

hormones secretion<sup>(17)</sup>. Nevertheless, direct and/or indirect role, also there could be probably an induction of Sertoli cells to secrete increasing amount of androgen binding protein (Abp), which binds testosterone and hydroxytestosterone produced outside the genital ducts, high concentration of these hormones are required within the genital epithelium and lumen for normal function<sup>(18, 19)</sup>. The epididymal wall thickness was decreased with 750 µg/kg doses and a great regression noticed at 1000 µg/kg dose. This could be due to the concept that melatonin is stimulating at normal level and harmful at higher doses<sup>(14, 15)</sup>.

The suggestion for those findings could be through suppression of hormone inhibin, which is secreted by Sertoli cells normally, inhibiting the secretion of FSH by the pituitary under control of hypothalamus and therefore plays an important feedback role in controlling the suppression of inhibin, which could be the cause of that regression consequently<sup>(4, 13)</sup>.

The number of points overlying the spermatozoa clump within the duct was increasing incrementally in the groups treated with the dose of 125 and 250 µg/kg, then at the dose of 500 µg/kg, it was adversely proportionate with those points on the wall & lumen of the tubules, this may be due to the effect of melatonin either directly on the main cells of spermatogenic lineage, through melatonin receptors proposed to be present in all body tissues and cells<sup>(16)</sup>, and / or indirectly by melatonin effect on hypothalamic-hypophyseal axis suppresses the secretion of FSH, hence decreases cells of spermatogenic lineage activity and number<sup>(20)</sup>. The other proposed explanation could be through over stimulation of these

Leydig cells by melatonin inducing over secretion of androgen; which acts by its negative feedback mechanism on hypothalamus leading to suppression of FSH secretion also<sup>(1, 4)</sup>.

The increase in frequency of apoptotic and pyknotic cells seen in groups treated with 250 µg/kg, might be caused by the effect of melatonin on Sertoli cells to control the large number of spermatogenic cells competing for survival in a so called programmed cell death (apoptosis) which is very different from that which occurs as a direct result of deleterious events to the cells, termed necrosis<sup>(1, 4, 13)</sup>.

In the group treated with 1000 µg/kg dose, some areas showed fibrosis & necrotic changes, this picture offers the extent of the highly damaging effect exerted by that dose of melatonin, since in any damaging events to any given tissue, a similar histological view will be sighted<sup>(1, 13, 17, 21)</sup>. Those results could be explained by the fact that melatonin has damaging effects only when it is administered in high doses<sup>(14, 15)</sup>. The thickening of the basement membrane could be resulted from the increase in production of fibrocollagenous tissues, since melatonin hormone has special effect on fibroblasts<sup>(22)</sup>, which are the active collagen – secreting cells and the basic forming cells of the connective tissues<sup>(1, 4, 23)</sup>. The increase in spermatozoa clump might be the consequence of decrease in motility of the spermatozoa so accumulated inside the widened lumen<sup>(13, 17)</sup>.

### References

1. Junqueira LC, Carneiro J, and Kelley RO. Genital system in Basic Histology, 10th Ed. A Lange Medical Book. 2003; P: 102-247.
2. Ebadi M. Hypothalamus, In Pharmacology. An Illustrated Review with Questions and