Research Journal of Recent Sciences _____ ISSN 2277-2502
Vol. **1(3),** 26-30, March **(2012)** *Res.J.Recent Sci.*

Hypervitaminosis - A causes Degenerative changes in Thyroid of Mouse

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Available online at: www.isca.in
(Received 5th February 2012, revised 13th February 2012, accepted 15th February 2012)

Abstract

Retinol Palmitate (RP) is known for its effects on differentiation and morphogenesis during vertebrate development, as it is important for reproduction development and growth, hyper and hypo-vitaminosis- A both provoke epithelial pathologies in animal and human being. So a critical value of RP is required in vivo for the maintenance of normal architecture and function of many body tissues. Thyroid gland is unique among vertebrate endocrine glands is that it stores its secretary products i.e. thyroid hormone. The thyroid influence reproduction, growth and differentiation. The group of adult mouse was treated 4 IU/ day concentration of RP by intubations for 7 days. This constituted the treated group. A similar number of mice were considered as controlled group, and were not given any RP treatment. The animal were observed for their growth, behavior and weight, during the period of treatment. On 8th day of the experiment thyrodactomy was done to both treated as well as controlled mice. The thyroid tissues taken were processed and sectioned for both light as well as electron microscopy. Following observation was made. In treated case hypertrophy of thyroid gland was seen. The thyroid follicle of the treated mice showed disorganization of their cells and the cells changed their cuboidal shape to an irregular shape. Ultra structure studies showed an irregular shaped nucleus. The studies concluded that RP treatment results in a reduced activity of thyroid follicles i.e. reduced synthesis of thyroxin.

Key words: Retinol palmitate/ hypothyroidism/ mouse).

Introduction

Vitamin A and its derivatives called retinoids are play important role in maintaining normal growth, regulating proliferation and differentiation of epithelial tissues, and maintaining visual and reproductive functions. Hypovitaminosis –A, leads to night blindness[1,2].

Recently many other functions of vitamin-A has been added during the vertebrate development. These includes its role in morphogenesis, maintained the healthy epithelium, regeneration of limbs[3]. McCollum and Davis[4] were the first to report that frog tadpoles fed with vitamin-A rich diet showed delayed metamorphosis. Niazi and Saxena[5] carried out systematic studies on vitamin-A induced delayed metamorphosis in buffo tadpoles and caused many histological changes in the thyroid. Such effects were consistent in other anurans[6]

In Rats Vitamin A repletion with concurrent vitamin A and iodine deficiency affects pituitary TSHß gene expression and reduces thyroid hyperstimulation and thyroid size[7].

Vitamin A supplementation in human beings has been promoted by much health organization to control nightblindness and other diseases related to vision[8]. It happens quite often due to ignorance that vitamin A supplementation is given overdosing in the young children, which some time leads to death. Even slightly higher dose then the required may cause damaged to certain vital organ including the endocrine glands[9]. Goswami and Choudhury established interrelationship between retinoid and thyroxin hormone. This study was carried out to find how RP, ester form of vitamin-A, influence thyroid gland of mouse when given in excess.

Material and Methods

Experimental work was carried out on adult Swiss albino mouse (4 weeks old). The mice were divided into two groups. The first group of four animals was not given any treatment and was considered as control. The other group of four animals was treated with 4 IU/day concentration of retinol palmitate by oral intubation for 7 days continuously.

Morphology and Histology: On the 8th day of experiment thyroid glands were removed from both controlled and treated animals after anesthetizing in ether, these were photographed then fixed in Bouin's for histological studies. For this purposes thyroid wax embedded 7 µm thick sections were stained with NFR (Nuclear fast red) and counter stain with Azan using Domagk[9] staining technique.

Ultra-structural study: The remaining thyroid from each groups were used for ultra-structural studies, for this these were fixed in glutaraldehyde and postfixed in osmium tetra-oxide. After embedding in Epoxy resin, semi-thin sections were cut using ultramicrotome with glass knife and stained with Touledene Blue. Some semi-thin sections were selected to identify the particular area for ultra-thin sectioning. The ultra-

thin sections were stained with double staining method using Uranyl acetate and Lead citrate and observed under transmission electron microscope.

