Original Article

Effect of Sodium Fluoride Administration During Pregnancy and Lactation on the Structure of the Submandibular Gland in Rat Offspring

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ABSTRACT

Aim of the work: This study was carried out to investigate the effect of gestational and lactational administration of sodium fluoride on the rat submandibular gland and its reversibility after fluoride withdrawal.

Materials and Methods: Thirty mature female albino rats were used and allowed for mating. Then the known pregnant rats were divided into three groups. The control group (group I) and their offspring were sacrificed at the age of two months. The treated group (group II) received a daily oral dose of 40mg/kg body weight sodium fluoride dissolved in distilled water via gastric tube. Drug administration started from the gestational day 10 up to the weaning on the postnatal day 21 then their offspring were administered the drug up to the age of two months then they were sacrificed. The third group (rehabilitated group) was treated in the same regimen as the second group, but their offspring were left without treatment after the weaning on the postnatal day 21 then they were sacrificed at the age of two months. Samples of the submandibular salivary gland were taken and prepared for light and electron microscopic studies. Histomorphometric technique was done to estimate the height, diameter and volume proportion of submandibular acinar and striated duct cells.

Results: Prominent changes were observed in the granular convoluted tubules (GCTs), in the acini and in the striated ducts. There was reduction in the amount of secretory granules content of the GCT of the sodium fluoride treated group. This reduction was associated with signs of degeneration and vacuolation of the cytoplasm. The GCT cells showed irregular contour of cell nuclei with clumping of the nuclear chromatin. Destruction of the mitochondria can be noticed in these cells. The acinar and striated duct cells showed degenerative changes in the form of irregular dark nuclei, variable staining and vacuolation of the cytoplasm and damaged mitochondria. Dissociation of cells from the basement membrane can be detected. On the other hand withdrawal of sodium fluoride reduced to a marked degree the structural changes induced by sodium fluoride.

Conclusion: It is concluded that administration of sodium fluoride in high dose in drinking water is associated with induction of destructive effect on the structure of the submandibular salivary gland. Withdrawal of sodium fluoride exposure can lead to recovery of the toxic effects of fluoride.

Key Words: Sodium fluoride, submandibular, rehabilitation, ultrastructure, albino rats.

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INTRODUCTION

Fluoride has been described as an essential element essential for normal development and growth of the animals and extremely useful for human beings. Fluoride is abundant in the environment, and the drinking water is the main source of fluoride to humans (Dhar & Bhantagar, 2009). Sodium fluoride has been known to be effective in caries prophylaxis, so it is still used for caries prevention in the form of fluoridated drinking water, fluoride tablets, fluoridated salt or milk (Dabrowska et al., 2006-a). Fluoride has been proved to be beneficial in recommended doses but at the same time its toxicity has also been well established at higher levels. Fluoride has been known that it gets accumulated in hard tissue of the body and plays an important role in mineralization of bone and teeth. At high levels there are suggested effects of fluoride on various body organs and genetic material (Dhar & Bhantnagar, 2009).
Amory et al. (1982) stated that absorption of high doses of sodium fluoride induced morphological changes in the secretory cellular units of the submandibular and sublingual salivary glands. Universal use of fluorine compounds in dentistry, as well as industrial and civilization-related exposures may produce undesirable effects of fluorine action. Fluoride ions effects depend on the dose and exposure time. Some may be positive for example in prevention of caries, while others are harmful when maximum prophylactic and therapeutic doses have been used (Dabrowska et al., 2006-b). The fluoride exposure results in slightly elevated steady-state level of fluoride in the oral fluids, primarily in saliva and plaque fluid. Following intake of fluoride, the remaining fluoride in the oral cavity is diluted by the saliva pool. Fluoride may be ionized in saliva, ionized in plaque, bound as calcium fluoride, bound to soft tissue and bound to enamel (Ekstrand & Oliveby, 1999).

