Perinatal Exposure to Sodium Fluoride with Emphasis on Territorial Aggression, Sexual Behaviour and Fertility in Male Rats

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Abstract: Territorial aggression, sexual behaviour and fertility parameters were evaluated at adulthood of male rats previously exposed to different concentrations of sodium fluoride (Na-F) at their gestation, lactation and post-weaning period till maturation. Sixty weanling male Wistar rats were received Na-F via their dams from second trimester of their pregnancy onward till weaning at 30 days of age at one of three different concentrations; 0, 50 and 100 ppm, 20 pups for each dose. Na-F was then administered in drinking water, at the same doses, to the three experimental groups throughout the course of the study till completing all investigations. Na-F treatment significantly diminished territorial aggressive behaviour parameters in adult male rats as indicated by reduced lateralization, boxing bouts, fighting as well as ventral presenting postures compared with controls. Likewise, a significant decline in sexual behaviour was also noted for Na-F-exposed rats, where latencies to first mount, intromission and ejaculation were significantly prolonged, and notably for the higher incorporated dose. Moreover, a significant decrease was evident for frequencies of mounts, intromissions and ejaculations when Na-F was given to males compared to their untreated counterparts. Higher post-ejaculatory intervals were observed with Na-F group, particularly at high dose. Compared to control group, high Na-F-treated rats displayed a significant inhibited profile of fertility as reflected in reduced number of impregnated females, implantations as well as viable fetuses, along with increased number of resorptions. Relative weights of reproductive organs were also lessened in Na-F-administered males. Histopathological examination showed degenerative changes in testes, seminal vesicles and prostate gland of Na-F-exposed males with varied degree of severity according to incorporated dose. Our study clearly signifies the adverse effect of fluoride on territorial aggression, sexual performance with inhibited fertility in adult male rats.

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1. Introduction:

Fluoridation of water supplies is practiced in many parts of the world, where fluoride is recognized as the most effective caries preventive agent (Mahejabeen and Hajira, 2007). Further fluoride sources, other than drinkable water are drinks, tooth pastes, mouth rinses and dietary supplements. There is growing evidence that serious overall health consequences of excessive fluoride intake are significant enough to warrant further precautionary measures with the consumption of fluoride **(**Spittle, 2009). Maternal-fetal transport of fluoride across human and rat placenta during pregnancy have been reported, with subsequent transfer of fluoride through milk, comprising a real threat for progeny health (Drinkard et al., 1985; Fassman, 1993; Hassunuma et al., 2007). This problem should become the concerns of many researchers dealing with fluoride, particularly with regard to its effects on susceptible generations.

Androgen hormones play a crucial role in control of aggressive and sexual behaviour in males (Clark and Henderson, 2003). Moreover, anterior hypothalamic-preoptic area was proved to be the primary site of androgen action in the mediation of both types of behaviours in males (Yahr, 1981; Barfield, 2011).

Exposure to toxic elements has been reported to affect both aggressive and antisocial violent behaviours (Werbach, 1995; Mysterud, 2003). However, a paucity of literature is available concerning the influence of Na-F on parameters of aggressive behaviour in male rats, namely territorial aggression.

Among the different effects fluoride can produce in different organ systems of the body, the reproductive tract is susceptible to disruption by fluoride at a concentration sufficient to produce other manifestations of toxicity (Spittle, 2007). A number of animal studies indicated the occurrence of adverse reproductive and developmental outcomes in individuals exposed to relatively high concentrations of fluorides (Dhar and Bhatnagar, 2009). Most of these investigations with diverse animal species, rat,

mice and rabbits, were associated with alterations in reproductive hormones, fertility, histological structure and developmental outcomes (Kumar & Susheela 1994, 1995; Elbetieha et al., 2000; Collins et al. 2001; Zhang et al. 2006). However, little is known about Na-F-induced alterations in sexual behaviour of male rats. Developmental Na-F exposure was shown to induce sexual behaviour deficits in male offspring (Bera et al., 2007), yet more research need to be done in order to further identify Na-F toxicity in animals exposed to its hazard throughout different developmental stages of their life, in particular its perinatal exposure.

