3.1  Introduction

3.1.1. General toxicity

The animals exposed to low (20mg/kg body weight), medium (200 mg/kg body weight) and high dose (1000 mg/kg body weight) of ELAP and animals exposed to 25 mg/kg body weight of Andrographolide (purity $\geq 98.0\%$) for 65 days did not show any clinical signs of toxicity (salination, eye size - dilation/shrinking, urination - increase/decrease, loss of fur, vocalization, head flicking, circling and walking backwards and redness around eyes, mouth, nose) or none of the rats were excluded from the experiment. No treatment related mortality was observed in the rats during the study. All pregnant rats were allowed to complete the gestation period half of the rats for 8 days and remains for 18 days for the observation of pups.

3.2.1.2. Effect of ELAP and Andrographolide on body weights, food and water intake in male rats

3.2.1.2.1 Body weights

The mean body weight of control rats is 219.1 ± 29.89 g. The mean body weights of rats subjected to low, medium and high doses of ELAP individually are 230.0 ± 33.06, 265.2 ± 30.55 and 257.8 ± 32.27 respectively. No significant difference in the final body weights were observed in rats subjected to low dose of ELAP compared to the controls. A significant (p<0.05) increase was observed in the final body weights of rats subjected to medium and high doses of ELAP compared to the controls (Table 3.1).

The mean body weight of the rats subjected to Andrographolide treatment is 238.0 ± 13.85 respectively. No significant (p<0.05) difference in the final body weights
was observed in the rats subjected to Andrographolide treatment compared to the controls (Table 3.1).

3.2.1.2.2 Food intake

The mean food intake of control rats is 16.55 ± 6.63 g. The mean food intake of rats subjected to low, medium and high doses of ELAP individually are 20.9±5.70, 23.36 ± 5.51 and 22.0±5.52 respectively. No significant difference in the food intake was observed in rats subjected to low and high doses of ELAP compared to the controls. A significant (p<0.05) increase was observed in the food intake of rats subjected to medium dose of ELAP compared to the controls (Table 3.1).

The mean food intake of the rats subjected to Andrographolide treatment is 22.9 ± 6.60 respectively. No significant (p<0.05) difference in the food intake was observed in the rats subjected to Andrographolide treatment compared to the controls (Table 3.1).

3.2.1.2.3 Water intake

The mean water intake of control rats is 26.22 ± 6.11 ml. The mean water intake of rats subjected to low, medium and high doses of ELAP individually are 27.93 ± 5.65, 29.28±4.75 and 29.92 ± 2.72 respectively. No significant difference in the water intake was observed in rats subjected to low, medium and high doses of ELAP compared to the controls (Table 3.1).

The mean water intake of the rats subjected to Andrographolide treatment is 29.53 ± 8.75 respectively. No significant (p<0.05) difference in the water intake was observed in the rats subjected to Andrographolide treatment compared to the controls (Table 3.1).
Results

3.2.1.3. Effect of ELAP and Andrographolide on tissue indices of male rats

3.2.1.3.1 Tissue indices

3.2.1.3.1a. Liver

The mean index of the liver is 3.546 ± 0.15 g % in the control rats. The mean indices of the liver are 3.915 ± 0.55, 3.164 ± 0.59 and 2.846 ± 0.61 g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in liver indices of rats subjected to low and medium doses of ELAP whereas a significant (p<0.05) decrease was observed in the liver index of rats subjected to high dose of ELAP (Table 3.2) compared to the controls.

The mean index of the liver is 3.072±0.530 g% in the rats subjected to Andrographolide treatment. A significant (p<0.05) decrease was observed in the liver index of rats subjected to Andrographolide treatment (Table 3.2) compared to the controls.

3.2.1.3.1b. Spleen

The mean index of the spleen is 0.423 ± 0.03 g % in the control rats. The mean indices of the spleen are 0.443 ± 0.09, 0.402 ± 0.04 and 0.420 ± 0.08 g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in spleen indices of rats subjected to low, medium and high doses of ELAP (Table 3.2) compared to the controls.

The mean index of the spleen is 0.395±0.058 g% in the rats subjected to Andrographolide treatment. No significant difference was observed in spleen indices of rats subjected to Andrographolide treatment (Table 3.2) compared to the controls.
3.2.1.3.3c. Kidney

The mean index of the kidney is $0.763 \pm 0.03$ g % in the control rats. The mean indices of the kidney are $0.715 \pm 0.08$, $0.727 \pm 0.09$ and $0.688 \pm 0.08$ g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in kidney indices of rats subjected to low and medium doses of ELAP whereas a significant ($p<0.05$) decrease was observed in the kidney index of rats subjected to high dose of ELAP (Table 3.2) compared to the controls.

The mean index of the kidney is $0.701\pm0.046$ g% in the rats subjected to Andrographolide treatment. A significant ($p<0.05$) decrease was observed in the kidney index of rats subjected to Andrographolide treatment (Table 3.2) compared to the controls.

3.2.1.3.3d. Brain

The mean index of the brain is $0.785 \pm 0.08$ g % in the control rats. The mean indices of the brain are $0.718 \pm 0.06$, $0.564 \pm 0.06$ and $0.568 \pm 0.09$ g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in brain index of rats subjected to low dose of ELAP whereas a significant ($p<0.05$) decrease was observed in the brain indices of rats subjected to medium and high doses of ELAP (Table 3.2) compared to the controls.

The mean index of the brain is $0.682\pm0.233$ g% in the rats subjected to Andrographolide treatment. No significant difference ($p<0.05$) was observed in brain index of rats subjected to Andrographolide treatment (Table 3.2) compared to the controls.
3.2.1.3.3e. Testis

The mean index of the testis is 1.259 ± 0.06 g % in the control rats. The mean indices of the testis are 1.214 ± 0.13, 1.100 ± 0.14 and 0.951 ± 0.37 g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in testis indices of rats subjected to low dose of ELAP whereas a significant (p<0.05) decrease was observed in the testis indices of rats subjected to medium and high doses of ELAP (Table 3.3) compared to the controls.