Fluoride is known by its efficacy in improving the remineralization process by the deposition of phosphate and calcium ions. The formation of calcium fluoride on the surface of the enamel is the main product of all types of topical fluoride systems containing fluoride ions (Poureslami et al., 2007). It has been reported that there are interactions of fluoride ions with the activity of many enzymes and indirectly with cellular metabolism (Dabrowska et al., 2006-b). It has been stated that the effect of fluorides on various metabolic levels in hard and soft tissue, namely respiration as well as carbohydrate, protein, enzymatic and vascular metabolism, can disturb detoxication of fluorine compounds administered orally (Dabrowska et al., 2006-a).

The aim of this work was to study the effect of sodium fluoride administration during pregnancy and lactation on the submandibular gland of the albino rat and its reversibility after fluoride withdrawal.

**MATERIALS AND METHODS**

A total number of 30 pregnant Wister-albino rats were chosen and kept under good environmental nutritional and hygienic conditions at the animal house of Faculty of Medicine, Assiut University. They were allowed for matting. Pregnant females were identified by using vaginal smear examination. Then they were separated and divided into three groups. The control Group: 10 dams received distilled water daily from the 10th day of gestation up to the weaning on the postnatal day 21 and then the offspring were administered distilled water until the age of two months, then they were sacrificed. The treated Group: 10 dams were treated with a daily oral dose of 40mg/kg body weight sodium fluoride dissolved in distilled water via gastric tube for the same period mentioned above then the offspring were administered the same dose up to the age of two months then they were sacrificed. The third recovered Group: 10 dams were treated in the same regimen as the second group, but the offspring were left without treatment after weaning on the postnatal day 21, then they were sacrificed at the age of two months.

After transcardiac perfusion of the animals with isotonic saline followed by 5% coccodylate buffered gluteraldehyde, the submandibular glands were removed and dissected in the same fixative. About two mm-thick slices were cut from the glands and postfixed in 1% osmium tetroxide. The specimens were dehydrated in ascending grades of ethanol and embedded in Araldite mixture. Semithin sections of one-micron thickness were cut with a glass knife in KLB ultramicrotome and stained with toluidine blue. Other ultrathin sections were cut, stained with uranyl acetate and lead citrate and examined with JEM-100 CX11 electron microscope.

**Morphometric methods:**

The acinar and striated duct cells height, diameter and volume proportion were measured in a light microscopic equipped with Olympus WFX10 calibrated ocular micrometer coupled to X40 or 100 objectives. Statistical analysis was evaluated by ANOVA test (LSD).

**RESULTS**

**Light microscopic results:**

Control group: The semithin sections obtained from the submandibular salivary gland in control group revealed the normal histological picture of the gland. The acini were formed of regular basement membrane lined by a group of pyramidal secretory cells surrounding a nar-
The intralobular duct segment of the gland was composed of three parts: intercalated duct, striated duct and Granular Convoluted Tubule (GCT). The striated duct cells were characterized by tall columnar epithelium with a characterized striated pattern of the basal cytoplasm (fig. 3). The GCT cells were columnar and distinguished by basal vesicular nucleus and abundant membrane-bound secretory granules occupying the apical part of the cell. These granules were round in shape and variable in size (fig. 4).

Treated group: In the treated group, the gland appeared with shrunken irregular degenerated acini (fig. 5). The lining epithelium is detached and dissociated from the basement membrane (figs. 5, 6). The cytoplasm showed vacuolation of different sizes and irregular staining. The nuclei were irregular and dark (fig. 6).

The striated duct cells showed also signs of degeneration and the ducts appeared with irregular outline and their epithelium detached from the basement membrane (figs. 6, 7). Their cytoplasm showed vacuolation, the nuclei appeared irregular and deeply stained (fig. 8). The GCT cells revealed vacuolation of the cytoplasm and small amount of secretory granules with some of them appeared degranulated (fig. 6).