Therefore, in the presented work we aimed to study the impact of fluoride toxicity in adult male rats perinatally exposed to different concentrations of Na-F (during their stages of gestation, lactation and post-weaning) till maturation on presentation of territorial aggressive and sexual behaviours. In addition, fertility indices of male rats as well as histopathological evaluation of male sex organs were also detected.

2. Materials and methods:

2.1. Animals and housing:

Rats used in this study were maintained and treated in accordance with ethical guidelines released by Cairo University Policy on Animal Care and Use. Adequate measures were taken to minimize pain, discomfort or stress of the animals. In addition, efforts were made to use only the minimal number of animals necessary to produce reliable scientific data.

Forty five mature female Wistar rats (Unit for Laboratory Animals at Faculty of Veterinary Medicine, Cairo University) weighing 200-220g were used. Animals were housed in polypropylene cages with stainless steel wire lids (bedded with wood shavings) and kept at a room temperature of 20-22°c, 60% humidity on a light cycle of 12 h/day. They were allowed free access to standard laboratory feed and water. Pairs of females were placed with single male rats of the same strain at night.

2.2. Administration of sodium fluoride:

Pregnant females were divided at random into three groups of 15 animals each and received Na-F at one of three different concentrations; 0 (control), 50 and 100 ppm on a mg/kg/day basis of 0, 5.15 and 10.77 Na-F, respectively). Sodium fluoride (Na-F, Sigma Chemical Company) was incorporated in drinking distilled water and administered to pregnant rats for a 44 days period (from day 8 of gestation till termination of lactation and weaning of pups at 30 days of age).

After weaning, all male pups were then collected and distributed into three groups of 20 animals each, divided on 2 replicates, each of 10, as following:

Group (1) control, n=20: weanling males were derived from control dams receiving no Na-F. These pups served as a control group.

Group (2) low-Na-F, n=20: weanling males were derived from dams receiving low dose of Na-F. Pups were then exposed to *ad libitum* supply of low dose of Na-F in drinking water, till completion of the study.

Group (3) high-Na-F, n=20: weanling males were derived from dams receiving high dose of Na-F. Males were then exposed to *ad libitum* supply of high dose of Na-F in drinking water, till completion of the study.

2.3. Behavioural assessment:

Male rats were exposed to different concentrations of Na-F (0, 50 or 100 ppm) during gestational, lactation and post-weaning stages of life until maturity. At 95 days of animals' age, adult male rats were then used for assessment of territorial aggression, sexual behaviour as well as fertility indices. All behavioural measurements were recorded by a single observer unfamiliar with the treated males.

2.3.1. Territorial aggressive behaviour testing:

A rectangular observation cage (45 x 27 x 40 cm: length x breadth x height) was used for testing rats' aggressive behaviour. A stud male rat was placed in the testing arena for 10 days. The tested male rat (control or Na-F-exposed) of no previous contact with the stud was then placed in the test arena, confronted with the stud male for 5-min test period. The following parameters were then recorded: lateralization by stud male (LSM), boxing bouts with stud male (BBSM), fights with stud male (FSM), ventral presenting posture (Supine posture) of the stud male (VP) (Bataineh et al., 1997, Bataineh et al., 1998; Khouri and El-Akawi, 2005). All testing was conducted between 09:00 and 12:00 h. All treatment groups were tested in a randomized order.

2.3.2. Sexual behaviour testing:

Sexual performance of each male rat per treatment groups was evaluated using a stimulus untreated female of the same strain. For induction of estrus in female rats, each female was subcutaneously injected with 5 mg estradiol benzoate and 0.5 mg progesterone (Misr Co. for Pharm. Ind., Cairo, Egypt), dissolved in 0.2 ml of sesame oil, at 54 and 6 h prior to test session, respectively. Male rat was kept alone in the mating cage (45 x 27 x 40 cm: length x breadth x height), 5 min before introducing the receptive female into the center of the arena. The sexual behaviour of the male was monitored during a 15-min

session and the following parameters were measured; mount latency (ML), intromission latency (IL), ejaculation latency (EjL), total mount frequency (TMF), total intromission frequency (TIF), ejaculation frequency (EjF) i.e. mating potential, post-ejaculatory interval (PEjI) i.e. latency period (Cagiano et al., 1998; Khouri and El-Akawi, 2005; Bataineh and Nusier, 2006). Intromissions were distinguished behaviorally from mounts by the presence of a rapid, springing dismount. Ejaculation patterns were characterized by longer, deeper thrusts, slow, relaxed dismounts and a prolonged period of rest (PEjI) following the ejaculation (Tsai et al., 2009). All testing was carried out between 09:00 and 15:00 h in a random order.