The mean index of the testis is 0.931±0.122 g% in the rats subjected to Andrographolide treatment. A significant (p<0.05) decrease was observed in the testis indices of rats subjected to Andrographolide treatment (Table 3.3) compared to the controls.

3.2.1.3.3f. Epididymis

The mean index of the epididymis is 1.124 ± 0.33 g % in the control rats. The mean indices of the epididymis are 1.023 ± 0.29, 1.086 ± 0.10 and 1.206 ± 0.35 g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in epididymis indices of rats subjected to low, medium and high doses of ELAP (Table 3.3) compared to the controls.

The mean index of the epididymis is 1.074±0.218 g% in the rats subjected to Andrographolide treatment. No significant difference was observed in epididymis indices of rats subjected to Andrographolide treatment (Table 3.3) compared to the controls.
3.2.1.3.3g. Vas deferens

The mean index of the vas deferens is \(0.126 \pm 0.42\) g% in the control rats. The mean indices of the vas deferens are \(0.116 \pm 0.01\), \(0.108 \pm 0.03\) and \(0.081 \pm 0.02\) g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in vas deferens indices of rats subjected to low, medium and high doses of ELAP (Table 3.3) compared to the controls.

The mean index of the vas deferens is \(0.118 \pm 0.043\) g% in the rats subjected to Andrographolide treatment. No significant difference was observed in vas deferens indices of rats subjected to low, medium and high doses of ELAP (Table 3.3) compared to the controls.

3.2.1.3.3h. Seminal vesicle

The mean index of the seminal vesicle is \(0.459 \pm 0.03\) g% in the control rats. The mean indices of the seminal vesicle are \(0.370 \pm 0.13\), \(0.349 \pm 0.08\) and \(0.191 \pm 0.09\) g% respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in seminal vesicle index of rats subjected to low dose of ELAP (Table 3.3) whereas a significant (p<0.05) decrease was observed in the seminal vesicle indices of rats subjected to medium and high doses of ELAP (Table 3.3) compared to the controls.

The mean index of the seminal vesicle is \(0.243 \pm 0.116\) g% in the rats subjected to Andrographolide treatment. A significant (p<0.05) decrease was observed in the seminal vesicle indices of rats subjected to Andrographolide treatment (Table 3.3) compared to the controls.
3.2.1.3.3i. Prostate gland

The mean index of the prostate gland is $0.131 \pm 0.04 \text{ g %}$ in the control rats. The mean indices of the prostate gland are $0.125 \pm 0.06$, $0.137 \pm 0.02$ and $0.121 \pm 0.02 \text{ g%}$ respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in prostate gland indices of rats subjected to low, medium and high doses of ELAP (Table 3.3) compared to the controls.

The mean index of the prostate gland is $0.125\pm0.015 \text{ g%}$ in the rats subjected to Andrographolide treatment. No significant difference was observed in prostate gland index of rats subjected to Andrographolide treatment (Table 3.3) compared to the controls.

3.2.1.3.3j. Penis

The mean index of the penis is $0.135 \pm 0.01 \text{ g %}$ in the control rats. The mean indices of the penis are $0.152 \pm 0.01$, $0.114 \pm 0.03$ and $0.103 \pm 0.02 \text{ g%}$ respectively in the rats subjected to low, medium and high doses of ELAP individually. No significant difference was observed in penis indices of rats subjected to low and medium doses of ELAP (Table 3.3) whereas a significant ($p<0.05$) decrease was observed in the penis index of rats subjected to medium dose of ELAP (Table 3.3) compared to the controls.

The mean index of the penis is $0.113\pm0.008 \text{ g%}$ in the rats subjected to Andrographolide treatment. A significant ($p<0.05$) decrease was observed in the penis index of rats subjected to Andrographolide treatment (Table 3.3) compared to the controls.
3.2.1.4. Effect of ELAP and Andrographolide on the sperm parameters in male rats

3.2.1.4.1 Daily sperm production

The average daily sperm production in the control rats is 21.3 ± 2.34 millions/g testes, whereas the daily sperm production in the rats exposed to low, medium and high doses of ELAP is 16.3 ± 1.73, 14.20 ± 2.12 and 13.08 ± 3.23 millions/g testes respectively. There is a significant (p<0.05) decrease (-23.4, -33.3, -38.5 %) in the testicular daily sperm production in all the experimental rats subjected to in low, medium and high doses of ELAP compared to that of the control rats (Table 3.4).

The average daily sperm production in the rats exposed to Andrographolide is 10.43±1.74 millions/g testes. There is a significant (p<0.05) decrease (-51.03 %) in the testicular daily sperm production in the experimental rats subjected to Andrographolide compared to that of the control rats (Table 3.4).

3.2.1.4.2 Epididymal sperm count

The average sperm count in the control rats is 68.5±3.23 millions/ml. The sperm count in the rats exposed to low, medium and high doses of ELAP is 48.6±2.32, 39.80±2.24 and 39.57±1.45 millions/ml respectively. There is a significant (p<0.05) decrease (-29, -41.8,- 42.2%) in the sperm count in all the experimental rats subjected to low, medium and high doses of ELAP when compared to that of the control rats (Table 3.4).

The average sperm count in the rats exposed to Andrographolide is 32.80±3.62 millions/ml respectively. There is a significant (p<0.05) decrease (-52.11 %) in the
sperm count in all the experimental rats subjected to Andrographolide when compared to that of the control rats (Table 3.4).

3.2.1.4.3 Sperm viability

The average viable sperm in the control rats is 82.22±2.88 %. The percent of viable sperm in the rats subjected to low, medium and high doses of ELAP is 38.00±2.54, 37.5±2.03 and 27.16±3.12 % respectively. A significant (p<0.05) decrease (-53.7, -54.3, -66.9 %) in the number of viable sperm was observed in all the rats subjected to low, medium and high doses of ELAP respectively when compared to that of viable sperm in control rats (Table 3.4).

