Vet.Med.J.,Giza. Vol.50, No.4. (2002):843-861.

# SEMEN CHARACTERISTICS, BLOOD CONSTITUENTS AND TESTICULAR PATHOLOGY IN BALADI BUCKS INJECTED WITH FLUNIXIN MEGLUMINE (FINADYNE®).

W.M. AHMED, R.I. EL-SHESHTAWY, H.M. DESOUKY, E.M. HANAFI and G.A. ALI

Department of Animal Reproduction and A.I., National Research Center, Cairo, Egypt.

Received: 7.8.2002.

Accepted: 8.9.2002.

## SUMMARY

Finadyne is one of the most commonly used non-steroidal anti-inflammatory drugs (NSAID). It is used in farm animals for treatment of stressful conditions. The present study aimed to clarify the effect of Finadyne injection on semen characteristics, blood constituents and testicular pathology of Baladi bucks.

Nine Baladi bucks raised at the National Research Center farm were divided into two groups, experimental (n =5) and control (n =4) groups. Experimental bucks were injected intramuscularly with 2 mg / kg. live body weight Flunixin meglumine (FM) every 2 weeks up to 2 months, while the control bucks were injected similarly with saline. A single semen sample was collected weekly from each buck using A.V. and subjected for evaluation. Blood samples were collected before, one and 2 months after treatment and complete blood picture was performed. Moreover, seminal and blood plasma were separated for determination of testosterone level (RIA), total proteins, glucose, lipids, calcium and inorganic phosphorus (colorometrically). Additional blood samples were collected at the end of the experiment every half an hour up to 6 hours for further testosterone evaluation. At the end of the experiment, bucks were subjected for open unilateral castration. The obtained testes were examined grossly and tissue samples were taken and processed for histopathological examination.

Results indicated that Baladi bucks injected with Finadyne showed inferior libido and semen characteristics as indicated by long reaction time, low production of alive sperm cells with high sperm abnormalities as compared to the control group. Injection of Finadyne did not significantly affect the haemogram except for increasing the prothrombin time at the end of the experiment. Tes-

tosterone levels decreased and cholesterol concentrations increased in both blood and seminal plasma of Finadyne injected bucks. High blood glucose value and low total proteins, globulin and triglycerides, and high total lipid concentrations in the seminal plasma were recorded in experimental bucks. Finadyne injection induced moderate testicular and epididymal changes in the form of vacuolar degeneration together with depletion and decrease in the number of the epithelial layers lining the seminiferous tubules

In conclusion, Flunixin meglumine (Finadyne ®843843) injection was found to have some side effects on male fertility as indicated by relatively inferior libido and semen quality and some pathological changes in the testis.

## INTRODUCTION

Flunixin meglumine (FM) is a potent non-steroidal anti-inflammatory drug (NSAID) that acts by inhibiting the synthesis of prostanoids, and their unique analgesic effect is mediated through prostaglandins, thromboxanes or leukotrienes (Wasfi et al., 1998). As NSAID, Flunixin has anti - inflammatory, analgesic and antipyretic properties, it has been used extensively to treat number of conditions in various species. Of these conditions, mastitis and fever in cows and mastitis in goats (Anderson et al., 1986 ; 1991), endotoxaemia in calves and mares (Luthman et al., 1989 ; Daels et al., 1991) and colic in mares (Jacot et al., 1999).

Flunixin meglumine and diclofenac are considered among the commonly used NSAID that act through inhibition of the enzyme prostaglandin cyclo-oxygenase. It was reported that these drugs decrease the formation of prostaglandins and related metabolites (Davidson et al., 1992; Gerdmann et al., 1997 ; Al-Matubsi and Fairclough, 2001), despite EL-Azab et al. (1996) found that prostaglandins improved semen characteristics and fertility in Friesian cattle.

Regarding male fertility, NSAIDs were reported to induce impairment in the reproductive function (Afifi et al., 1996 ; El-Far, 1996), as well as inducing pathological changes in the testis and accessory glands (El-Ashmawy et al., 1994 ; El-Far, 1996).

From the clinicopathological point of view, many authors reported that NSAIDs induce changes in the cellular and non-cellular components of the blood (El-Said, 1992; El-Ashmawy et al., 1994 ; Wintrobe, 1999). Also, pharmacokinetic studies in sheep revealed slower excretion rate of Flunixin from plasma after long term treatment (Cheng et al., 1998).

Nowadays NSAIDs are extensively used in animal farms. So, the current study aimed to investigate the effect of FM (Finadyne®) on male fertility monitored by changes in semen quality, some

blood and semen constituents and the microscopical structure of the testis in Baladi bucks.

## MATERIALS AND METHODS

The current study was carried out on Baladi bucks raised at the National Research Center Experimental Farm , Abou Rawashî, Giza, Egypt, during the green season (December to May) of the year.

**Experimental Animals:**

Nine healthy mature Baladi bucks (2-3 years old and 30-35 kg live body weight) were used in the present experiment. Bucks were kept free away from females in an open shed. Animals were fed on commercial concentrate mixture (1 kg/head / day. protein not less than 15 %). Egyptian clover (*Trifolium alexandrinum*), rice straw and water were provided *ad libitum*.

**Finadyne ®:**

Finadyne® (Schering-Plough Veterinary, France) is a non-steroidal anti-inflammatory sterile injectable solution. Each 1ml contains 50 mg Flunixin meglumine and 5 mg phenol as preservative.

**Experimental design:**

Bucks were divided into two groups:

1- Experimental group of five animals: each animal was injected intramuscularly with the recommended dose (2 mg / kg live body weight) every 2 weeks up to 2 months.

2- Control group of four animals: each animal was injected intramuscularly with saline (1.5 ml / animal) using the same schedule of the experimental group.

Libido was expressed by estimating the reaction time in seconds (after performing the false mounting) as the interval of time between introducing the buck to the teaser (an oestrous doe) till ejaculation (Singh et al., 2000).

**Samples:**

**Semen samples:**

Semen samples were collected from each buck using an oestrous doe as a teaser. Semen collection was performed indoors, early in the morning, by using artificial vagina at 44-45°C according to Leboeuf et al. (2000). Collection of semen (a single ejaculate) was carried out once a week from each buck after a false mounting through out the experimental period. Part of the sample was used for performing complete semen picture including acrosomal integrity (Sansone et al., 2000) and the other part was centrifugated (X 1500 g/15 minutes at 4°C) for separation of seminal plasma and kept frozen at -20°C till analysis.

**Blood samples:**

Blood samples were collected, after semen collection, by jugular venepuncture into heparinized ( for hormonal assay) or citrated (for hematological study) tubes, once a month for two consecutive months. Moreover, for testosterone evaluation,

additional heparinized samples were collected every half an hour up to 6 hours from both groups, 60 days following the first Finadyne® injection. Samples were kept in an ice box during transportation. Parts of the samples were centrifugated (X 3000 g/15 minutes at 4°C) to separate plasma and kept in Eppendorff vials at -20°C until biochemical analysis.

**Analysis:**

Testosterone levels were assayed by radioimmunoassay (RIA; Abraham, 1981) in both seminal and blood plasma using commercial kits from Diagnostic Product Corporation (Los Angles, USA). Assay had sensitivity of 0.04 ng/ml with inter-and intra-assays C.Vs. both being <13 %.