2.4. Fertility assessment:

To evaluate the fertility, each male was housed with two virgin untreated females of the same strain for ten days to ensure two successive estrus cycles (Amann, 1982). One week after removal of the males, all females were killed by cervical dislocation under light ether anesthesia. Numbers of pregnant females, implantation sites, viable fetuses as well as fetal resorptions were recorded after cesarean sections (Bataineh et al., 1998).

2.5. Relative weights of male reproductive organs:

Five males per treatment were sacrificed by cervical dislocation under light ether anesthesia. The reproductive tract was then dissected, trimmed free of fat and each organ was weighed separately on electronic balance in relation to body weight. The reproductive organs taken into account for study included testes, seminal vesicles and prostate gland.

2.6. Histopathological examination:

After completion of all assessments, tissue specimens from testes, seminal vesicles and prostate glands were collected and fixed in 10% neutral buffer formalin. The tissue specimens were processed by the convention method and stain with Hematoxylin and Eosin **(**Bancroft and Gamble, 2008**)**.

2.7. Statistical analysis:

In order to evaluate the influence of Na-F administration, data for all collected variables were analyzed by analyses of variance (AVOVA), using the general linear models procedure in SPSS® statistical software (SPSS, 2006). Comparisons between the groups after ANOVA were made using post hoc Tukey HSD test. A p value of <0.05 was required to consider the difference as significant. All data are expressed as mean ± SEM.

3. Results:

3.1. Territorial aggressive behaviour parameters:

Table 1 illustrates the influence of Na-F on the parameters of territorial aggression in adult male rats. There was a significant marked decline in lateralization, boxing bouts, fighting as well as number of ventral presenting postures ($p < 0.001$) in males treated with Na-F, at both dose levels, compared to their counterparts in the control group.

3.2. Sexual behaviour:

The results presented in Table 2 show the effect of Na-F on male rats' sexual behaviour. Na-F administered dose significantly affect latencies to first mount, intromission and ejaculation, where higher latencies ($p < 0.001$) were observed with high Na-F-treated rats compared to other groups. However, a significant reduction in frequencies of mounts, intromissions and ejaculations ($p < 0.001$) were recorded in Na-F-exposed males when compared with controls, regardless of the incorporated dose. Moreover, Na-F treatment significantly prolonged the post-ejaculatory intervals ($p<0.001$), where increased intervals were found in high Na-F group. The number of animals ejaculating was reduced in Na-F-treated groups, particularly at high level.

3.3. Male rats' fertility:

Results in Table 3 indicate that Na-F administration to male rats significantly diminished their fertility parameters. Na-F treatment at high dose caused a significant decrease in number of females impregnated by male treated rats ($p < 0.05$) compared to untreated one. A significant reduction in number of implantations as well as number of viable fetuses ($p < 0.01$) accompanied by a significant increase in total number of resorptions sites ($p < 0.05$) was noticed in females impregnated by high Na-F-exposed males when compared to controls. Fertility parameters measured in low Na-F-administered males were not statistically different from those of control group, except for number of viable fetuses, where a significant decrease was found evident in low Na-F treated rats when compared with control rats.

3.4. Reproductive organs weights:

The relative weights of testes, seminal vesicles and prostate gland are demonstrated in Table 4. Regardless of the incorporated level of Na-F, relative weights of all selected reproductive organs were significantly diminished ($p < 0.001$) when male rats were exposed to Na-F compared to their counterparts in control group.

3.5. Histopathological examination:

No pathological changes could be detected in the testes, seminal vesicle and prostate glands of rats in control group receiving no Na-F.