Rehabilitated group: The mucous acini and striated ducts showed recovery and appeared more or less normal with regular appearance and less prominent vacuolation of the cytoplasm as compared with the treated group (figs. 9, 10). The nuclei of the striated duct appeared more regular and vesicular (fig. 10). The GCTs appeared more or less normal with relative increase in the amount of the secretory granules as compared with the treated group and their lining cells contained vesicular nuclei (figs. 10, 11).

**Ultrastructural results:**

**Control group:** Ultrastructural examination of the gland of the control animals showed that the acinar secretory cell was pyramidal in shape and contained abundant mucous-like secretory granules with a flocculent content of low electron density in the apical region of the cytoplasm (fig. 12). The cell had a flattened basally located nucleus, mitochondria and abundant closely-packed cisternae of Rough Endoplasmic Reticulum (RER) (fig. 13).

The GCT cell was characterized by basal euchromatin nucleus and abundant membrane-bound uniformly electron-dense secretory granules variable in sizes in the apical three quarters of the cell (fig. 18). RER was located in the basal perinuclear regions of the cell. Mitochondria were scattered throughout the cytoplasm (fig. 18).

Treated group: Ultrastructural examination of the gland of the treated animals showed that the acinar secretory cells had irregular, basally located nucleus with peripheral aggregates of dense chromatin. Destruction of the mitochondria can be noticed. Multiple cytoplasmic vacuoles were observed (figs. 14, 15, 16).

The GCT cells had remarkable changes. In contrast to the control group, the treated GCT cells showed prominent reduction in the amount of the secretory granules (fig. 19). Regressed GCT cells contained few secretory granules near the apical rim. These granules were variable in size and their electron density was not uniform. Some granules showed lightly-stained density while others showed deeply-stained density (fig. 20). Multiple cytoplasmic vacuoles were frequently observed. RER was less developed (fig. 20). Some mitochondria were damaged. The cell nuclei showed clumping of nuclear chromatin in the periphery (fig. 20).

Rehabilitated group: Ultrastructural examination of the gland of the rehabilitated animals showed that the acinar secretory cells had flattened basally-located electron-dense nucleus. Mitochondria appeared more or less normal but some few small dense mitochondria were seen. Well-defined considerable RER can be detected in the infranuclear region (fig. 17).

The GCT cells contained numerous large secretory granules in their apical cytoplasm (fig. 21). Mitochondria appeared more or less healthy. Less marked cytoplasmic vacuolation was noticed as compared with the treated group (fig. 21).
Morphometric results:

There was significant decrease in the mean diameter, volume proportion and cell height of acini and striated ducts in the treated group as compared with the control group. In group III, there was a significant increase in the mean cell height, diameter and volume proportion of acini and striated ducts compared with the treated group (Tables 1, 2; figs. 22, 23).

Fig. 1: Semithin section of submandibular salivary gland of control male albino rat showing mucous acini (A) and striated duct (st). Toluidine blue; X 400

Fig. 2: Semithin section of submandibular salivary gland of control male albino rat showing mucous acini (A). The acinar cells contain pale foamy cytoplasm with flattened basally located nuclei. Toluidine blue; X 1000

Fig. 3: Semithin section of submandibular salivary gland of control male albino rat showing striated duct (st) cells with striated pattern of the basal cytoplasm and round vesicular nuclei. Toluidine blue; X 1000

Fig. 4: Semithin section of submandibular salivary gland of control male albino rat showing GCT cells (G) filled with secretory granules (arrows), their nuclei are round with prominent nucleoli (arrow heads). Toluidine blue; X 1000

Fig. 5: Semithin section of submandibular salivary gland of treated male albino rat showing mucous acini (A). The acinar cells are dissociated from the basement membrane (arrow heads). Notice destruction and cavitation of these cells (V). Toluidine blue; X 400
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Fig. 6: Semithin section of submandibular salivary gland of treated male albino rat showing granular convoluted tubule (G) with small amount of secretory granules, some cells show vacuolation (V) of their cytoplasm with irregular deeply stained nuclei. Irregular acini with vacuolated cytoplasm can be detected. Notice irregular staining of the cytoplasm in the acinar and GCT cells. Toluidine blue; X 1000