Result and Discussion

Morphological Studies show hypertrophy in the thyroid gland of retinol palmitate treated mouse (figure 1a and figure1b).

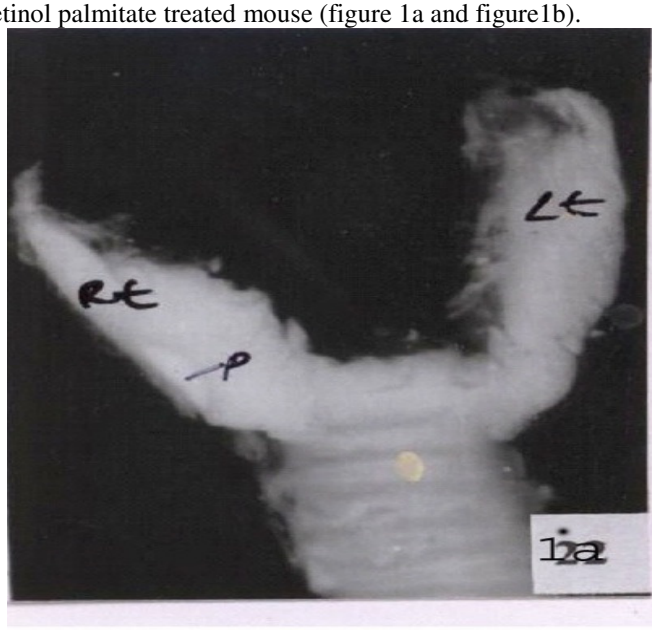

Figure-1(a)

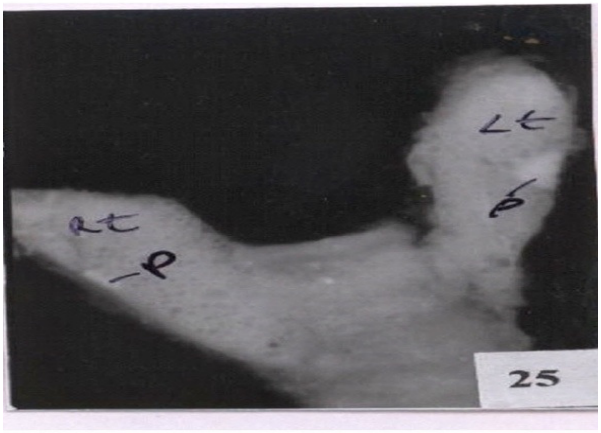

Fig. 1b (Treated) 4X

Figure-1(b)

The light microscopical histological studies of the thyroid gland of the controlled mouse at 10x magnification show that the follicles are well organized and the follicles at the boarder are of bigger size. These follicles are active follicles. In case of treated mouse the follicles get disorganized and become non-active. (figure 2a and 2b)

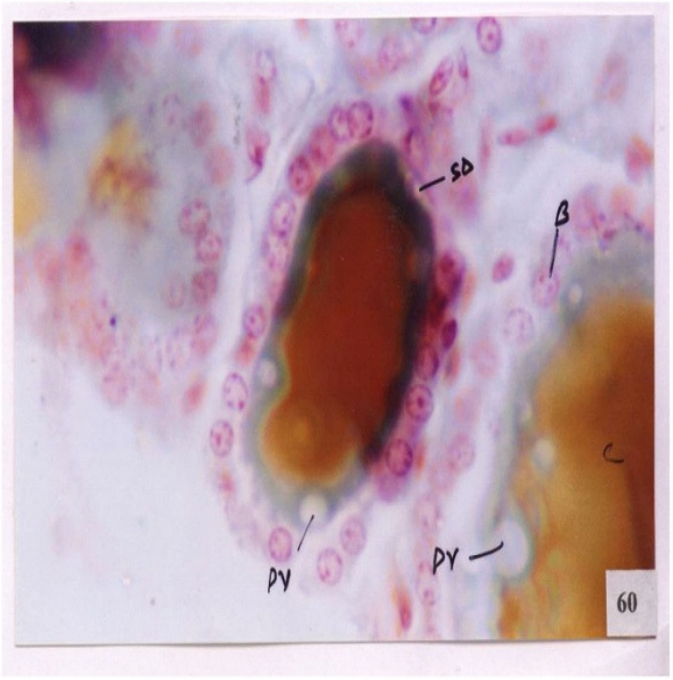

Figure-2(a)