Total proteins (Bakerman, 1984), albumin (Doumas et al., 1971), glucose (Henery, 1981), total lipids (Frings and Dunn, 1970), triglycerides (Wahlefeld, 1974), cholesterol (Stein, 1986) and calcium and inorganic phosphorus (Henery, 1981) concentrations were colorometrically determined in seminal and blood plasma samples using commercial chemical kits from Stainbio, Texas, USA. Globulin was determined by subtracting albumin from total protein of each sample.

Complete blood picture including erythrogram, leucogram and thrombocytic counts were performed as outlined by Jain (1997). Prothrombin time (PT) was measured colorometrically according to Van der Besselaar (1988), while partial thromboplastin time (PPT) was measured according to Hoffman and Neulendijk (1978).

**Pathological study:**

Following open castration at the end of the experiment, testes were grossly examined and samples were taken from different parts of the testes and epidydimis as well as from the spermatic cords. Samples were fixed in 10% buffered formalin and prepared for histopathological examination according to Bancroft et al. (1996).

**Statistical analysis:**

Data were computed (SAS, 1989), and statistically analysed using Student (t) test and regression analysis (Snedecor and Cochran, 1980).

## RESULTS

**Effect of Finadyne® injection on Baladi bucks:**

**Libido and semen characteristics:**

The current study indicated that Finadyne® injection relatively affected both the libido and semen characteristics of Baladi bucks (Table, 1).

The reaction time of Finadyne® injected bucks obviously prolonged as shown by the overall means as well as during the first ($P<0.05$) and the second ($P < 0.01$) months of the experiment as compared to the control group.

Concerning semen characteristics, Finadyne® injection markedly decreased the production of nor-

**Table (1):** Effect of Finadyne® injection on semen characteristics of Baladi bucks (Mean ± SE)

| Parameters | First Month | | Second Month | | Overall means | |
|---|---|---|---|---|---|---|
| | Control group | Exp. group | Control group | Exp. group | Control group | Exp. group |
| Reaction Time (second) | 94.20± 12.40 | 123.0± 9.60* | 78.60± 9.60 | 120.0± 11.40** | 86.40± 11.00 | 121.0± 10.5** |
| Volume (ml) | 0.73± 0.04 | 0.87± 0.16 | 0.85± 0.05 | 0.69± 0.08* | 0.79± 0.05 | 0.78± 0.12* |
| Mass Activity (0-5) | 2.69± 0.28 | 2.90± 0.18 | 2.54± 0.32 | 2.430± 0.17 | 2.62± 0.30 | 2.67± 0.18 |
| Individual Motility (%) | 70.33± 1.28 | 66.0± 2.34 | 70.70± 1.56 | 62.14± 2.01** | 70.52± 1.42 | 64.07± 2.18** |
| Sperm Con.($X10^6$/ml) | 2971.88± 64.63 | 2735.0± 55.84** | 2875.0± 108.99 | 2601.4± 44.46* | 2923.44± 86.76 | 2668.20± 50.15* |
| Alive sperm (%) | 83.29± 2.17 | 74.86± 2.15** | 84.09± 2.86 | 73.02± 2.78** | 83.69± 2.52 | 73.94± 2.74** |
| Abnormal sperm (%) | 5.39± 0.74 | 9.03± 1.00 | 7.50± 1.46 | 15.16± 1.86** | 6.45± 1.15 | 15.16± 1.43** |
| Acrosomal damage (%) | 5.16± 1.11 | 7.39± 0.99 | 6.52± 1.12 | 10.26± 1.01* | 5.79± 1.12 | 8.83± 1.0* |

* P<0.05 ** P<0.01

mal alive sperm cells as indicated by low conctration and alive sperm percent as well as high incidence of sperm cell abnormalities. Moreover, decreased semen volume ($P < 0.05$) and individual sperm motility ($P < 0.01$) and increased percent of acrosomal damage ($P < 0.05$) were recorded in samples obtained during the second month and for the overall means following Finadyne® injection in comparison with the control group.

**Haemogram:**

Injection of Finadyne® induced non significant changes in both erythrogram and leucogram (Table, 2).

At the end of the experiment, prothrombin time was found to increase significantly ($P<0.05$) from 15.16 ± 0.17 to 19.40 ± 0.24 seconds. While the thrombocytic count ($X10^5$) was 688.0 ± 39.02 in the control and 776.0 ± 47.60 in the experimental group. The partial thromboplastin time (PTT, seconds) were 20.60 ± 0.69 and 21.52 ± 0.53 in the control and the experimental groups respectively. However, both thrombocytic count and thromboplastin time did not show significant changes.

**Table (2):** Effect of Finadyne® injection on blood profile of Baladi bucks (Mean ± SE).

| Parameters | First Month | | Second Month | | Overall means | |
|---|---|---|---|---|---|---|
| | Control group | Exp. group | Control group | Exp. group | Control group | Exp. group |
| RBCs Count ($10^6$/ml) | 12.96± 0.44 | 14.78± 0.52 | 13.75± 0.39 | 12.53± 0.89 | 13.36± 0.42 | 13.66± 0.71 |
| Hb (g/dl | 10.82± 0.42 | 11.30± 0.36 | 10.20± 0.27 | 9.19± 0.34 | 10.82± 0.35 | 10.25± 0.35 |
| PCV (%) | 31.80± 0.87 | 30.00± 1.04 | 32.01± 1.30 | 29.90± 0.38 | 31.91± 1.09 | 29.95± 0.94 |
| MCV (%) | 24.68± 1.28 | 23.60± 0.46 | 23.60± 0.68 | 21.42± 1.19 | 24.14± 0.96 | 22.51± 0.83 |
| MCH (pg) | 8.40± 0.49 | 7.68± 0.39 | 8.75± 0.47 | 7.45± 0.40 | 8.58± 0.48 | 7.57± 0.40 |
| MCHC (g/dl) | 34.00± 0.53 | 34.19± 1.60 | 34.08± 0.50 | 32.51± 09 | 34.04± 0.52 | 33.35± 1.35 |
| WBCs Count ($10^3$/ml) | 6.64± 0.06 | 6.66± 0.40 | 7.15± 0.62 | 6.86± 0.45 | 6.89± 0.34 | 6.76± 0.43 |
| Lymphocytes (%) | 59.80± 0.67 | 60.00± 1.85 | 62.40± 0.83 | 63.00± 1.82 | 61.10± 0.75 | 61.50± .84 |
| Neutrophiles (%) | 34.40± 1.63 | 35.40± 1.04 | 35.00± 0.90 | 36.80± 1.34 | 34.7± 1.27 | 36.10± 1.19 |
| Monocytes (%) | 1.60± 0.24 | 1.80± 0.37 | 1.70± 0.37 | 1.60± 0.25 | 1.65± 0.31 | 1.70± 0.31 |
| Eosinophiles (%) | 1.45± 0.45 | 1.00± 0.32 | 1.40± 0.41 | 1.00± 0.45 | 1.20± 0.43 | 1.00± 0.39 |
| Basophils (%) | 0.00± 0.00 | 0.00± 0.00 | 0.00± 0.00 | 0.00± 0.00 | 0.00± 0.00 | 0.00± 0.00 |

**Blood and semen constituents:**

The effect of Finadyne® injection on some seminal (Table, 3) and blood (Table, 4) biochemical constituents including proteins, glucose, lipids, calcium and inorganic phosphorous of Baladi bucks was recorded.