The histopathological examination of the testes of rats in high Na-F-treated group revealed severe pathological lesions represented by severe disorganization and denudation of germinal epithelial cells of most seminiferous tubules with absence of sperm in the lumina. Most of semineferous tubules appeared atrophied with complete absence of germinal epithelium and Sertoli cells (Fig. 1). Only the basement membranes were detected with multiple numbers of spermatid giant cells (Fig. 2).

Congestion of blood vessels in tunica albuginea and edematous fluid were detected in-between the interstitial tissues. Moreover, some tubules were completely destructed. The seminal vesicle showed hyperplasia of the epithelial lining with desquamated epithelial cells in the lumen mixed with its secretion (Fig. 3).

Edema in the lamina propria with congestion of submucosal blood vessels was also noticed. The prostate gland revealed edema in the interstitial tissues dispersed the glands. There was severe hyperplasia of epithelium lining as folds in the lumen (Fig. 4). Also, few numbers of inflammatory cells was detected in the interstitial tissues (Fig. 5).

Concerning low Na-F-exposed rats, the testes showed moderate pathological changes as indicated by necrosis in the layers of germinal epithelium of seminiferous tubules and decreased numbers or absence of mature sperms in the lumen (Fig 6). Few numbers of spermatid giant cells were also present in the lumen of some seminiferous tubules. The seminal vesicle appeared normal while the prostate displayed moderate hyperplasia in its epithelial lining (Fig. 7).

Table 1. Effect of perinatal Na-F exposure at different doses on territorial aggression in adult male rats during a 5 min session.

	Experimental Groups		
	(C) Group	(Low Na-F) Group	(High Na-F) Group
LSM	**5.2±0.73[a]**	**2.1±0.35[b]**	**0.9±0.28[b]**
BBSM	**4.7±0.73[a]**	**1.8±0.33[b]**	**0.7±0.22[b]**
FSM	**2.8±0.53[a]**	**1.1±0.28[b]**	**0.4±0.13[b]**
VP	**1.9±0.38[a]**	**0.6±0.22[b]**	**0.1±0.03[b]**

(C) Group: Animals received plain water without any treatment and served as a control.
(Low Na-F) Group: Animals received 50 ppm Na-F.
(High Na-F) Group: Animals received 100 ppm Na-F.
[a-c]Values within row with unlike superscripts differ significantly ($p<0.05$), according to ANOVA. Data are expressed as mean±SEM of 10 animals per treatment.
(LSM = lateralization by stud male, BBSM = boxing bouts with stud male, FSM = fights with stud male, VP = ventral presenting posture (supine posture) of the stud male.

Table 2. Effect of perinatal Na-F exposure at different doses on sexual behaviour in adult male rats during a 15 min session.

	Experimental Groups		
	(C) Group	(Low Na-F) Group	(High Na-F) Group
ML (s)	**102.7±18.64[a]**	**165.2±9.78[b]**	**231.5±12.58[c]**
IL (s)	**126±14.26[a]**	**187.4±10.17[b]**	**272.8±20.09[c]**
EjL (s)	**170.5±9.63[a]**	**240.8±10.85[b]**	**306.7±23.79[c]**
TMF	**13.7±0.76[a]**	**6.8±1.23[b]**	**3.6±0.92[b]**
TIF	**11.1±0.69[a]**	**5.1±1.07[b]**	**2.3±0.83[b]**
EjF	**5.8±0.76[a]**	**1.7±0.47[b]**	**0.6±0.27[b]**
PEjI	**73.2±5.31[a]**	**170.8±10.21[b]**	**274.4±14.84[c]**
PME	**90%**	**50%**	**40%**

(C) Group: Animals received plain water without any treatment and served as a control.
(Low Na-F) Group: Animals received 50 ppm Na-F.

(High Na-F) Group: Animals received 100 ppm Na-F.
[a-c]Values within row with unlike superscripts differ significantly ($p<0.05$), according to ANOVA. Data are expressed as mean±SEM of 10 animals per treatment.
(ML = mount latency, IL = intromission latency, EjL = ejaculation latency, TMF = total mount frequency, TIF = total intromission frequency, EjF = ejaculation frequency (mating potential), PEjI = post-ejaculatory interval (latency period), PME = % of males ejaculating).