The percent of viable sperm in the rats exposed to Andrographolide is 36.50±2.61 %. A significant (p<0.05) decrease (-55.60 %) in the number of viable sperm was observed in all the rats subjected to Andrographolide respectively when compared to that of viable sperm in control rats (Table 3.4).

3.2.1.4.4 Sperm Motility

The average motile sperm in control rats is 78.23±3.32 %. The percent of motile sperm in rats subjected to low, medium and high doses of ELAP is 31.33±2.21, 22.16±2.23 and 16.37±1.96 % respectively. The decrease in the number of motile sperm is -59.9, -71.6 and -79 % in rats exposed to low, medium and high doses of ELAP respectively when compared to that of controls. A significant (p<0.05) decrease in the motile sperm concentration was observed in rats subjected to low, medium and high doses of ELAP compared to that of the control rats (Table 3.4).

The percent of motile sperm in rats exposed to Andrographolide is 32.50±2.08. The decrease in the number of motile sperm is -58.45 % in rats exposed to
Andrographolide respectively when compared to that of controls. A significant (p<0.05) decrease in the motile sperm concentration was observed in rats exposed to Andrographolide compared to that of the control rats (Table 3.4).

3.2.1.4.5 HOS tail coiled sperm

The average HOS tail coiled sperm in the control rat is 79.32±3.01 %. The number of tail coiled sperm is 37.12±3.12, 35.16±2.92 and 25.35±1.90 % in rats subjected to low, medium and high doses of ELAP respectively. A significant (p<0.05) decrease in HOS tail coiled sperm was observed in rats exposed to low, medium and high doses of ELAP compared to that of controls. The decrease in the number of HOS tail coiled sperm is -53.2, -55.6 and -68 % in in rats exposed to low, medium and high doses of ELAP respectively when compared to that of control rats (Table 3.4).

The average number of tail coiled sperm is 24.66±1.82 % in rats subjected to Andrographolide. A significant (p<0.05) decrease in HOS tail coiled sperm was observed in rats exposed to Andrographolide compared to that of controls. The decrease in the number of HOS tail coiled sperm is -68.91 % in in rats exposed to Andrographolide respectively when compared to that of control rats (Table 3.4).

3.2.1.4.6 Sperm Morphology

All the rats exposed to low, medium and high doses of ELAP showed abnormalities in the sperm morphology like balloon shape (Figure 3.1b), amorphic spiral bend (Figure 3.1c), double and poly headed (Figure 3.1d) sperm when compared to that of control rats (Figure 3.1a).

Rats exposed to Andrographolide on the other hand also showed abnormalities in the sperm morphology like balloon shape (Figure 3.1b), amorphic spiral bend (Figure
3.1c), double and poly headed (Figure 3.1d), acephalic (Figure 3.1e), bent tail (Figure 3.1f), gigantic twirling (Figure 3.1g), gigantic (Figure 3.1h), amorphic (Figure 3.1i), sticky (Figure 3.1j), multiple fission headed (Figure 3.1k), bisectated (Figure 3.1l), detoriated (Figure 4.1m), fragile (Figure 3.1n), HOS coil (Figure 3.1o), sperm when compared to that of control rats (Figure 3.1a).

3.2.2. Effect of ELAP and Andrographolide on the serum testosterone levels in male rats

The average level of the circulating testosterone is 6.03 ± 0.57 ng/ml in the control rats. The levels of serum testosterone in rats exposed to low, medium and high doses of ELAP are 3.16 ± 0.82, 2.28 ± 0.74 and 2.64 ± 1.74 ng/ml respectively (Table 3.5). The decrease in the levels of the serum testosterone is -47.5, -62.18 and -56.21 % in rats exposed to low, medium and high doses of ELAP respectively when compared to that of the control rats (Table 3.5, Figure 3.2). A significant (p<0.05) decrease is observed in the circulating levels of serum testosterone in rats subjected to the low, medium and high doses of ELAP.

The level of serum testosterone in rats exposed to Andrographolide is 4.65±0.12 ng/ml respectively (Table 3.5). The decrease in the levels of the serum testosterone is -22.88 % in rats exposed to Andrographolide respectively when compared to that of the control rats (Table 3.5, Figure 3.2). A significant (p<0.05) decrease is observed in the circulating levels of serum testosterone in rats subjected to Andrographolide treatment.

3.2.3. Effect of ELAP and Andrographolide on the lipid peroxidation in male rats

Table 3.6 and Figure 3.3 summarizes the effect of ELAP and Andrographolide on the lipid peroxidation in male rats.
3.2.3.1 Testis

The average level of malondialdehyde in the testis of the control rats is 0.44±0.40 µmol MDA/g. The levels of malondialdehyde in the testis of rats exposed to low, medium and high doses of ELAP are 0.77±0.10, 1.04±0.23 and 1.28±0.45 µmol MDA/g, respectively. The increase in the levels of MDA in the testis of rats exposed to low, medium and high doses of ELAP is 75, 136.3 and 190.9 % respectively, when compared to that of the control rats (Table 3.6, Figure 3.3). A significant (p<0.05) increase in the levels of malondialdehyde is observed in the testis of all the experimental rats as compared to that of controls.

The level of malondialdehyde in the testis of rats exposed to Andrographolide is 0.85±0.20 µmol MDA/g. The increase in the levels of MDA in the testis of rats exposed to Andrographolide is 93.18 %, when compared to that of the control rats (Table 3.6, Figure 3.3). A significant (p<0.05) increase in the levels of malondialdehyde is observed in the testis of Andrographolide treatment rats as compared to that of controls.