Fig. 7: Semithin section of submandibular salivary gland of treated male albino rat showing striated duct (st) cells with marked dissociation form the basement membrane (arrowhead). Some nuclei are irregular and deeply stained. The acinar cells (A) show vacuolated cytoplasm (V) and dark degenerated nuclei. Toluidine blue; X 1000

Fig. 8: Semithin section of submandibular salivary gland of treated male albino rat showing striated duct (st). The striated duct cells appear degenerated with vacuolated cytoplasm (V) and irregular darkly stained nuclei (arrows). Toluidine blue; X 1000

Fig. 9: Semithin section of submandibular salivary gland of rehabilitated male albino rat showing mucous acini (A) and granular convoluted tubules (G) which appear more or less normal in comparison with the control group. Toluidine blue; X 400

Fig. 10: Semithin section of submandibular salivary gland of rehabilitated male albino rat showing mucous acini (A), striated duct (st) and a group of GCTs (G). The mucous acini and striated duct cells show regular, more or less normal appearance with very scanty areas of vacuolated cytoplasm (V). GCT cells show recovery as compared with the treated group as regard the amount of secretory granules which show much increase (arrow heads). Their lining cells contain vesicular nuclei. Some GCT cells show small amount of secretory granules (arrows). Toluidine blue; X 1000
Fig. 11: Semithin section of submandibular salivary gland of rehabilitated male albino rat stained with showing mucous acini (A) and GCT (G) which show recovery as compared with the treated group and appear more or less normal. Toluidine blue; X 1,000

Fig. 12: An electronmicrograph of acinar cell of control animal showing flattened and basally located nucleus (N). Notice abundant secretory granules with a flocculent content of low electron density in the apical region of the cytoplasm. X 5,000

Fig. 13: An electronmicrograph of acinar cell of control animal showing flattened and basally located nucleus (N), mucus like secretory granules in the supranuclear region (arrow head), perinuclear mitochondria (mi) and abundant closely packed cisternae of RER (arrow) X 8,000

Fig. 14: An electronmicrograph of acinar cell of treated animal showing irregular shaped basally located nucleus (N). Vacuolations of the cytoplasm (V) and destruction of the mitochondria (mi) can be noticed. X 4,000

Fig. 15: An electronmicrograph of acinar cell of treated animal showing irregular shaped basally located nucleus (N) with dense clumps of chromatin. Highly destroyed mitochondria (mi) can be detected and other organelles are hardly recognizable. X 5,000

Fig. 16: An electronmicrograph of acinar cell of treated animal showing flattened basally located nucleus (N) with peripheral condensation of chromatin and multiple cytoplasmic vacuoles (V). X 8,000
Fig. 17: An electronmicrograph of acinar cell of rehabilitated animal showing flattened basally located nucleus (N). The apical region of the cytoplasm is occupied by electron lucent secretory granules. Mitochondria (mi) and arrays of RER (arrow) can be seen in the infranuclear region. X 8,000

Fig. 18: An electronmicrograph of GCT cells of control animal showing basal euchromatic nucleus (N) with dispersed chromatin. An electron-dense secretory granules of variable sizes in the supranuclear region (arrow heads). Mitochondria (mi) and arrays of RER (arrow) can be detected in the infranuclear and perinuclear regions. X 4,000

Fig. 19: An electronmicrograph of GCT of treated animal showing nuclei (N) with peripheral aggregates of dense clumps of chromatin. GCT cells show few electron dense secretory granules. X 4,000

Fig. 20: A magnified part of the previous section showing electron dense nucleus (N) with clumps of chromatin. Multiple cytoplasmic vacuoles (V) are observed. Some mitochondria are damaged (mi). Some secretory granules are electron-dense (arrow) while others are of low electron density (arrowhead). X 8,000

Fig. 21: An electronmicrograph of GCT of rehabilitated animal showing many electron-dense granules are packed in the cytoplasm (arrow heads). The nucleus (N) appears round with relatively dispersed chromatin. Healthy mitochondria similar to the control group (mi) and few vacuoles (V) can be detected. X 5,000
Fig. 22: Histogram showing the height, diameter and volume proportion of acini in the control, treated and rehabilitated groups.