Testosterone levels decreased significantly in blood plasma of the treated bucks after the first ($P < 0.01$) and the second month ($P < 0.05$) as well as for the overall means. While, it decreased in seminal plasma after the second month and in the overall means ($P < 0.01$) compared to the control group. However, blood samples frequently collected every half an hour up to 6 hours revealed low plasma testosterone levels especially during the first 2 hours, 3.5, 5 and 6 hours ($P < 0.01$) (Fig. 1). Moreover, regression analysis indicated that testosterone levels decreased significantly ($P<0.01$) with the advance of time in the Finadyne® injected bucks.

Finadyne® injection increased cholesterol values in both semen and blood plasma especially during the second month and for the overall means (at least $P< 0.05$). Glucose increased in blood plasma especially during the second month and in the overall means.

**Table (3):** Effect of Finadyne ® injection on some biochemical levels in semenal plasma of Baladi bucks (Mean ± SE).

| Parameters | First Month | | Second Month | | Overall means | |
|---|---|---|---|---|---|---|
| | Control group | Exp. group | Control group | Exp. group | Control group | Exp. group |
| Testosterone (ng/ml) | 0.39± 0.01 | 0.36± 0.02 | 0.40± 0.01 | 0.35± 0.01 | 0.39± 0.01** | 0.36± 0.02** |
| Total proteins (g/dl) | 61.63± 1.66 | 12.52± 1.35** | 52.20± 2.20 | 15.60± 2.00** | 56.92± 1.93 | 14.06± 1.68** |
| Albumin (g/dl) | 1.88± 0.06 | 2.15± 0.07 | 1.95± 0.07 | 2.30± 0.09 | 1.92± 0.07 | 2.23± 0.08 |
| Globulins (g/dl) | 60.25± 1.60 | 9.97± 1.26** | 50.70± 2.13 | 13.10± 1.45** | 44.48± 1.87** | 11.45± 1.36** |
| Glucose (mg/dl) | 17.28± 3.62 | 12.75± 2.13 | 19.20± 2.02 | 14.30± 2.20* | 18.24± 2.82 | 13.53± 2.17 |
| Total lipids (mg/dl) | 119.33± 0.87 | 139.20± 4.34** | 122.50± 1.00 | 132.00± 3.50* | 120.92± 0.94 | 135.60± 3.92* |
| Triglycerides (mg/dl) | 95.82± 4.44 | 80.59± 2.41* | 92.00± 3.50 | 82.22± 2.30* | 93.91± 3.97 | 81.41± 2.40* |
| Cholesterol (mg/dl) | 800.0± 60.0 | 840.0± 60.0** | 700.0± 30.0 | 900.0± 70.0** | 750.0± 50.0 | 870.0± 70.0* |
| Calcium (mg/dl) | 6.12± 0.77 | 5.80± 0.70 | 5.80± 0.80 | 5.50± 0.70 | 5.96± 0.79 | 5.65± 0.7 |
| In.Phosphorus (mg/dl) | 16.80± 1.78 | 15.76± 1.77 | 15.20± 1.80 | 16.00± 2.00 | 16.0± 1.79 | 15.88± 1.89 |

* P<0.05 * P<0.01

**Table (4):** Effect of Finadyne® injection on some biochemical levels in blood plasma of Baladi bucks (Mean ± SE).

| Parameters | First Month | | Second Month | | Overall means | |
|---|---|---|---|---|---|---|
| | Control group | Exp. group | Control group | Exp. group | Control group | Exp. group |
| Testosterone (ng/ml) | 0.69± 0.01 | 0.33± 0.12** | 0.48± 0.06 | 0.24± 0.09* | 0.59± 0.04 | 0.29± 0.11* |
| Total protein (g/dl) | 7.58± 0.36 | 7.37± 0.38 | 7.20± 0.40 | 7.07± 0.13 | 7.39± 0.38 | 7.22± 0.26 |
| Albumin (g/dl) | 2.52± 0.16 | 2.84± 0.20 | 2.52± 0.20 | 2.91± 0.20 | 2.52± 0.18 | 2.88± 0.20 |
| Globulins (g/dl) | 5.06± 0.20 | 4.53± 0.18 | 4.70± 0.20 | 4.09± 0.36 | 4.88± 0.20 | 4.31± 0.27 |
| Glucose (mg/dl) | 120.26± 13.06 | 206.72± 29.11* | 118.00± 12.20 | 227.63± 22.61** | 119.13± 12.20 | 217.18± 25.86** |
| Total lipids (mg/dl) | 226.75± 15.39 | 238.96± 6.52 | 223.00± 14.20 | 232.96± 13.13 | 224.88± 14.80 | 235.96± 9.83 |
| Triglycerides (mg/dl) | 116.90± 11.63 | 113.17± 22.41 | 115.00± 10.20 | 148.80± 35.27 | 115.95± 10.92 | 130.00± 28.84 |
| Cholesterol (mg/dl) | 90.0± 10.0 | 130.0± 10.0 | 80.0± 10.0 | 120.0± 10.0** | 90.00± 10.0 | 130.0± 10.0 |
| Calcium (mg/dl) | 8.28± 0.26 | 8.69± 0.46 | 8.00± 0.30 | 8.92± 0.59 | 8.14± 0.28 | 8.81± 0.53 |
| In.Phosphorus (mg/dl) | 2.86± 0.09 | 3.14± 0.09 | 2.70± 0.08 | 2.58± 0.13 | 2.77± 0.09 | 2.86± 0.11 |

* $P < 0.05$ ** $P < 0.01$

On the other hand, significant decrease in total protein ($P < 0.01$), globulin ($P < 0.01$) and triglycerides ($P < 0.05$) and increase in total lipids ($P < 0.05$) were recorded in seminal plasma in the experimental group

**Pathological changes:**

Testes obtained from FinadyneÆ injected bucks appeared slightly oedematous, enlarged in size and soft in consistency.

Microscopical examination of the testes indicated that Finadyne injection had a moderate degenerative changes in most of the examined testes of Baladi bucks. Most of the seminiferous tubules appeared relatively small in size, meanwhile, others appeared shrunken, collapsed, irregular in outline and widely separated from each others (Fig. 2). The spermatogenic epithelial lining of seminiferous tubules showed vacuolar degeneration and necrotic changes represented by pyknosis and lysis of their nuclei I focal manners (Fig. 3). There were moderate depletion and /or decrease in the