Table 3. Effect of perinatal Na-F exposure at different doses on fertility in adult male rats.

	Experimental Groups		
	(C) Group	(Low Na-F) Group	(High Na-F) Group
No. of males	**10**	**10**	**10**
No. of females	**20**	**20**	**20**
No. of pregnant females	**16/20[a] (80%)**	**13/20[ab] (65%)**	**8/20[b] (40%)**
No. of implantation sites	**7.2±0.88[a]**	**4.95±0.77[ab]**	**3.4±0.97[b]**
No. of viable fetuses	**6.35±0.78[a]**	**3.85±0.62[b]**	**2.8±0.81[b]**
Rats with resorptions	**2/20 (10%)**	**5/20 (25%)**	**6/20 (30%)**
No. of resorption sites/total no. of implantation sites	**2/144[a] (1.39%)**	**6/99[ab] (6.06%)**	**17/68[b] (25%)**

(C) Group: Animals received plain water without any treatment and served as a control.
(Low Na-F) Group: Animals received 50 ppm Na-F.
(High Na-F) Group: Animals received 100 ppm Na-F.
[a-c]Values within row with unlike superscripts differ significantly ($p<0.05$), according to ANOVA. Data are expressed as mean±SEM.

Table 4. Effect of perinatal Na-F exposure at different doses on reproductive organs weights (g/100g b.wt) in adult male rats.

	Experimental Groups		
	(C) Group	(Low Na-F) Group	(High Na-F) Group
Testes	**1.32±0.06[a]**	**1.08±0.07[b]**	**0.87±0.05[b]**
Seminal vesicles	**0.59±0.05[a]**	**0.40±0.01[b]**	**0.32±0.03[b]**
Prostate gland	**0.31±0.02[a]**	**0.18±0.01[b]**	**0.14±0.01[b]**

(C) Group: Animals received plain water without any treatment and served as a control.
(Low Na-F) Group: Animals received 50 ppm Na-F.
(High Na-F) Group: Animals received 100 ppm Na-F.
[a-c]Values within row with unlike superscripts differ significantly ($p<0.05$), according to ANOVA. Data are expressed as mean±SEM of 5 animals per treatment.

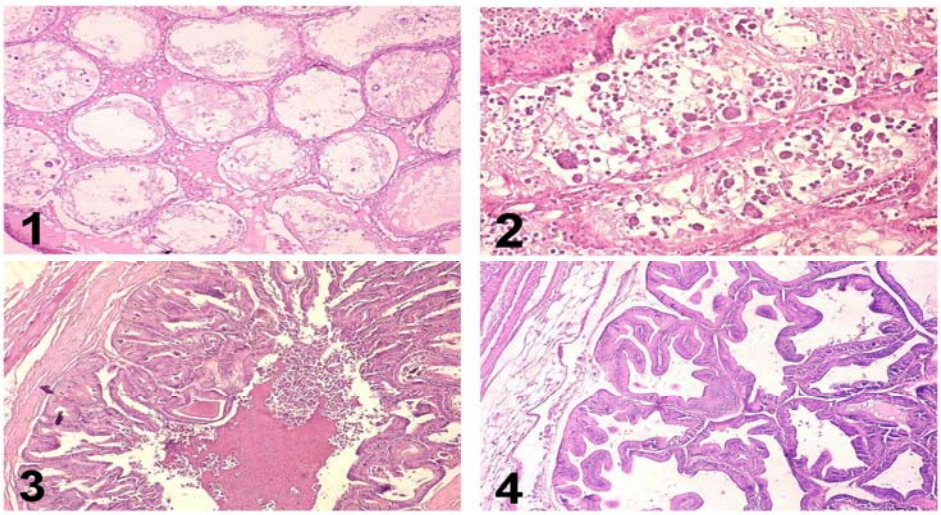

Figure 1: Testes of high Na-F-treated rats showing atrophy of semineferous tubules with complete absence of germinal epithelium and Sertoli cells. Notice the edema in-between the interstitial tissues. H&E X 200.
Figure 2: Testes of high Na-F-treated rats showing multiple numbers of spermatid giant cells. Notice the congestion of blood vessels in the interstitial tissues. H&E X 400.
Figure 3: Seminal vesicles of high Na-F-treated rats showing hyperplasia of the epithelial lining with desquamated epithelial cells in the lumen mixed with its secretion. H&E X 200.
Figure 4: Prostate gland of high Na-F-treated rats showing severe hyperplasia of epithelium lining forming finger like projection in the lumen. H&E X 200.