Fig. 23: Histogram showing the height, diameter and volume proportion of striated ducts in control, treated and rehabilitated groups.

Table 1: Height, diameter and volume proportion of acini in the control, treated and rehabilitated groups.

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<td>Group II (Treated)</td>
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<td>I vs. III</td>
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<td>Volume proportion</td>
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<td>33.46±3.98</td>
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<td>II vs. III</td>
<td>0.038*</td>
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ANOVA test (LSD)
* Statistical significant difference
Table 2: Height, diameter and volume proportion of striated ducts in the control, treated and rehabilitated groups

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<td>Group II (Treated)</td>
<td>6.03 ± 0.34</td>
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<td>Group III (Rehabilitated)</td>
<td>17.8 ± 2.4</td>
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<td><strong>Height</strong></td>
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<td>I vs. III</td>
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<td>Group I (Control)</td>
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<td>Group III (Rehabilitated)</td>
<td>55.41 ± 8.93</td>
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<td>Group II (Treated)</td>
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<td>Group III (Rehabilitated)</td>
<td>11.49 ± 0.69</td>
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<td><strong>Volume proportion</strong></td>
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ANOVA test (LSD)
* Statistical significant difference

**DISCUSSION**

In the present study, the morphological organization of the albino rat submandibular salivary glands is in agreement with that reported by previous authors (Srinivasan & Chang, 1975; Barka, 1980; Gresik, 1994; Fawcett & Jensh, 1997).

The present study revealed that the rat submandibular gland was composed of seromucous secretory cells. In semithin sections stained with toluidine blue, the cells contained abundant pale foamy cytoplasm due to the presence of a large number of mucous-like secretory granules which appeared faintly and moderately stained. Qwarnstrom and Hand (1983) stated that the intercalated ducts of the salivary glands constitute the first portion of the intralobular duct system, connecting the acini with the striated ducts. In the submandibular gland of the adult rat, the intercalated duct empties into the granular convoluted tubule which develops at puberty from the proximal portion of the striated duct.

The granular convoluted tubule (GCT) is located at the junction between the intercalated duct and the striated duct (Abdollahi & Simaiee, 2003). Hand (1979) and Barka (1980) reported that the duct system has been thought to play a role in not only conveying saliva from the secretory endpieces to the mouth but also by active transport of sodium and potassium ions. Tamarin and Sreebny (1965) stated that the intercalated duct cell of rat submandibular gland is low cuboidal in shape. The striated duct epithelium is columnar and the cells show characteristic basal infolding (basal striation) (Sato & Miyoshi, 1998).

The striation of the basal cytoplasm detected with the light microscope was found in electron micrographs to be due to the vertical alignment of numerous long mitochondria in narrow compartments formed by deep invaginations of the plasma membrane at the cell base (Bloom & Fawcett, 1994).

Abdollahi and Simaiee (2003) found that the GCT consists of cells with large secretory granules that contain a variety of bioactive peptides such as growth factors as EGF, NGF (epidermal growth factor) and (nerve growth factor). In accordance, Gresik et al. (1996)
reported that the GCT is a special segment of the duct system which is under hormonal regulation and synthesize many biologically potent proteins such as NGF, EGF, TGF-α, hepatocyte growth factor, insulin like growth factor, and kallikrein- like proteases. Kaiho et al. (1975) claimed that the size and granularity of this tubular portion depend on circulating levels of certain hormones (e.g. testosterone and thyroxin).