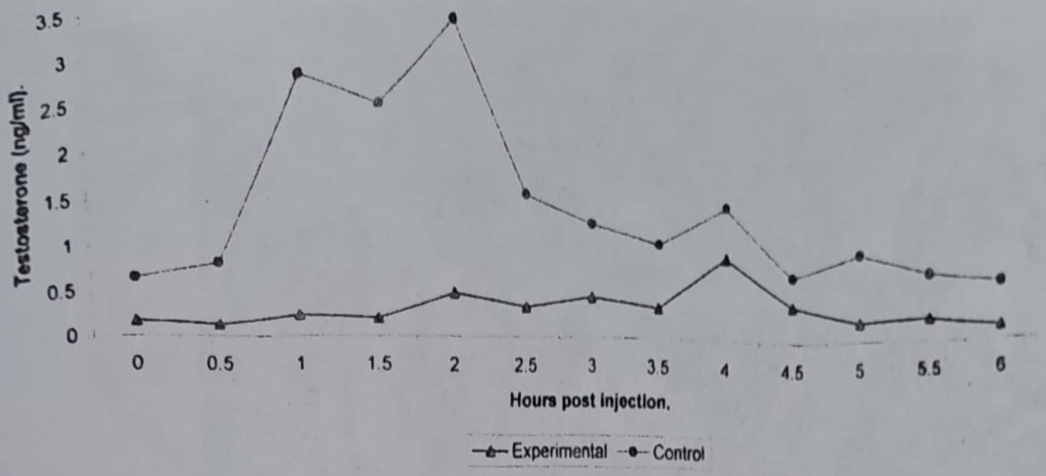



**Fig. (1):** Mean plasma testosterone level (ng/ml) in Baladi bucks after Finadyne injection.

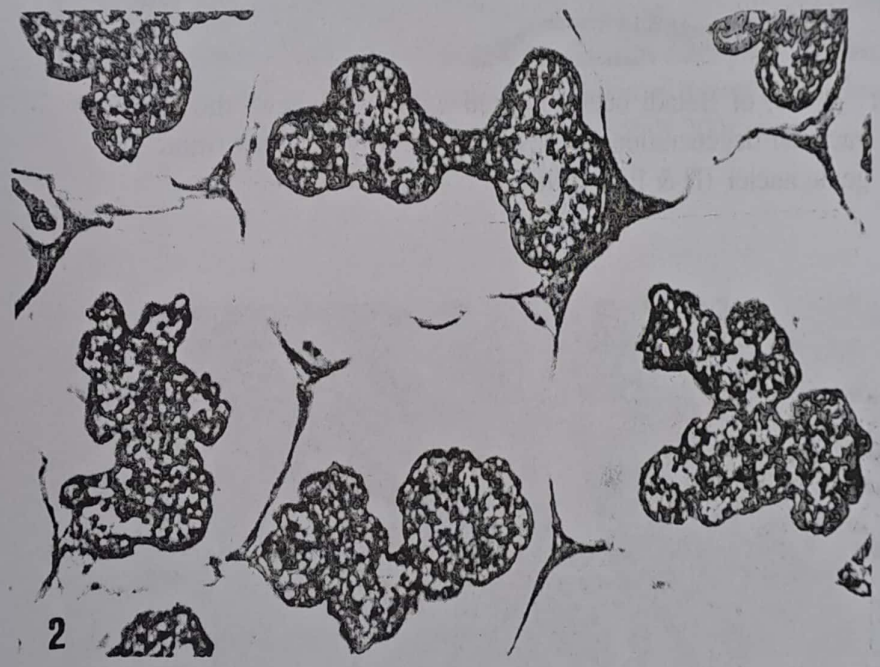



**Fig. (2):** Testis, of Baladi bucks injected with finadyne® showed shrunken, irregular outline and collapsed seminferous tubules (H & E, X 100)

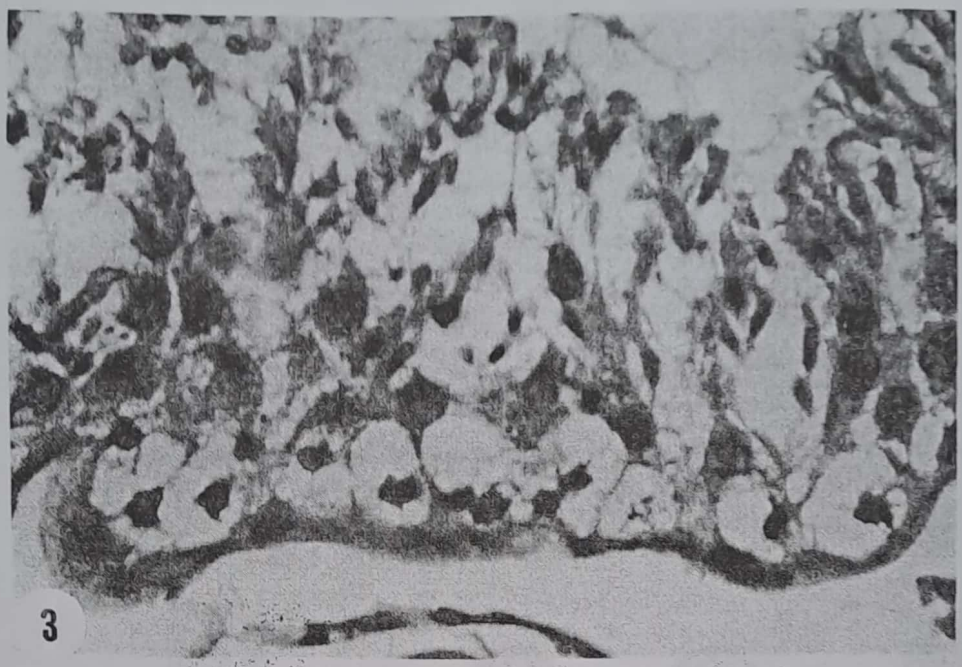



**Fig. (3):** Testis, of Baladi bucks injected with finadyne® showed vacuolar degeneration, pyknosis and karyolysis of spermatogenic nuclei (H & E, X 400)

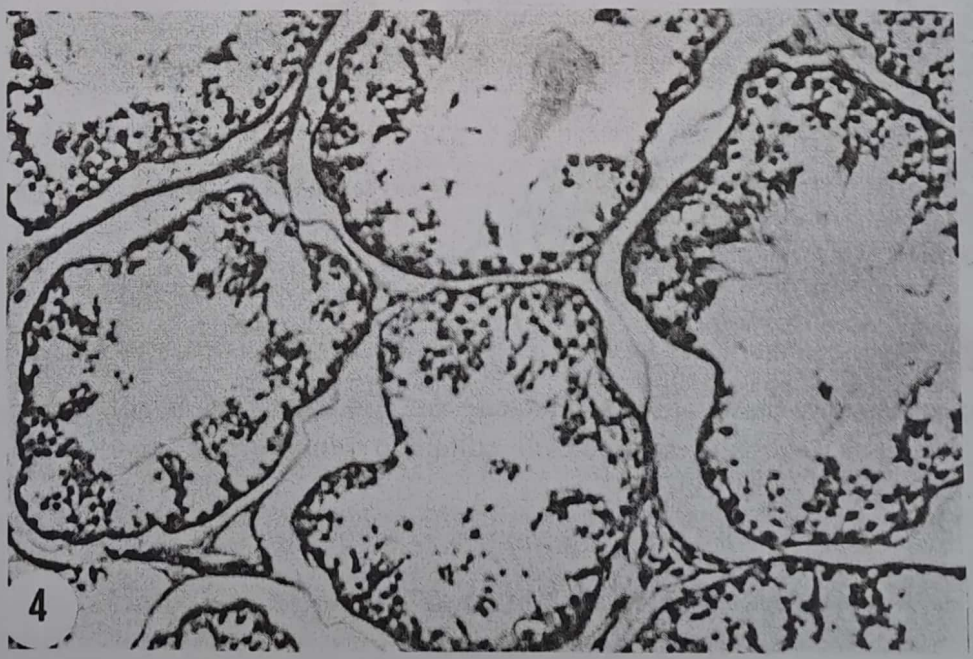



**Fig. (4):** Testis, of Baladi bucks injected with finadyne® showed moderate depletion and decreas ein the number of epithelial layers lining the seminferous tubules (H & E, X 400)