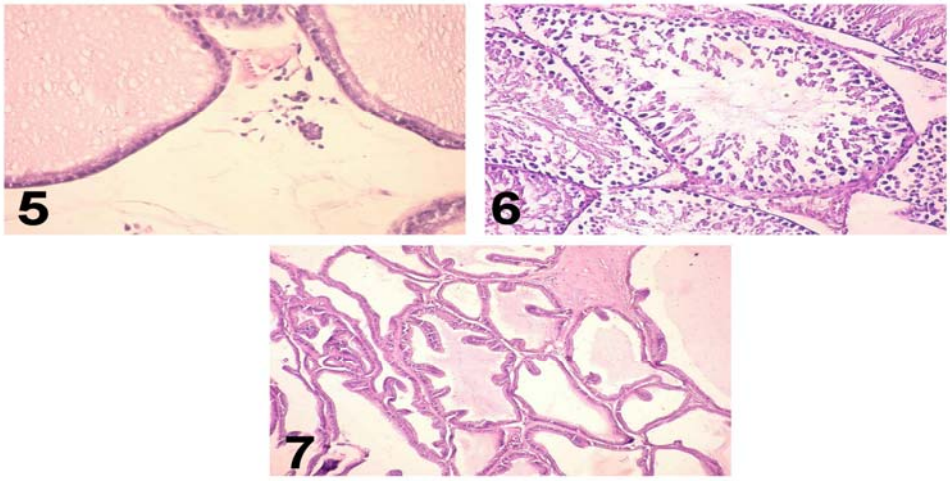

Figure 5: Prostate gland of high Na-F-treated rats showing edema in-between the glands with few numbers of inflammatory cells. H&E X 400.
Figure 6: Testes of low Na-F-treated rats showing necrosis in the layers of germinal epithelium of seminiferous tubules with absence of mature sperms in the lumen. H&E X 200.
Figure 7: Prostate gland of low Na-F-treated rats showing moderate hyperplasia of epithelium lining. Notice the edema in-between the glandular tissues. H&E X 200.

4. Discussion:

The animal model used in the present study has been previously employed in several investigations to evaluate the adverse effects of different compounds on reproductive function in male (Otoom et al., 2004; Bataineh and Nusier, 2006). Furthermore, the applied concentration of Na-F was selected carefully and according to our former studies with rats reporting no toxicity potentials of the chosen dose, with no side

effects as well (El-lethey et al., 2010, Kamel et al., 2010).

Marked decline in all parameters of territorial aggression in Na-F-treated males was revealed in the present study. This was reflected in reduced lateralization, boxing bouts and fights. Ventral presenting posture (supine posture) has been evidenced to announce for submission of the target during attack (Scott, 1970). Since behaviour modulating phermones are proved to control fighting and other behaviours, reduced aggression-stimulating phermones in Na-F-treated males are assumed to be responsible for altered incidence of supine posture displayed by the stud male (Tirindelli et al., 2009). These results are in accordance with previous research with rats, where ingestion of Na-F greatly abolished aggressive behaviour postures in males (Bataineh and Nusier, 2006).

The latencies to show the first mounts, first intromission, and the post-ejaculatory interval are commonly used for evaluating male's sexual motivation (Everitt, 1990). Negative impact of Na-F administration was shown in sexual behaviour displayed by adult male rats used in the current study. Marked suppression of sexual performance was evidenced by prolonged time to first mount, intromission and ejaculation, accompanied by reduction in total numbers of these parameters. More interestingly, significant increase in post-ejaculatory interval was also noticed in Na-F-exposed males. A significant impairment of sexual behaviour was reported in former study with male rats exposed to different levels of NaF (Bataineh and Nusier, 2006; Bera et al., 2007).