In the present work, treatment with sodium fluoride resulted in alterations in the cells of submandibular salivary gland in the form of irregular staining of the cytoplasm with the presence of multiple cytoplasmic vacuoles. The nuclei appeared irregular. Morphometric study augmented these observations since there were marked reduction in mean cell height, diameter and volume proportion in the acini and intercalated ducts. In harmony with these findings, Amory et al. (1982) reported that the morphometric study showed a strong decrease of the acinar and canalicular surfaces in the submandibular gland of rats treated with sodium fluoride. These findings are also supported and explained by Ogilvie (1951) who stated that there is evidence of cytological change in the rat submandibular salivary gland in the form of vacuolation and unusual staining of the cytoplasm and the enlarged and irregular shape of many cell nuclei pointed to degeneration possibly of a fatty nature.

Everett (1944) proved that the sharp histological picture of cell derangement in the submandibular gland may be found to arise from the adverse effects of fluoride upon metabolic systems within the cell. Glandular tissue has a secretory function that can be done by the metabolic activity of their component cells. Fluoride can block the reformation of adenosine triphosphate, so it can prevent optimum cellular oxidation. Moreover, fluoride is a known inhibitor of lipase. If inhibition of oxidase is likewise effective a biochemical reason of fatty degeneration would be established.

In the present study, the ultrastructural examination revealed signs of degeneration as multiple cytoplasmic vacuolation, damaged mitochondria and irregular contours of cell nucleus and This was supported by Dabrowska et al. (2004) who studied the effect of sodium fluoride on the ultrastructural changes in the rat submandibular gland and found that mitochondria were most damaged.

The present study revealed striking cytological changes in the GCT in the form of appearance of cytoplasmic vacuoles and obvious reduction in the amount of their granules with alteration in the staining intensity of these granules. The reduction in the amount of the GCT cells may be due to the toxic effect of sodium fluoride on the reproductive system since the maintenance and development of the granular tubules in the rat, as well as the level of some submandibular proteases are known to be androgen dependent (Chretein, 1977). This is in agreement with the work of Gupta et al. (2007) who concluded that sodium fluoride administration in drinking water was associated with toxic effect on the reproductive system of male rats and testicular disorders. In accordance with that, Ortiz-Perez et al. (2003) observed a decreased serum testosterone levels in human population exposed to high doses of fluoride.

The alteration in staining density of the granules in the granular ducts could be due to alteration of their contents by hormone disturbance. Mucin, glycoprotein rich in sialic acid, has been localized in these ducts (Ravetto et al., 1966). Keryer et al. (1973) found that the amine sugars and sialic acid in mucin increase greatly after puberty in male and female rats. So, disturbance in level of testosterone due to exposure to fluoride might also alter the sugar content of the granules, changing their staining density.

In the present work, withdrawal of sodium fluoride resulted in improvement in the acinar, striated ducts and GCT cells in the form of less marked cavitation, a visible increase in the amount of intracellular granules and a marked improvement in the cellular damage induced by sodium fluoride. These observations are supported by Ekambaram and Paul (2002), who reported that the toxic effects of fluoride are reversible if its exposure is withdrawn for two months. In accordance with that, Verma and Gunia Sherlin (2002) found that withdrawal of sodium fluoride treatment of rats during lactation caused significant amelioration in feed consumption. In support of this, Ekambaram and Paul (2002) explained that withdrawal of sodium fluoride for two months
can decrease availability of fluoride in the gastrointestinal tract. As a result, absorption of fluoride has been disturbed in these animals. These results indicate that the changes produced by fluoride are transient and withdrawal of sodium fluoride exposure lead to reduction in serum fluoride to a lesser toxic concentration so these effects can be reverted.

REFERENCES


تأثير إعطاء فلوريد الصوديوم أثناء الحمل والرضاعة على تركيب الغدة اللعابية تحت الفكية 

في أجيال الفئران البيضاء

هبه كمال محمد، وفاء علاء الدين مبارك، درية عبد الله زغلو

قسم التشريح - كلية الطب - جامعة أسيوط

ملخص البحث

تهدف هذه الدراسة إلى التعرف على تأثير إعطاء فلوريد الصوديوم أثناء الحمل والرضاعة على الغدة اللعابية تحت الفكية في أجيال الفئران البيضاء ومدى انعكاسه بعد توقف إعطائه.