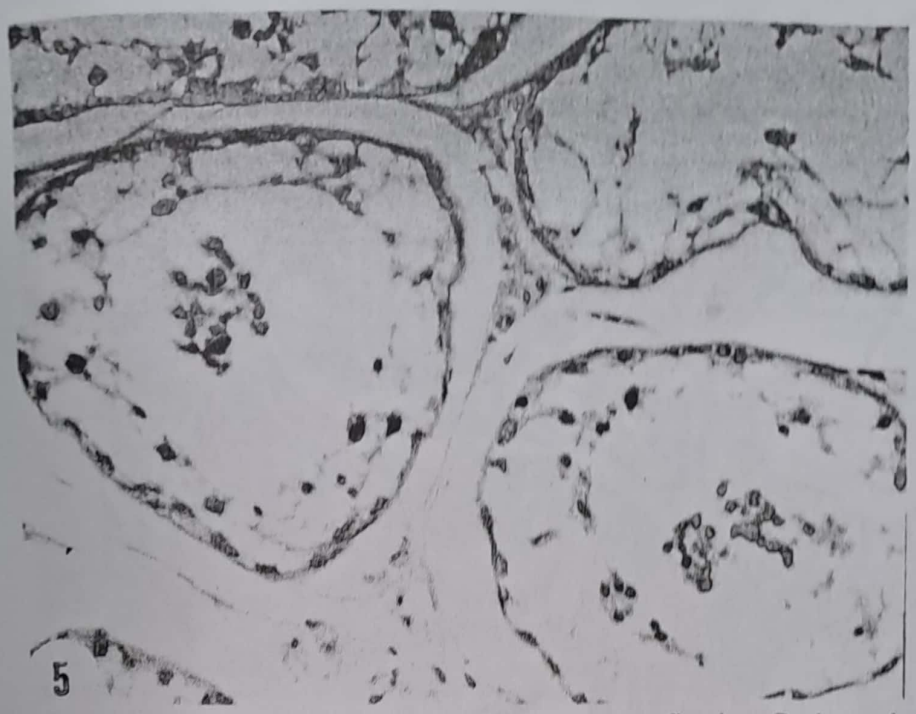



**Fig. (5):** Testis, of Baladi bucks injected with finadyne® showed necrosis, disappearance and exfoliation of necrotic cells into lumina of seminiferous tubules (H & E, X 200)

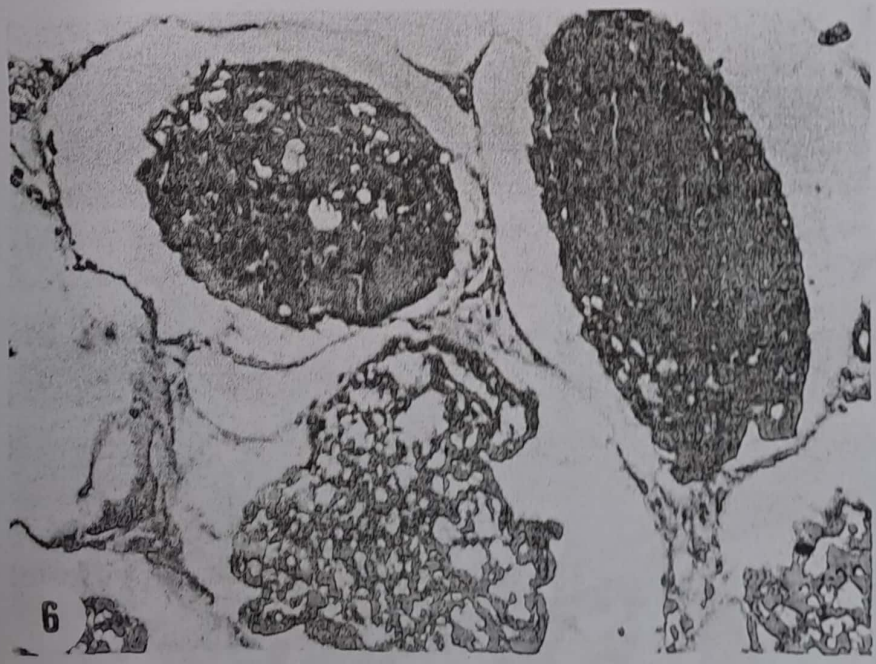



**Fig. (6):** Testis, of Baladi bucks injected with finadyne® showed hyalinized homogenous eosinophilic material within the lumen of seminferous tubules

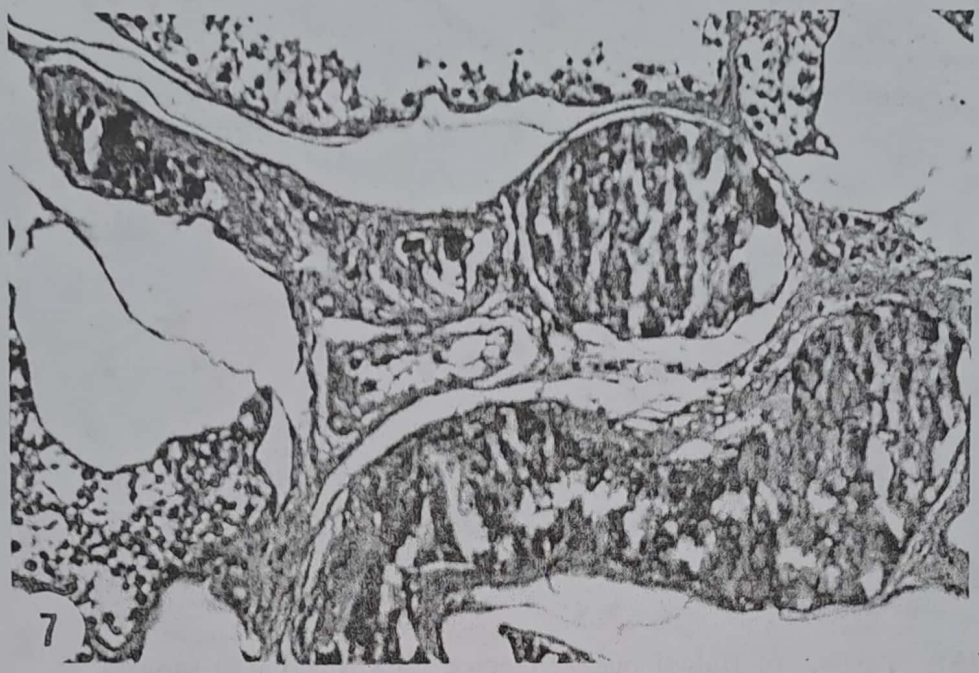


**Fig. (7):** Testis, of Baladi bucks injected with finadyne® showed necrosis and mineralization of seminferous tubules associated with proliferation of inter tubular connective tissue (H & E, X 100)