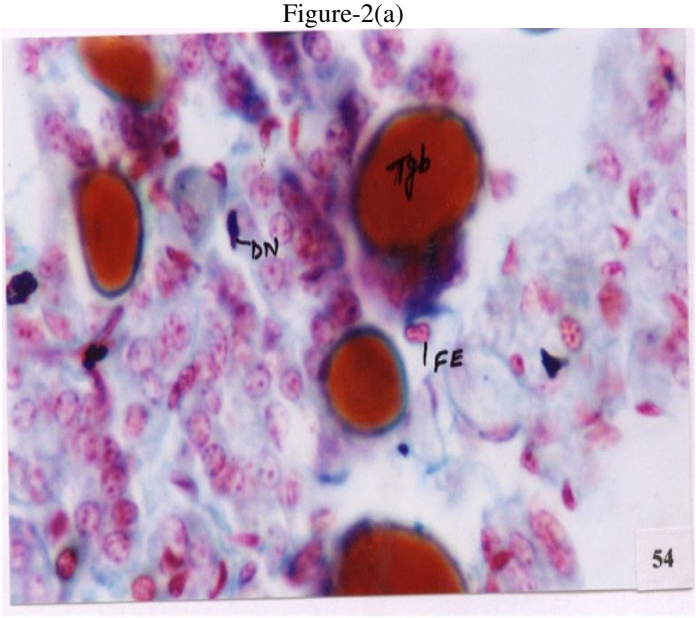

Fig. 2b (Treated) 10X

Figure-2(b)

Similar studies at 40x magnification show circularly arranged follicular cells i.e. cuboidal epithelial cells. The colloid is rich in thyroglobulin. Due to pinocytosis by follicular cells there are empty spaces at the boarders of the colloid which show that the thyroid is an active thyroid where as in RP treated mouse the follicular cells disorganized. And as a result the colloid also disperses away (figure 3a and 3b)

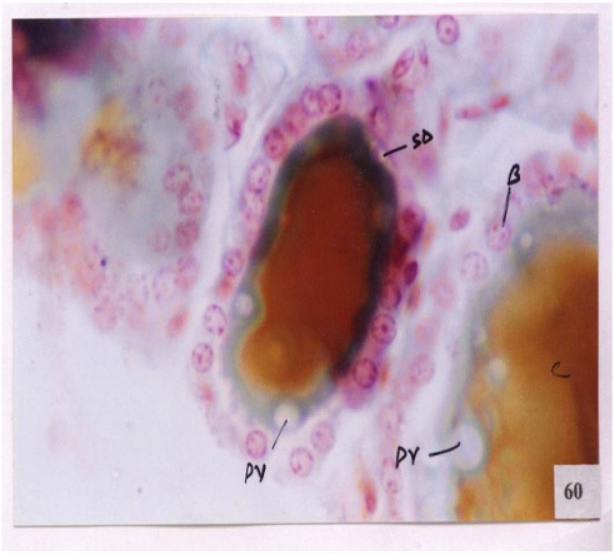

Fig. 3a (control) 40X

Figure-3(a)

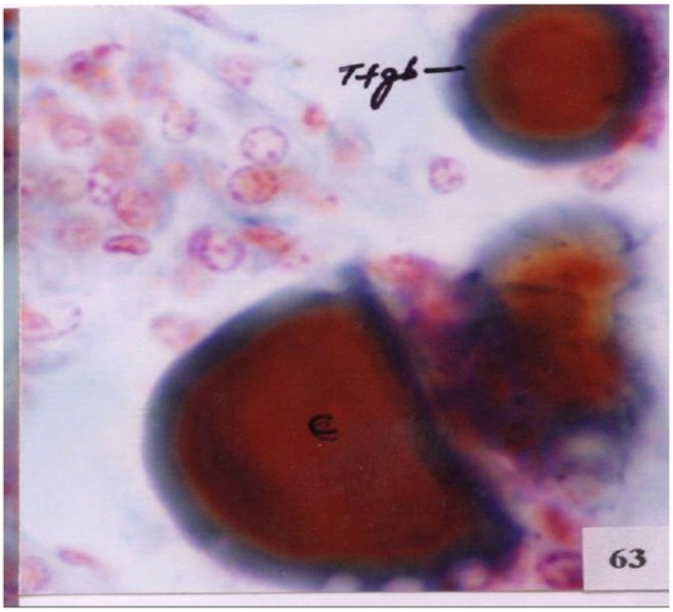

Fig. 3b (Treated) 40X

Figure-3(b)