3.2.3.2 Epididymis

The average level of malondialdehyde in the epididymis of the control rats is 0.27±0.02 µmol MDA/g. The levels of malondialdehyde in the epididymis of rats exposed to low, medium and high doses of ELAP are 0.45±0.22, 0.55±0.10 and 0.97±0.46 µmol MDA/g, respectively. The increase in the levels of MDA in the epididymis of rats exposed to low, medium and high doses of ELAP is 66.6, 103.7 and 259.2 % respectively, when compared to that of the control rats (Table 3.6, Figure 3.3). A significant (p<0.05) increase in the levels of malondialdehyde is observed in the epididymis of all the experimental rats as compared to that of controls.
The level of malondialdehyde in the epididymis of rats exposed Andrographolide is 1.60±0.14 µmol MDA/g. The increase in the levels of MDA in the epididymis of rats exposed to low, medium and high doses of ELAP is 492.59 % respectively, when compared to that of the control rats (Table 3.6, Figure 3.3). A significant (p<0.05) increase in the levels of malondialdehyde is observed in the epididymis of Andrographolide treatment rats as compared to that of controls.

### 3.2.4. Effect of ELAP and Andrographolide on the superoxide dismutase in male rats

Table 3.7 and Figure 3.4 summarizes the effect of ELAP and Andrographolide on the superoxide dismutase (SOD) in male rats

#### 3.2.4.1 Testis

The average level of SOD in the testis of the control rats is 6.09±0.20 Units/mg protein/min. The levels of SOD in the testis of rats exposed to low, medium and high doses of ELAP are 4.74±0.50, 4.20±0.12 and 3.37±0.62 Units/mg protein/min, respectively. The decrease in the levels of SOD in the testis of rats exposed to low, medium and high doses of ELAP is -22.16, -31.03 and -44.66 % respectively, when compared to that of the control rats (Table 3.7, Figure 3.4). A significant (p<0.05) decrease in the levels of SOD is observed in the testis of all the experimental rats as compared to that of controls.

The level of SOD in the testis of exposed to Andrographolide is 1.04±0.23 Units/mg protein/min, respectively. The decrease in the levels of SOD in the testis of rats exposed to Andrographolide is -82.92 %, when compared to that of the control rats (Table 3.7, Figure 3.4). A significant (p<0.05) decrease in the level of SOD is observed in the testis of all the Andrographolide treatment rats as compared to that of controls.
3.2.4.2 Epididymis

The average level of SOD in the epididymis of the control rats is 1.96±0.40 Units/mg protein/min. The levels of SOD in the epididymis of rats exposed to low, medium and high doses of ELAP are 1.53±0.30, 1.48±0.20 and 1.46±0.10 Units/mg protein/min, respectively. The decrease in the levels of SOD in the epididymis of rats exposed to low, medium and high doses of ELAP is -21.9, -24.48 and -25.51% respectively, when compared to that of the control rats (Table 3.7, Figure 3.4). A significant (p<0.05) decrease in the levels of SOD is observed in the epididymis of all the experimental rats as compared to that of controls.

The level of SOD in the epididymis of rats exposed to Andrographolide is 0.72±0.20 Units/mg protein/min. The decrease in the levels of SOD in the epididymis of rats exposed to Andrographolide is -63.26%, when compared to that of the control rats (Table 3.7, Figure 3.4). A significant (p<0.05) decrease in the level of SOD is observed in the epididymis of all the Andrographolide treatment rats as compared to that of controls.

3.2.5. Effect of ELAP and Andrographolide on the Catalase in male rats

3.2.5.1 Testis

The average level of catalase in the testis of the control rats is 0.087±0.007 µmoles of H₂O₂ metabolised/mg protein/min. The levels of catalase in the testis of rats exposed to low, medium and high doses of ELAP are 0.042±0.01, 0.032±0.07 and 0.028±0.01 µmoles of H₂O₂ metabolised/mg protein/min, respectively. The decrease in
the levels of catalase in the testis of rats exposed to low, medium and high doses of 
ELAP is -51.7, -63.2 and -67.8% respectively, when compared to that of the control rats 
(Table 3.8, Figure 3.5). A significant (p<0.05) decrease in the levels of catalase is 
observed in the testis of all the experimental rats as compared to that of controls.

The level of catalase in the testis of rats exposed to Andrographolide is 
0.018±0.01 μmoles of H₂O₂ metabolised/mg protein/min, respectively. The decrease in 
the levels of catalase in the testis of rats exposed to Andrographolide is -79.31%, when 
compared to that of the control rats (Table 3.8, Figure 3.5). A significant (p<0.05) 
decrease in the levels of catalase is observed in the testis of all the Andrographolide 
treatment rats as compared to that of controls.

3.2.5.4 Epididymis

The average level of catalase in the epididymis of the control rats is 0.10±0.06 
μmoles of H₂O₂ metabolised/mg protein/min. The levels of catalase in the epididymis 
of rats exposed to low, medium and high doses of ELAP are 0.027±0.05, 0.021±0.02 
and 0.018±0.01 μmoles of H₂O₂ metabolised/mg protein/min, respectively. The 
decrease in the levels of catalase in the epididymis of rats exposed to low, medium and 
high doses of ELAP is -73, -79 and -82% respectively, when compared to that of the 
control rats (Table 3.8, Figure 3.5). A significant (p<0.05) decrease in the levels of 
catalase is observed in the epididymis of all the experimental rats as compared to that of 
controls.

The level of catalase in the epididymis of rats exposed to Andrographolide is 
0.010±0.10 μmoles of H₂O₂ metabolised/mg protein/min, respectively. The decrease in 
the levels of catalase in the epididymis of rats exposed to Andrographolide is -90%, 
when compared to that of the control rats (Table 3.8, Figure 3.5). A significant (p<0.05)
decrease in the levels of catalase is observed in the epididymis of all the Andrographolide treatment rats as compared to that of controls.

3.2.6. Effect of low, medium and high doses of ELAP and Andrographolide on the testicular histology in male rats

Transverse section of testis of control rats show normal seminiferous tubular structure with spermatogenic cells at different stages and well developed interstitial cells (Figure 3.6A). The seminiferous tubules are closely packed with clusters of Leydig cells. Each tubule consists of tubular wall with the outer most basement membrane, spermatogonia and Sertoli cells resting on the membrane (Figure 3.6A). The transverse section of low dose ELAP administered rats testis shows atrophy of spermatogenic elements with degenerated appearance of germ cells (Figure 3.6B). The transverse section of medium dose ELAP administered rats testis shows decrease of spermatozoa in the lumen of seminiferous tubules (Figure 3.6C, D). The transverse section of high dose ELAP administered rats testis shows necrotic seminiferous tubules with giant cells (Figure 3.6E, F). The transverse section of Andrographolide administered rats testis shows absence of spermatozoa and giant cells in the seminiferous tubules (Figure 3.6G, H).