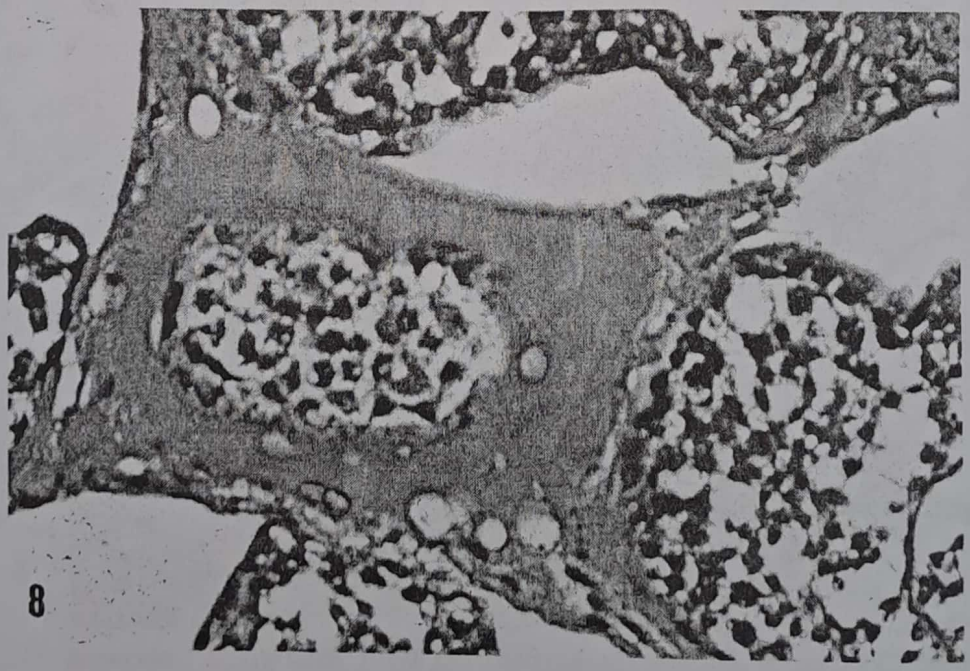


**Fig. (8):** Testis, of Baladi bucks injected with finadyne® showed interstitial oedema among the seminferious tubules (H & E, X 200)


**Fig. (9):** Testis, of Baladi bucks injected with finadyne® showed necrobiotic changes in leydig cells with vacuolar degeneration of spermatogonial cells (H & E, X 100)

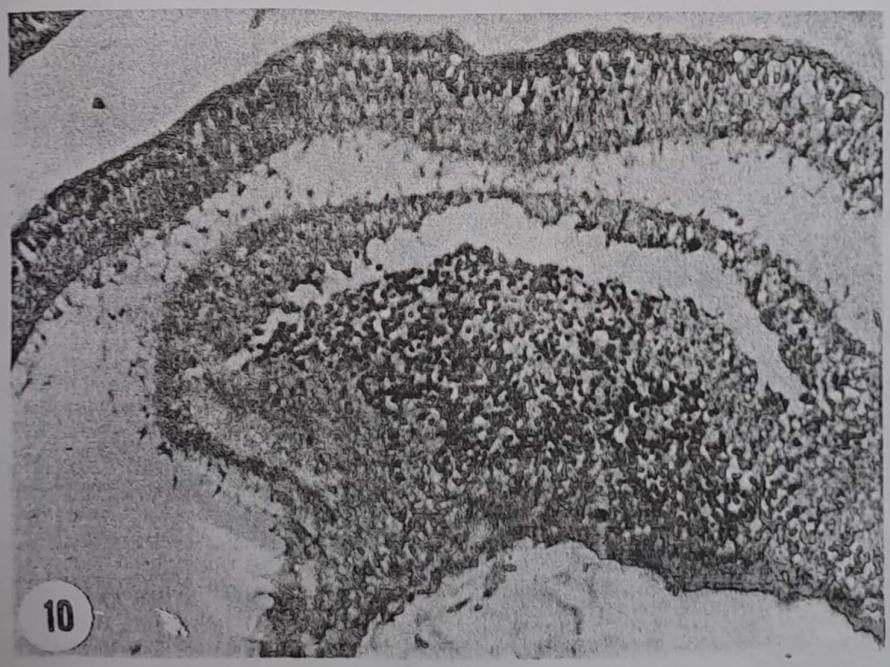



**Fig. (10):** Head of epididymis, of Baladi bucks injected with finadyne® showed focal hyperplasia of epithelial lining of ductul (H & E, X 100)

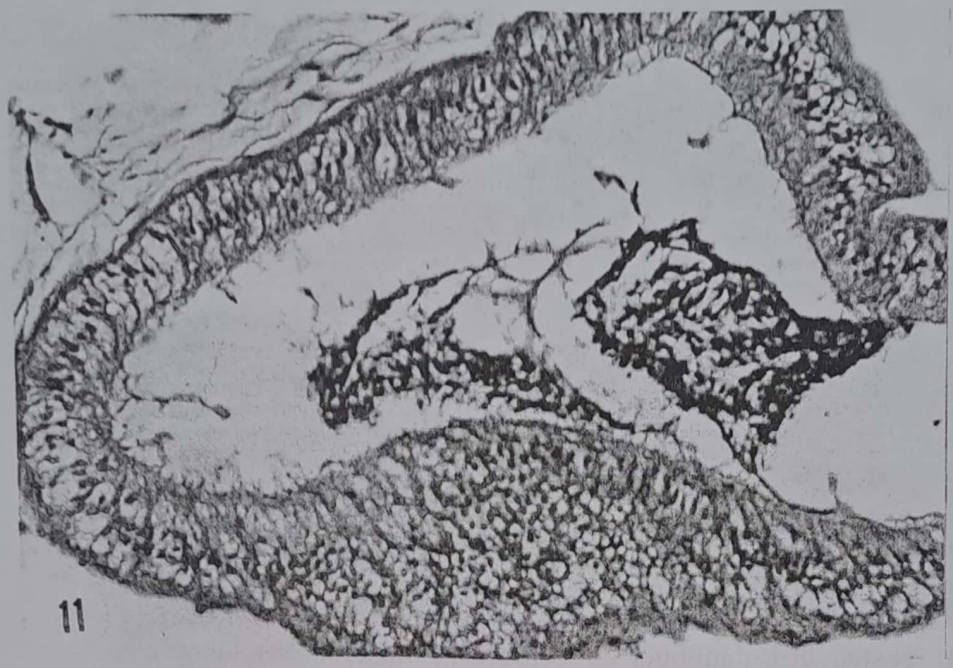
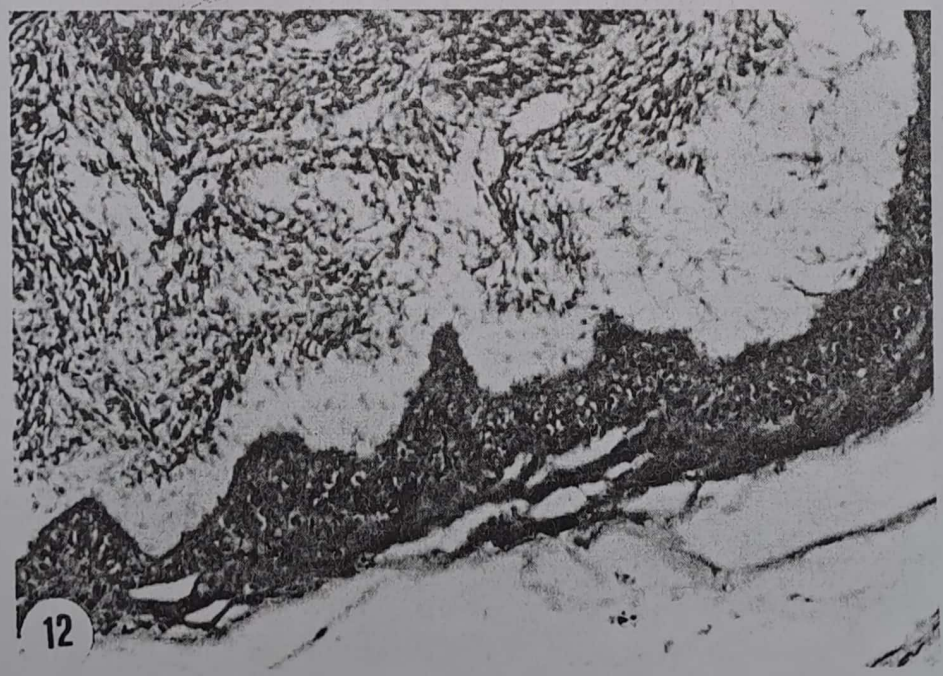
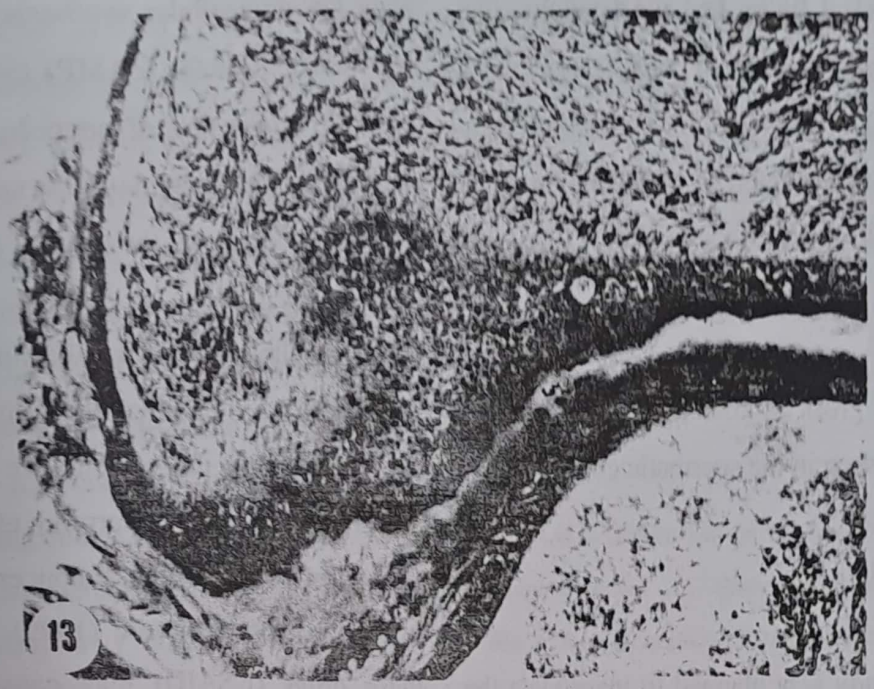