استخدم في هذا البحث ثلاثون من إناث الفئران البيضاء البالغة. وبعد التزاوج تم تقسيم الفئران الحوامل إلى ثلاث مجموعات. المجموعة الأولى (المجموعة الضابطة) وقُد أطعمت يومياً ماء مقطر بكميات مفهرسة (المجموعة المختبرة) حيث أعطيت يومياً جرعة من مادة فلوريد الصوديوم نقية بكميات مفهرسة (0.4 مجم / كلجم من وزن الجسم) بداية من اليوم العاشر من الحمل وحتى انتهاء فترة الرضاعة (اليوم الواحد والعشرون بعد الولادة). بينما أُلقت إعطاء فلوريد الصوديوم لمجموعة الفئران المولودة حتى عمر البلوغ. تم إعطاء فلوريد الصوديوم للكل الفئران الثلاثة. تم استخدام الفئران المولودة لمجموعات الفئران الأولى والثانية والثالثة عند عمر البلوغ. وقد تم أخذ العينات من الغدة اللعابية تحت الفكية من جميع الفئران المولودة. تم تحليل النتائج في الميكروسكوبين الضوئي والإلكتروني.

تعد هذه الدراسة الأولى من إثبات الفئران البيضاء البالغة. وبعد التزاوج تم تقسيم الفئران الحوامل إلى ثلاث مجموعات. المجموعة الأولى (المجموعة الضابطة) وقُد أطعمت يومياً ماء مقطر بكميات مفهرسة (المجموعة المختبرة) حيث أعطيت يومياً جرعة من مادة فلوريد الصوديوم نقية بكميات مفهرسة (0.4 مجم / كلجم من وزن الجسم) بداية من اليوم العاشر من الحمل وحتى انتهاء فترة الرضاعة (اليوم الواحد والعشرون بعد الولادة). بينما أُلقت إعطاء فلوريد الصوديوم لمجموعة الفئران المولودة حتى عمر البلوغ. تم إعطائ الفئران المولودة لمجموعات الفئران الثلاثة. تم استخدام الفئران المولودة لمجموعات الفئران الأولى والثانية والثالثة عند عمر البلوغ. وقد تم أخذ العينات من الغدة اللعابية تحت الفكية من جميع الفئران المولودة. تم تحليل النتائج في الميكروسكوبين الضوئي والإلكتروني.

أعدت شرائح بسمك 4 ميكرون وتم صباغتها باستخدام التوليودين بلو. كما تم عمل بعض القياسات لمقارنة المجموعات باستخدام محلل الصور ومقارنة جمع النتائج باستخدام الطرق الإحصائية. ولقد وجد أن التغيرات التي أحدثتها مادة فلوريد الصوديوم في الغدة اللعابية قد ظهرت في خلايا الحويض وقنوات الخلايا بالفروضات المفهرسة، وظهور أحيانًا تهالك في الشكل من خلايا الحويض وظهور نواة دقيقة، وظهور فضلات في السوائل المحيطة بالخلايا وظهور نواة دقيقة، وظهور نواة دقيقة، وظهور نواة دقيقة، وظهور نواة دقيقة، وظهور نواة دقيقة، وظهور نواة دقيقة. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على الغدة اللعابية في بعض الفئران. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على غدة الخلايا. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على الغدة اللعابية في بعض الفئران. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على غدة الخلايا. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على الغدة اللعابية في بعض الفئران. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على غدة الخلايا. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على الغدة اللعابية في بعض الفئران. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على غدة الخلايا. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على الغدة اللعابية في بعض الفئران. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على غدة الخلايا. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على الغدة اللعابية في بعض الفئران. وعند إيقاف إعطاء فلوريد الصوديوم حدث تحسن ملحوظ للتأثيرات الضارة لفلوريد الصوديوم على غدة الخلايا. وعند إيقاف إعطاء فلوريد الصودوم