The current suppression of aggression and sexual behaviour might be explained on the basis of Na-F-induced adverse effect on androgen biosynthesis controlling both types of behaviours. Na-F was shown to directly affect the brain, hypothalamus or anterior pituitary gland, which in turn possibly affect sexual behaviour (Bataineh and Nusier, 2006). Males with fluorosis also showed a marked reduction in testosterone hormone which plays an important role in this regulation process (Narayana and Chinoy, 1994; Susheela and Jethanandani, 1996; Huang et al., 2007). Confirmatory results derived from other study for Reddy et al. (2007), where serum testosterone, follicle stimulating hormone and lutenizing hormone were significantly altered in rats after exposure to Na-F. In addition, testicular disorders have been reported to be associated with Na-F-induced oxidative stress in reproductive organs along with possible adverse effects of fluoride on pituitary testicular axis (Ghosh et al 2002, Wan et al., 2006). Antioxidant defenses were also reduced with occurrence of oxidative stress in rats and mice exposed to Na-F (Zhang et al., 2006; Hunag et al., 2007). Germ cells, in comparison to somatic cells, are more susceptible to oxidative stress, relying on two main reasons. Firstly, germ cells are intimately associated with the free radical-generating phagocytic Sertoli cells (Bauche et al., 1994). Secondly, germ cell plasma membrane contains a higher amount of polyunsaturated fatty acids that are vulnerable to oxidation by free radicals (Lenzi et al., 2000). Supporting evidence derived from our histopathological analysis of reproductive organs; testes, seminal vesicles and prostate gland in Na-F treated males, where severe necrotic degenerative changes in seminiferous epithelium of testicular tissues, deficiency of sperms in lumina, complete absence of Sertoli cells along with multiple numbers of spermatid giant cells were also detected. Our results are in agreement with earlier reports (Ge et al., 2006; Wan et al., 2006; Gupta et al., 2007; Tiwari and Pande, 2009). These findings together with previously mentioned observations go hand in hand with and further confirm the androgenic effect on male reproductive function.

The results reported in this paper also showed a profound negative effect of high concentration of Na-F on male rats' fertility in terms of reduced numbers of females impregnation, decreased numbers of implantation and viable fetuses along with high resorption incidences. Even more compelling were the findings of numbers of viable fetuses which are proved to be the more responsive parameter for Na-F administration, even at low dose. Theses findings are in contradiction of other previous scientific reports where mating, fertility and survival indices were not affected in Na-F-administered rats (Collins et al., 1995). However, our reported results are in accordance with earlier research with rats and mice (Elbetieha et al., 2000; Bataineh and Nusier, 2006). Again, our histopathological findings of disorganization, decreased numbers of germinal epithelium of semineferous tubule along with absence of mature sperms in testicles, especially in high Na-F-treated males, confirm diminished male fertility observed in the current study. This diminution in male fertility parameters could be a reflect and might be due to an impairment in spermatogenesis and steroidogenesis of NaF-treated male rats (Pushpalatha et al., 2005). It has been reported that Na-F-generated testicular oxidative stress resulted in damage of sperm cell membrane which might be accountable for inhibition of testicular spermatogenesis with reduced sperm activity (Zhang et al., 2006). Decreased sperm quality (sperm count, sperm motility, sperm viability and sperm function with increased sperm abnormalities) was also formerly observed in male rats and mice exposed to Na-F, which might explain

the reproductive dysfunction experienced here by male rats (Collins et al. 2001; Wan et al., 2006; Huang et al., 2007).

In agreement with Gupta et al. (2007), our findings showed a clear lessening effect of Na-F on relative weight of reproductive organs. In view of the fact that, any decrease in weight of reproductive organs is under hormonal control, this observed diminution further confirmed androgen hormone decline. The weight, size and secretory function of testes, seminal vesicles, ventral prostate are well known to be closely regulated by androgens hormones (Sriraman et al., 2004). So, Na-F treatment might act directly or indirectly on pituitary gland secretory function leading to a decrease in the main hormones controlling spermatogenesis process.

In conclusion, it is hoped that the findings included in this article might help further understand and appreciate the negative outcomes of pre- and post-natal exposure to Na-F on socio-sexual health and fertility potential, ultimately at adulthood in male individuals.

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