3.2.7. Effect of low, medium and high doses of ELAP and Andrographolide on the Cauda epididymis histology in male rats

Transverse section of cauda epididymis of control rats shows normal sperms (Figure 3.7A). The transverse section of low dose ELAP administered rats cauda epididymis shows necrotic germinal layer (Figure 3.7B). The transverse section of medium, high dose ELAP administered rats and Andrographolide administered rats cauda epididymis shows debris and decrease in the number of sperms (Figure 3.6C, D, E).
3.2.8. Effect of low, medium and high doses of ELAP and Andrographolide on the reproductive performance in male rats

Table 3.9 summarizes the effect of low, medium and high doses of ELAP on the reproductive performance in adult male rats.

3.2.8.1. Time taken to impregnate female rats

The time taken to impregnate female rats mated with control male rats is found to be 1.235 ± 0.52 days, whereas the time taken to impregnate female rats cohabited with male rats exposed to low, medium and high doses of ELAP is 2.5 ± 0.83, 2.833 ± 0.13 and 4.142 ± 1.7 days respectively. The percent increase in the time taken to impregnate the female rat is 102.42, 129.39 and 235.38 in rats exposed to low, medium and high doses of ELAP during embryonic development respectively. There is a significant (p<0.05) delay to impregnate female rats exposed to low, medium and high doses of ELAP when compared to the control rats (Table 3.9).

The time taken to impregnate female rats cohabited with male rats exposed to Andrographolide is 2.5±1.224 days respectively. The percent increase in the time taken to impregnate the female rat is 102.42 in rats exposed to Andrographolide during embryonic development respectively. There is a significant (p<0.05) delay to impregnate female rats exposed to Andrographolide when compared to the control rats (Table 3.9).

3.2.8.2. Mating index

The percentage of mating index in female rats cohabited with control rats and female rats cohabited with rats exposed to low, medium and high doses of ELAP and Andrographolide during the embryonic development is found to be 100 (Table 3.9).
3.2.8.3. Fertility index

The fertility index in rats is calculated on their ability to impregnate female rats. The percentage of fertility index in female rats cohabited with control animals is found to be 100, whereas, the fertility indices of the female rats cohabited with male rats exposed to low, medium and high doses of ELAP are 87.5, 87.5 and 75 % respectively during the embryonic development (Table 3.9).

The fertility indices of the female rats cohabited with male rats exposed to Andrographolide is 75 % respectively during the embryonic development (Table 3.9).

3.2.8.4. Number of corpora lutea

The number of corpora lutea in the female rats cohabited with control rats is found to be 14.01± 0.89 whereas in the female rats cohabited with male rats exposed to low, medium and high doses of ELAP during embryonic development is found to be 13.81 ± 0.10, 13.70 ± 0.20 and 13.16 ± 0.18 respectively. There is a significant decrease in the number of corpora lutea in the female rats cohabited with male rats exposed to high dose of ELAP (Table 3.9).

The number of corpora lutea in the female rats cohabited with male rats exposed to Andrographolide during embryonic development is found to be 13.10±0.20 respectively. There is a significant decrease in the number of corpora lutea in the female rats cohabited with male rats exposed to Andrographolide (Table 3.9).

3.2.8.5. Number of implantations

The number of implantations in the female rats mated with control rats is found to be 12 ± 0.58 (Figure 3.7A), whereas the number of implantations in the females
mated with males to low, medium and high doses of ELAP during embryonic development are 11 ± 0.57, 10.5 ± 0.21 and 9.66 ± 0.57 respectively (Figure 3.7B, C, D). The percent decrease in the number of implantations is -8.33, -12.5 and -19.5 respectively in the female rats mated with the male rats to low, medium and high doses of ELAP during prenatal period. There is a significant (p<0.05) decrease in the number of implantations in female rats mated with male rats exposed to low, medium and high doses of ELAP during embryonic development when compared to controls (Table 3.9).

The number of implantations in the females mated with males exposed to Andrographolide during embryonic development are 6.16 ± 0.37 respectively (Figure 3.7E). The percent decrease in the number of implantations is -48.6 respectively in the female rats mated with the male rats exposed to Andrographolide during prenatal period. There is a significant (p<0.05) decrease in the number of implantations in female rats mated with male rats exposed to Andrographolide during embryonic development when compared to controls (Table 3.9).

3.2.8.7. Number of live fetuses

The number of live fetuses in female rats mated with the control rats is 11.03 ± 0.04 (Figure 3.8A), whereas the number of live fetuses is 10.01 ± 0.82, 9.13 ± 0.76 and 7.38 ± 0.12 (Figure 3.8B, C, D) in the female rats mated with male rats exposed to low, medium and high doses of ELAP during embryonic period respectively. The percent decrease in the number of live fetuses is -9.24, -17.22 and -33.09 in female rats mated with the male rats exposed to low, medium and high doses of ELAP during prenatal period respectively. There is a significant (P<0.05) decrease in the number of live fetuses in female rats mated with male rats exposed to low, medium and high doses of ELAP during prenatal period when compared to the control rats (Table 3.9).
The number of live fetuses in female rats mated with male rats exposed to Andrographolide during embryonic period is $4 \pm 0.10$ (Figure 3.8E). The percent decrease in the number of live fetuses is -63.73 in female rats mated with the male rats exposed to Andrographolide during prenatal period respectively. There is a significant ($P<0.05$) decrease in the number of live fetuses in female rats mated with male rats exposed to Andrographolide during prenatal period when compared to the control rats (Table 3.9).