**Fig. (11):** Head of epididymis, of Baladi bucks injected with finadyne® showed vacuolar degeneration associated with hyperplasia (H & E, X 200)




**(Fig. 12):** Tail of epididymis, of Baladi bucks injected with finadyne® showed papillary like projections of the epithelial lining (H & E, X 100)/




**(Fig. 13):** Tail of epididymis, of Baladi bucks injected with finadyne®showed partial hyperplasia of epithelial lining

number of the epithelial layers lining the tubules of most cases (Fig. 4). Moreover, the tubular lumen is markedly dilated and the epithelium become partitioned into individual Sertoli cells with their associated germ cells separated from each other by distended inter cellular spaces.

In one case, the epithelial lining was necrosed and disappeared and the remnants were vacuolated. The tubules were lined by few stem spermatogonial cells in addition to exfoliation of some necrotic spermatogenic cells within the tubular lumina (Fig. 5). At the same time, some tubules contained homogenous hyalinised eosinophilic material with no sperm as a result of coagulative necrosis of tubular elements (Fig. 6). Also, few seminiferous tubules showed severe necrosis associated with mineralization (Fig. 7). There were dilatations and congestion of blood vessels in addition to focal interstitial oedema among the tubules (Fig. 8). Leydig cells showed necrotic changes (Fig. 9). The cells appeared small in size with pyknotic nuclei and deeply eosinophilic cytoplasm.

Grossly, epididymis showed non-pronounced lesions. The histopathological examination of the head region showed focal hyperplasia accompanied with hydropic degeneration of lining epitheli-

um of some tubules (Figs.10 & 11). In the tail region, the epithelial lining had short villous- like projections associated with focal hyperplasia (Figs. 12& 13). Moreover, the number of spermatozoa within the lumen of epididymal tubules was generally lowered in experimental than control bucks.

No prominent gross or histopathological alterations could be seen in the spermatic cord.

## DISCUSSION

The current study was planned to investigate the effect of one of the common non-steroidal anti-inflammatory drugs (Finadyne®) on male fertility in farm animals.

In this study injection of Finadyne® was found to induce prolonged libido and inferior semen characteristics and reduced testosterone levels in Baladi bucks as compared to the control group. To the best of our knowledge, little data were traced in the available literature regarding the effect of Finadyne on male fertility in animals. However, in rats, El-Ashmawy et al. (1994) and Afifi et al. (1996) reported that Finadyne® significantly reduced sperm cell concentrations and alive sperm, and increased the percent of total sperm abnormalities in addition to decrease plasma testosterone levels. They attributed such harmful effects to reduced synthesis of prostaglandins due to inhibition of prostaglandin synthetase. In this respect, it had been reported that prostaglandins regulate the intracellular synthesis of cyclic adenosine monophosphate (cAMP) (Selim et al., 1997) leading to releasing of adenohypophyseal gonadotrophins which regulate the spermatogenic and hormonal function of the testis.

From the clinicopathological point of view, it has been found that Finadyne had non-significant effect on blood picture despite the prolongation of prothrombin time. No harmful effect of NSAID was traced in the literature concerning blood picture. However, Wintrobe (1999) mentioned that these drugs (NSAID) may cause normoplastic anaemia after prolonged administration. On the other hand, the prolongation in prothrombin time could be explained in light of liver affection followed the administration of non-steroidal anti-inflammatory drugs (NSAID) (El-Ashmawy, et al., 1994 ; Wintrobe, 1999) and consequently reduced production of factor V and VII or deficient production of platelet factor III which is essential for transformation of prothrombin to thrombin (Wintrobe, 1999).

Concerning hyperglycemia in Finadyne® injected bucks similar results were reported in rats injected with NSAID by Roderick et al. (1985) and El-Said (1992) and they attributed the condition either to depletion of muscle glycogenesis (Roderick et al., 1985) or increased glyconeogensis, increased intestinal absorption of glucose or increased liver glycogenolysis (El-Said, 1992). On the other

hand, the present hypercholesterolemia agreed with the findings of Jeli et al. (1985) and contradicted the results of El-Said (1992). However, this hypercholesterolemia may be associated with hyperglycemia ( Stein, 1986).Regarding biochemical analysis of seminal plasma, Finadyne injection induced marked increase in lipids and decrease in proteins. These findings may be related to the direct effect of the drug on testicular function as indicated by histopathological picture as well as due to indirect effect on pituitary gland secretion following reduced production of prostaglandins and consequently low secretion of gonadotrophins (El-Ashmawy et al., 1994, El-Far, 1996 ; Selim, et al., 1997).

The most common histopathological findings in the current study were vacuolar degeneration and necrosis of epithelial lining of seminiferous tubules with focal hydropic degeneration in the epididymal epithelium. These findings are in agreement with the observations recorded by El-Ashmawy et al. (1994) and El-Far (1996) in rats. However, such changes may be attributed to inhibition of prostaglandin $F_{2\alpha}$ with subsequently alteration in the intracellular cAMP affecting the activity of various cellular protein kinase which produce alterations in cell function, swelling and necrosis (Selim et al., 1997). On the other hand, the observed pathological changes in the interstitial cells correlated well with the decreased testosterone level.