The electron micrograph at 1900x of the controlled mouse show secretary granules and droplets of thyroglobulin. Nucleus is almost spherical. In case of the treated mouse at the same magnification the nucleus gets deformed and looses its spherical shape. (figure 4a and 4b) At a higher magnification i.e.3800x the microvilli are very closely visible in controlled case. The small dots on these microvilli show that the iodination of thyroglobulin is taking places there. Where as in treated mouse the nucleus is deformed. Secretary granules are relatively smaller and lesser in number. Microvilli are also not very clear. No nuclear pore can be seen (figure 5a, 5a' and 5b).

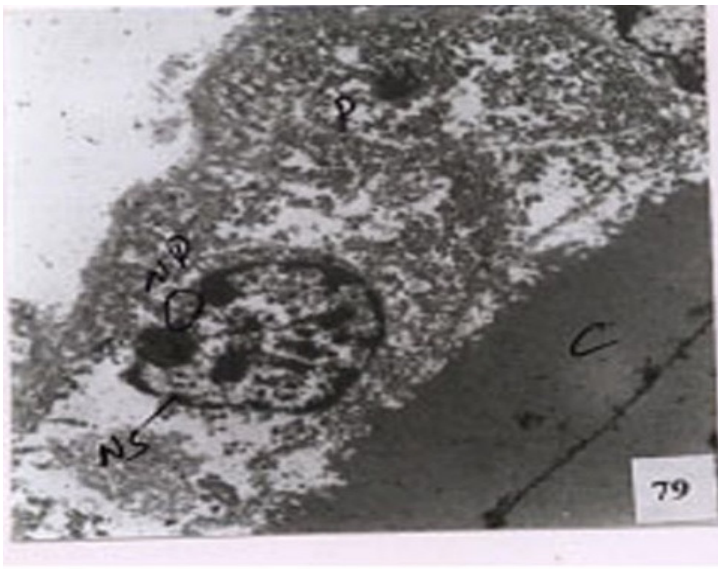

Fig. 4b (control) 1900X

Figure-4(a)

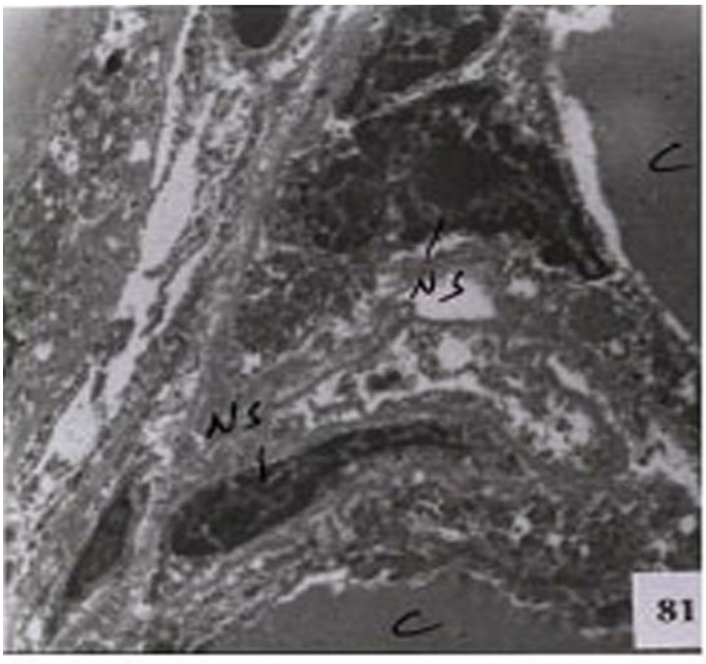

Fig. 4b (Treated) 1900X

Figure-4(b)