### 3.2.8.8. Pre-implantation loss

The mean pre-implantation loss is 14.35 % in the female rats mated with the control rats, whereas mean pre-implantation loss is 20.34, 23.35 and 26.59 % respectively in the female rats cohabited with the male rats exposed to low, medium and high doses of ELAP during embryonic development respectively (Table 3.9).

The mean pre-implantation loss in the female rats mated with the rats exposed to Andrographolide during embryonic development is 52.97 % (Table 3.9).

### 3.2.8.9. Post-implantation loss

The mean post-implantation loss is 8.08 % in the female rats mated with the control rats, whereas, mean post-implantation loss is 9, 13.04 and 23.6 respectively in the female rats mated with the male rats exposed to low, medium and high doses of ELAP during embryonic development (Table 3.9).

The mean post-implantation loss in the female rats mated with the rats exposed to Andrographolide during embryonic development is 35.06 respectively (Table 3.9).
Table 3.1. Effect of graded doses of ELAP and Andrographolide on the body weights (g), food (g) and water intake (ml) in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract</th>
<th>Andrographolide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>200</td>
</tr>
<tr>
<td>Body weight</td>
<td>219.1 ± 29.89</td>
<td>230.0 ± 33.06 (5.02)</td>
<td>265.2* ± 30.55 (21.0)</td>
</tr>
<tr>
<td>Food intake</td>
<td>16.55 ± 6.63</td>
<td>20.9 ± 5.70 (28.2)</td>
<td>23.36* ± 5.51 (41.1)</td>
</tr>
<tr>
<td>Water intake</td>
<td>26.22 ± 6.11</td>
<td>27.93 ± 5.65 (6.5)</td>
<td>29.28 ± 4.75 (11.6)</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.
Values in the parentheses are percent change from that of control.

* Significantly different from control at P<0.05.
**Table 3.2.** Effect of graded doses of ELAP and Andrographolide on the tissue somatic indices (w/w %) in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract</th>
<th>20 mg/Kg body weight</th>
<th>200 mg/Kg body weight</th>
<th>1000 mg/Kg body weight</th>
<th>Andrographolide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>3.546±0.15</td>
<td>3.915±0.55 (10.40)</td>
<td>3.164±0.59 (-10.77)</td>
<td>2.846 *±0.61 (-19.74)</td>
<td>3.072 *±0.530 (-13.36)</td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>0.423±0.03</td>
<td>0.443±0.09 (4.72)</td>
<td>0.402±0.04 (-4.96)</td>
<td>0.420±0.08 (-0.70)</td>
<td>0.395±0.058 (-6.61)</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>0.763±0.03</td>
<td>0.715±0.08 (-6.29)</td>
<td>0.727±0.09 (-4.71)</td>
<td>0.688 *±0.08 (-9.82)</td>
<td>0.701 *±0.046 (-8.12)</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>0.785±0.08</td>
<td>0.718±0.06 (-8.53)</td>
<td>0.564 *±0.06 (-28.15)</td>
<td>0.568 *±0.09 (-27.64)</td>
<td>0.682±0.233 (-13.12)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.

Values in the parentheses are percent change from that of control.

* Significantly different from control at P<0.05.
Table 3.3. Effect of graded doses of ELAP and Andrographolide on the reproductive tissue indices (w/w %) in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract 20</th>
<th>Leaf Extract 200</th>
<th>Leaf Extract 1000 mg/Kg body weight</th>
<th>Andrographolide 2000 mg/Kg body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testis</td>
<td>1.259±0.06</td>
<td>1.214±0.13</td>
<td>1.100* ±0.14</td>
<td>0.951 * ±0.37</td>
<td>0.931* ±0.122</td>
</tr>
<tr>
<td></td>
<td>(-3.54)</td>
<td>(-3.54)</td>
<td>(-12.6)</td>
<td>(-24.46)</td>
<td>(-26.05)</td>
</tr>
<tr>
<td>Epididymis</td>
<td>1.124±0.33</td>
<td>1.023±0.29</td>
<td>1.086±0.10</td>
<td>1.206±0.35</td>
<td>1.074±0.218</td>
</tr>
<tr>
<td></td>
<td>(-8.98)</td>
<td>(-8.98)</td>
<td>(-3.38)</td>
<td>(7.29)</td>
<td>(-4.44)</td>
</tr>
<tr>
<td>Vas deferens</td>
<td>0.126±0.42</td>
<td>0.116±0.01</td>
<td>0.108±0.03</td>
<td>0.081±0.02</td>
<td>0.118±0.043</td>
</tr>
<tr>
<td></td>
<td>(-7.93)</td>
<td>(-7.93)</td>
<td>(-14.28)</td>
<td>(-35.71)</td>
<td>(-6.34)</td>
</tr>
<tr>
<td>Seminal vesicle</td>
<td>0.459±0.03</td>
<td>0.370±0.13</td>
<td>0.349*±0.08</td>
<td>0.191*±0.09</td>
<td>0.243*±0.116</td>
</tr>
<tr>
<td></td>
<td>(-19.38)</td>
<td>(-19.38)</td>
<td>(-23.96)</td>
<td>(-58.3)</td>
<td>(-47.05)</td>
</tr>
<tr>
<td>Prostate gland</td>
<td>0.131±0.04</td>
<td>0.125±0.06</td>
<td>0.137±0.02</td>
<td>0.121±0.02</td>
<td>0.125±0.015</td>
</tr>
<tr>
<td></td>
<td>(-4.58)</td>
<td>(-4.58)</td>
<td>(4.58)</td>
<td>(-7.63)</td>
<td>(-4.58)</td>
</tr>
<tr>
<td>Penis</td>
<td>0.135±0.01</td>
<td>0.152±0.01</td>
<td>0.114±0.03</td>
<td>0.103*±0.02</td>
<td>0.113*±0.008</td>
</tr>
<tr>
<td></td>
<td>(-12.59)</td>
<td>(-12.59)</td>
<td>(-15.55)</td>
<td>(-23.73)</td>
<td>(-16.29)</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.
Values in the parentheses are percent change from that of control.
* Significantly different from control at P<0.05.
Table 3.4. Effect of graded doses of ELA P and Andrographolide on testicular daily sperm production and epididymal sperm parameters in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract</th>
<th>Andrographolide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>200</td>
</tr>
<tr>
<td>DSP (millions/g testis)</td>
<td>21.3 ±2.34</td>
<td>16.3 * ±1.73</td>
<td>14.20 * ±2.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-23.4)</td>
<td>(-33.3)</td>
</tr>
<tr>
<td>Sperm count (millions/ml)</td>
<td>68.5 ±3.23</td>
<td>48.6 * ±2.32</td>
<td>39.80 * ±2.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-29)</td>
<td>(-41.8)</td>
</tr>
<tr>
<td>Viable sperm (%)</td>
<td>82.22 ±2.88</td>
<td>38.00 ±2.54</td>
<td>37.5 ±2.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-53.7)</td>
<td>(-54.3)</td>
</tr>
<tr>
<td>Motile sperm (%)</td>
<td>78.23 ±3.32</td>
<td>31.33 * ±2.21</td>
<td>22.16 * ±2.23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-59.9)</td>
<td>(-71.6)</td>
</tr>
<tr>
<td>HOS-tail coiled sperm (%)</td>
<td>79.32 ±3.01</td>
<td>37.12 ±3.12</td>
<td>35.16 ±2.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-53.2)</td>
<td>(-55.6)</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.
Values in the parentheses are percent change from that of control.
* Significantly different from control at P<0.05.
Table 3.5. Effect of graded doses of ELAP and Andrographolide on the serum testosterone levels in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract</th>
<th>Andrographolide</th>
<th>20</th>
<th>200</th>
<th>1000 mg/Kg body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone (ng/ml)</td>
<td>6.03 ± 0.57</td>
<td>3.16* ± 0.82</td>
<td>2.28* ± 0.74</td>
<td>2.64* ± 1.7</td>
<td>4.65* ± 0.12</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.