In conclusion, application of Finadyne® therapy in farm animals has side effects on testicular function as indicated by decreased libido, inferior semen characteristics, and some blood and seminal constituents as well as pathological changes in the testis. Further investigations on the prolonged administration of this drug in different farm animals are considered later on.

## REFERENCES


Abraham, G.E. (1981): The application of natural steroid radioimmunoassay to gynecologic endocrinology. In ìRadio Assay System in Clinical Endocrinologyî. Marcel Dekker, Basle, pp: 783-800.

Afifi, N.A.; Attia, K.A. and Attia, M.Z. (1996): Effect of Flunixin meglumine on fertility of male rats. Vet. Med. J., Giza. , 44: 463-469.

Al-Matubsi, H.Y. and Fairclough, R.J. (2001): Effect of Finadyne on oestradiol induced ovarianoxytocin and uterine PGF2α secretory system on day 15 after oestrus in ovarian autotransplanted ewes. J. Reprod., Fet. 121: 429-434.

Anderson, K. L. Hunt, E. and Davis , B.J. (1991): The influence of anti-inflammatory therapy on bacterial clearance following intrammary Escherichia coli challenge in goats . Vet. Res. Common., 15: 147-161.

Anderson, K. L.; Smith, A. and Shanks, R.D. (1986): Efficacy of Flunixin meglumine for the treatment of endotoxin-induced bovine mastitis.Amer. J.Vet. Res., 47: 1366-1372.

Bakerman, A.S. (1984): A colorometric method for the determination of seminal total protein. ABC's of Interpretive Laboratory Dataî, 2nd ed., Griffin and Tilghman , p.

347.

ancroft, J. D.; Stevens, A. and Turner, D.R (1996): Theory and Practice of Histological

echniques, 4th ed. Churchill Livingstone Co., New York, London, San Fransisco, Tokyo.

Cheng, Z.; McKeller, Q. and Nolan, A. (1998): Pharmacokinetic studies of flunixin meglumine and phenylbutazone in plasma, exudate and transudate in sheep. J. Vet. Pharmacol. Therap., 21: 315-321.

Daels, P. F.; Stabenfeldt, G.H. and Hughas, P. (1991): Effect of Flunixin meglumine one ndotoxin- induced prostaglandin F2a secretion during early pregnancy in mares. Amer. J.Vet. Res., 52: 276-281.

Davidson, J. R.; Lantz, G.C.; Salisbury, S.K.; Kasacox, E.A. and Bottoms, G.D. (1992): Effect of fluunixin meglumine on dogs with experimental gastric dilatation - volvulus. Vet Surg., 21: 131-120.

Doumas, B.T.; Watson, W.A. and Biggs, H.G. (1971): A colorometric method for the determination of serum albumin. Clin. Chem. Acta, 31: 87.

El-Ashmawy, I.M.; Fayed, A.H. and Zakaria, A.D. (1994): Effect of Flunixin meglumine (Finadyne®) on the reproductive organs and gonadotrophin levels in male rats. Proc.The 6th Ann. Congr.,Egyptian soc. Anim. Reprod. Fert., Cairo , pp. 27-36.

El-Azab, A.I.; Abdel-Ghafar, A.E.; Nasr, M.T. and Issa, E.S. (1996): Effect of exogenous PGF2-alpha and /or GnRH on libido and semen production of aged Friesian bulls. Vet. Med. J., Giza. , 44: 529-533.

El-Far, F. I. (1996): Effect of some antirheumatics on some hormones and testicular functions of male albino rats. M.V.Sc. Thesis (Animal Physiology), Cairo Univ., Egypt.

El-Said, E. M. (1992): Biochemical studies on the effect of aspirin in relation to nutrition.M.V.Sc. Thesis (Biochemistry),Cairo Univ., Egypt.

Frings, C.S. and Dunn, R.T. (1970): Calorimetric determination of total lipid in serum. Am. J. Clin. Pathol., 53: 89.

Gerdmann, R.; Deegen, E.; Kietzmann, M. and Venner, M. (1997): Effect of Flunixin

Melgumine on plasma prostanoid concentrations in colic horses within the pri-operative period. Deutsche-Tierarztliche- Wochenschrift., 104: 365-368.

Henery, R.J. (1981): Clinical Chemistry, Principals and Techniques. Harper and Row Publisher; N.J. USA.

Hoffman, J. J.M. and Neulendijk, P.N. (1978): Thrombos. Haemostas., 39: 640.

Jacot, S.; Gluntez, X. and Battail, G. A. (1999): Evaluation of the benefit/risk ratio of anlgesics as a fist line of treatment in colic: a clinical case treated with flunixin. Pratique Vet. Equine., 31: 433-438.

Jain, N.C. (1997): Essentials of Veterinary Haematology. 4th ed., Lee and Febiger, Philadelphia, USA.

Jeli, I. Z. ; Spasi, S. ; Majki, S. N. and Todorovi, P. (1985): Clin. Chem. 31, 1141.

Leboeuf, B; Restall, B.and Salamon, S. (2000): Production and storage of goat semen for artificial insemination. Anim. Reprod. Sci., 62: 113-141.

Luthman, J.; Kindahl, H. and Jacobsson, S.O. (1989): The influence of Flunixin on the response to salmonella typhimurium endotoxin in calves. Acta Vet. Scand., 30: 295-300.

Rodrick, J. F.; Salvador, M. and John, R .V. (1985): In: Goodman and Gilman's. The Pharmacological Basis of Theraputics. Goodman L.S. and Gilman A. (Eds.), Macmillan, Newyork, P. 684.

Sansone, G.; Nastri, M.J.F. and Fabbrocini, A. (2000): Storage of buffalo (Bubalus bubalis) semen. An. Rep. Sci., 62: 55-76.

SAS (1989): Statistical Analysis System. SAS userís guid- SAS Inst., Cary, N.C., USA.

Selim, A.G.; Mokhbatly, A.A. and Mohammed, A.H. (1997): Clinicopathological and histopathological studies on diclofenac sodium in albino rat. Egypt. J. Comp. Path. And Clin. Path., 10: 119-129.

Singh, P; Sengupta, B.P. and Tripathi, V.N. (2000): Effect of supplemental amino acid feeding on sexual behaviour, quality and freezability of buffalo bull semen. Buffalo J., 16: 41-46.

Snedecor, G.W. and Coheran, W.G. (1980): Statistical Methods. 6th ed. Iowa State University press, Ames Iowa, USA.

Stein, E. A. (1986): Textbook of Clinical Chemistry. 3rd ed. NW Tietz (Ed.) W.B. Sounders,Philadelphia, USA.

Van der Besselaar, A. M. (1988): The certification of the second reference material for rabbit thromboplastin. CRM 1491. Commission of the European Communities, BCR information. Report Eur. 11686.

Wasfi, I.A.; Boni, N.S.; Abdel Hadi, A.A.; Elghazali, M.; Zorob, O.; Alkatheeri, N.A. and Barezaiq, I.M. (1998): Pharmacokinetics, metabolism and urinary detection time of Flunixin after intravenous administration in camels. Vet. Pharmacol. Therap., 21: 203-208.

Wahlefeld, A.W. (1974): Methods of Enzymatic Analysis. H.U. Bregmeyer (Ed.) Acad. Press. N.Y., USA. pp: 1831-1853.

Wintrobe M. M. (1999): Wintrobesí Clinical Haematology. P.1459. 10th Ed. Baltimor, Maryland, USA.