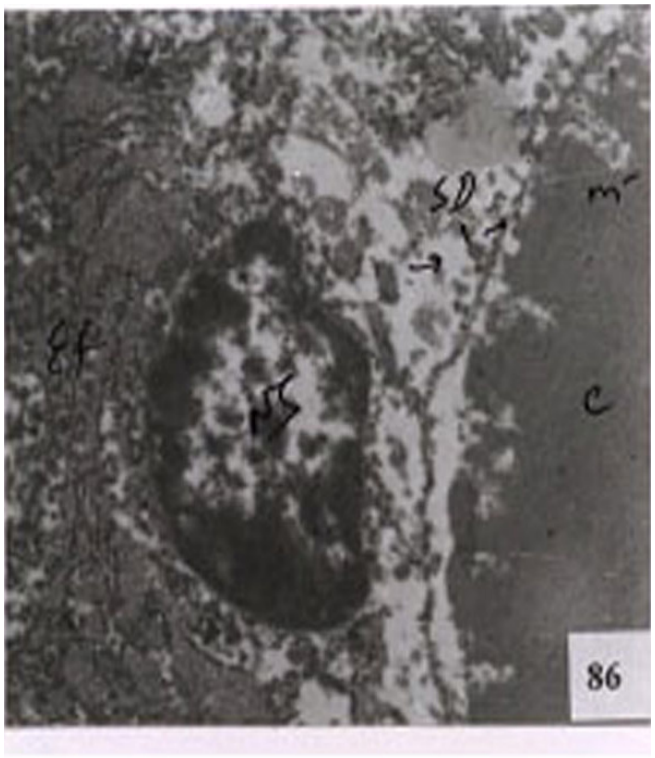

Fig. 5a (control) 3800X
Figure-5(a)

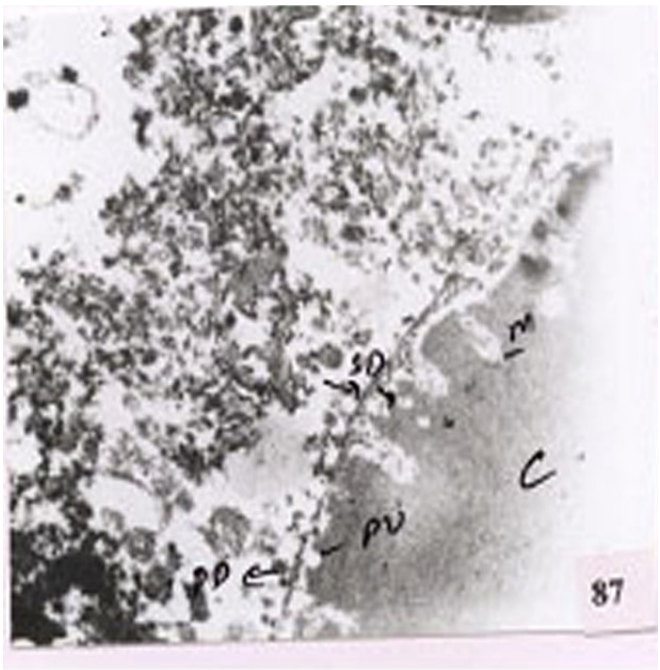

Fig. 5a' (control) 3800X
Figure-5(a)

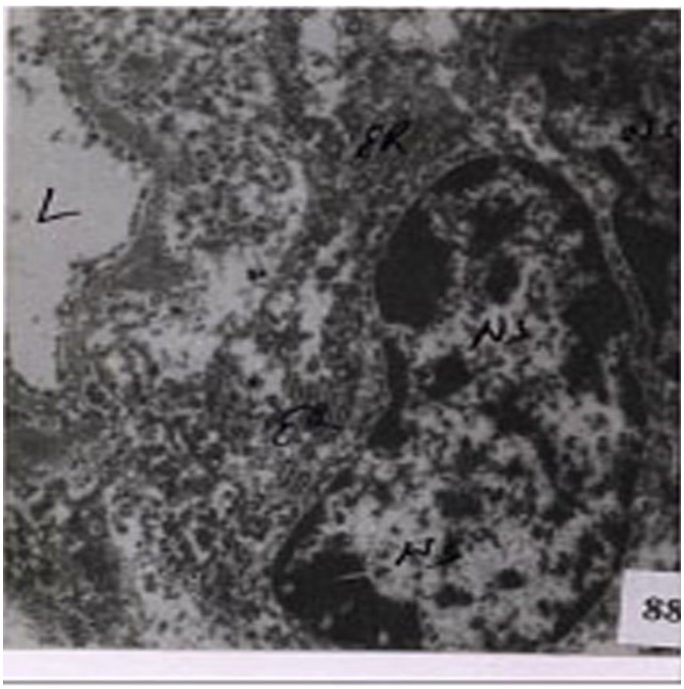

Fig. 5b (Treated) 3800X

Figure-5(B)