Values in the parentheses are percent change from that of control.

* Significantly different from control at P<0.05.
Table 3.6. Effect of graded doses of ELAP and Andrographolide on the lipid peroxidation (µmoles MDA/g) in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract 20</th>
<th>Leaf Extract 200</th>
<th>Leaf Extract 1000 mg/Kg body weight</th>
<th>Andrographolide body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testis</td>
<td>0.44±0.40</td>
<td>0.77*±0.10 (75)</td>
<td>1.04*±0.23 (136.3)</td>
<td>1.28*±0.45 (190.9)</td>
<td>0.85*±0.20 (93.18)</td>
</tr>
<tr>
<td>Epididymis</td>
<td>0.27±0.02</td>
<td>0.45*±0.22 (66.6)</td>
<td>0.55*±0.10 (103.7)</td>
<td>0.97*±0.46 (259.2)</td>
<td>1.60*±0.14 (492.59)</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.
Values in the parentheses are percent change from that of control.
* Significantly different from control at P<0.05.
Table 3.7. Effect of graded doses of ELAP and Andrographolide on the activity levels of SOD (Units/mg protein/min) in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract</th>
<th>Andrographolide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>200</td>
</tr>
<tr>
<td>Testis</td>
<td>6.09±0.20</td>
<td>4.74*±0.50</td>
<td>4.20*±0.12</td>
</tr>
<tr>
<td></td>
<td>(-22.16)</td>
<td>(-31.03)</td>
<td>(-44.66)</td>
</tr>
<tr>
<td>Epididymis</td>
<td>1.96±0.40</td>
<td>1.53*±0.30</td>
<td>1.48*±0.20</td>
</tr>
<tr>
<td></td>
<td>(-21.9)</td>
<td>(-24.48)</td>
<td>(-25.51)</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.
Values in the parentheses are percent change from that of control.
* Significantly different from control at P<0.05.
Table 3.8. Effect of graded doses of ELAP and Andrographolide on the activity levels of Catalase (µmoles of H\textsubscript{2}O\textsubscript{2} metabolised/mg protein/min) in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Leaf Extract</th>
<th>Andrographolide</th>
<th>Andrographolide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>200</td>
<td>1000 mg/Kg body weight</td>
</tr>
<tr>
<td>Testis</td>
<td>0.087±0.007</td>
<td>0.042±0.01</td>
<td>0.032±0.07</td>
<td>0.028±0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-51.7)</td>
<td>(-63.2)</td>
<td>(-67.8)</td>
</tr>
<tr>
<td>Epididymis</td>
<td>0.10±0.06</td>
<td>0.027±0.05</td>
<td>0.021±0.02</td>
<td>0.018±0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-73)</td>
<td>(-79)</td>
<td>(-82)</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.
Values in the parentheses are percent change from that of control.
* Significantly different from control at P<0.05.
### Table 3.9: Effect of low, medium and high doses of ELAP and Andrographolide on the reproductive performance in adult male rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls</th>
<th>Leaf Extract 20</th>
<th>Leaf Extract 200</th>
<th>Leaf Extract 1000 mg/Kg body weight</th>
<th>Andrographolide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception time (days)§</td>
<td>1.235 ± 0.52</td>
<td>2.5* ± 0.83</td>
<td>2.83* ± 0.13</td>
<td>4.14* ± 1.7</td>
<td>2.5*±1.224*</td>
</tr>
<tr>
<td></td>
<td>(102.42)</td>
<td>(129.39)</td>
<td>(235.38)</td>
<td>(102.42)</td>
<td></td>
</tr>
<tr>
<td>Mating index (%)</td>
<td>100 (8/8)</td>
<td>100 (8/8)</td>
<td>100 (8/8)</td>
<td>100 (8/8)</td>
<td>100 (8/8)</td>
</tr>
<tr>
<td>Fertility index (%)</td>
<td>100 (8/8)</td>
<td>87.5 (7/8)</td>
<td>87.5 (7/8)</td>
<td>75 (6/8)</td>
<td>75 (6/8)</td>
</tr>
<tr>
<td>No. of corpora lutea/rat</td>
<td>14.01 ± 0.89</td>
<td>13.81 ± 0.10</td>
<td>13.70 ± 0.20</td>
<td>13.16* ± 0.18</td>
<td>13.10* ± 0.20</td>
</tr>
<tr>
<td></td>
<td>(-1.42)</td>
<td>(-2.21)</td>
<td>(-6.06)</td>
<td>(-6.49)</td>
<td></td>
</tr>
<tr>
<td>No. of implantations/rat</td>
<td>12 ± 0.58</td>
<td>11* ± 0.57</td>
<td>10.5* ± 0.21</td>
<td>9.66* ± 0.57</td>
<td>6.16* ± 0.37</td>
</tr>
<tr>
<td></td>
<td>(-8.33)</td>
<td>(-12.5)</td>
<td>(-19.5)</td>
<td>(-48.6)</td>
<td></td>
</tr>
<tr>
<td>Pre-implantation loss (%)</td>
<td>14.35</td>
<td>20.34</td>
<td>23.35</td>
<td>26.59</td>
<td>52.97</td>
</tr>
<tr>
<td>No. of live pups/rat</td>
<td>11.03 ± 0.04</td>
<td>10.01* ± 0.82</td>
<td>9.13* ± 0.76</td>
<td>7.38* ± 0.12</td>
<td>4* ± 0.10</td>
</tr>
<tr>
<td></td>
<td>(-9.24)</td>
<td>(-17.22)</td>
<td>(-33.09)</td>
<td>(-63.73)</td>
<td></td>
</tr>
<tr>
<td>Post-implantation loss (%)</td>
<td>8.08</td>
<td>9</td>
<td>13.04</td>
<td>23.6</td>
<td>35.06</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. of 8 individuals.