Still a higher magnification 4800x show even more secretary granules which are larger in size. Microvilli are more prominent and nucleopore are also clearly visible in controlled mouse. In treated mouse the microvilli disappeared completely showing that no iodination process is taking place there. Lack of iodination process causes hypothyroidism (figure 6a and 6b)

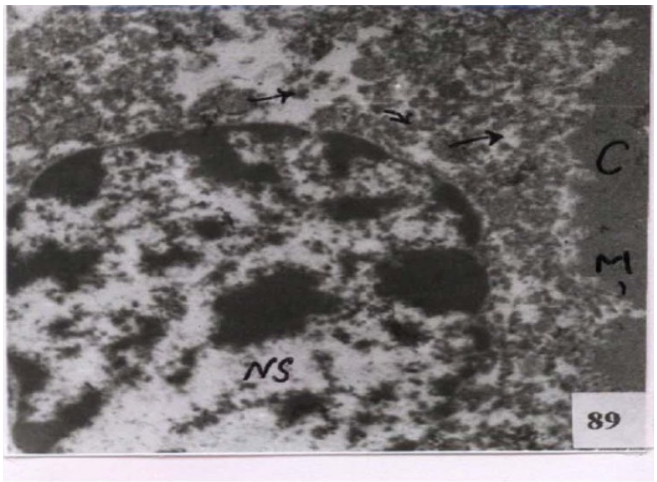

Fig.6a (control) 4800X

Figure-6(a)

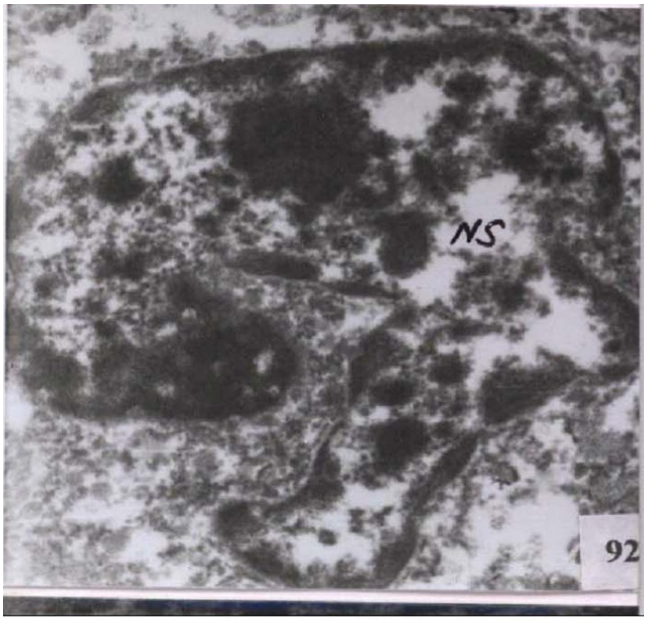

Fig. 6b (Treated) 4800X

Figure-6(b)

Thus it can be concluded that the RP if administrated orally in higher doses cause hypothyroidism by causing deformities in thyroid follicles.

Conclusion

RP causes disorganization of thyroid follicles. Disorganization of thyroid follicles, flattened epithelial cells, non-iodination of thyroglobulin, and prevention of re-absorption of thyroglobulin was observed. Ultra structural studies using transmission electron microscophy (TEM) revealed deformed nuclei, dilated and distorted endoplasmic reticulum, absence of Golgi bodies, and also absence of microvilli on acinar surface. In the RP treated cases iodination of colloid was inhibited. On the contrary untreated cases showed iodinated thyroglobulin in the colloid.

Acknowledgments

We are thankful to many persons who have made this research possible.

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