Values in the parentheses are percent change from that of control.

* Significantly different from control at P<0.05.
Figure 3.1. Sperm morphology a) Represents sperm morphology in control rats b) represents balloon shaped sperm c) represents amorphic spiral bend sperm d) represents double headed sperm e) represents acephalic sperm f) represents bent tail sperm g) represents gigantic twirling sperm h) represents gigantic sperm i) represents amorphic sperm j) represents sticky sperm
Figure 3.1. Sperm morphology j) represents sticky sperm k) represents multiple fission headed sperm l) represents bisectated sperm m) represents detoriated sperm n) represents fragile sperm o) represents HOS coil sperm in the rats exposed to graded doses of ELAP and Andrographolide.
**Results**

**Figure 3.2.** Effect of graded doses of ELAP and Andrographolide on the serum testosterone levels in male rats.

Bars are mean ± S.D. of 8 individuals.

Values in the parentheses are percent decrease from that of control.

Bars are significantly different from control at *P* < 0.05.

---

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Figure 3.3. Effect of graded doses of ELAP and Andrographolide on the lipid peroxidation in male rats

Bars are mean ± S.D. of 8 individuals.

Bars are significantly different from control at *P< 0.05.
**Figure 3.4.** Effect of graded doses of ELAP and Andrographolide on the SOD activity levels in male rats

Bars are mean ± S.D. of 8 individuals.

Bars are significantly different from control at *P< 0.05.
**Figure 3.5.** Effect of graded doses of ELAP and Andrographolide on the Catalase activity levels in male rats

Bars are mean ± S.D. of 8 individuals.

Bars are significantly different from control at *P< 0.05.
Figure 3.6.  

A: Transverse section of the testes of the control rat  

B: Transverse section of the testes of the rat administered with low dose of ELAP  

C, D: Transverse section of the testes of the rat administered with medium dose of ELAP
Results

a – represents non affected seminiferous tubules, b – represents atrophy of spermatogenic elements, c – represents degenerated appearance of germ cells, d – represents decrease of spermatozoa in the lumen of seminiferous tubules, e – represents foamy substance

**Figure 3.6.** E, F: Transverse section of the testes of the rat administered with high dose of ELAP

G, H: Transverse section of the testes of the rat administered with Adrographolide.
f – represents necrotic seminiferous tubules, g – represents absence of spermatozoa, h – represents foamy substance, i – represents giant cells in the seminiferous tubules, j – represents tail debris of spermatozoa in the lumen of seminiferous tubules

Figure 3.7. A: Transverse section of the cauda epididymus of the control rat
B: Transverse section of the cauda epididymus of the rat administered with low dose of ELAP
C: Transverse section of the cauda epididymus of the rat administered with medium dose of ELAP
D: Transverse section of the cauda epididymus of the rat administered with high
Results

dose of ELAP

**F:** Transverse section of the cauda epididymus of the rat administered with Adrographolide.
a – represents necrotic germinal layer, s – represents sperms, d – represents debris

Figure 3.8.  
A: Uterus of control rat showing normal implantations on 8th day pregnancy.  
B: Uterus of 8th day pregnant rat mated with rat exposed to 20 mg/kg BW of ELAP during embryonic development.  
C: Uterus of 8th day pregnant rat mated with rat exposed to 200 mg/kg BW of ELAP during embryonic development.
**Results**

D: Uterus of 8th day pregnant rat mated with rat exposed to 1000 mg/kg BW of ELAP during embryonic development.

E: Uterus of 8th day pregnant rat mated with rat exposed to 25 mg/kg BW of Andrographolide during embryonic development.

**Figure 3.9.**  
A: Uterus of control rat showing normal implantations on 18th day pregnancy.  
B: Uterus of 18th day pregnant rat mated with rat exposed to 20 mg/kg BW of ELAP during embryonic development.  
C: Uterus of 18th day pregnant rat mated with rat exposed to 200 mg/kg BW of ELAP during embryonic development.
**Results**

**D:** Uterus of 18th day pregnant rat mated with rat exposed to 1000 mg/kg BW of ELAP during embryonic development.

**E:** Uterus of 18th day pregnant rat mated with rat exposed to 25 mg/kg BW of Andrographolide during embryonic development.