MITIGATION OF SODIUM FLUORIDE INDUCED TOXICITY IN MICE BRAIN BY BLACK TEA INFUSION

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SUMMARY: In an extension of previous work on fluoride (F) toxicity in a group of 80 Swiss albino mice, the mitigating effects of polyphenols in black tea on the F-induced increase in glycogen, cholesterol, and total lipids in the cerebral hemisphere (CH), cerebellum (CB), and medulla oblongata (MO) regions of the brain were studied. Oral administration of sodium fluoride (6 and 12 mg NaF/kg bw/day) to the mice for 30 days resulted in a significant dose-dependent increase in the parameters studied. Withdrawal of treatment for 30 days caused significant but only partial recovery. Administration of a 2% black tea infusion alone for 30 days did not cause any significant alteration. However, concurrent administration of NaF and black tea infusion for 30 days produced significant mitigation in all the parameters.

Keywords: Black tea infusion; Cerebellum; Cerebral hemisphere; Fluoride and Mice brain; Medulla oblongata; Mitigation of fluoride toxicity.

INTRODUCTION

Fluoride (F) is a potent toxicant, which, when ingested through drinking water and food, often results in adverse health effects. F-induced glycogen accumulation has been observed in fishes[1] and in liver, muscle, vas deferens, and uterus in rats and mice.[2,3] F-treated rats exhibit a decreased capacity to synthesize glucose from glutamate, succinate, pyruvate, and glycerol.[4] Interaction of F and lipid metabolism assumes considerable significance since fluoride is involved in atherosclerosis.[5] Guan et al.[6] found that membrane lipids in brain, kidney, and liver could be affected in animals with chronic fluorosis. However, data revealing the effects of NaF on glycogen, cholesterol, and total lipids in different parts of the brain are limited and need further study.

After water, tea is one of the most common beverages consumed worldwide. The favorable properties ascribed to tea consumption are believed to relate to its bioactive components: catechins, and their derivatives, which have been shown to act directly as free radical scavengers and exert indirect antioxidant effects through activation of transcription factors and antioxidant enzymes.[7] In line with this evidence, particular attention has been placed on studying the neuroprotective action of antioxidants, tea polyphenols, and catechin.[8]

The aim of the present study was to evaluate the mitigating effect on the toxicity of NaF in mice by black tea infusion on glycogen, cholesterol, and total lipids in the cerebrum hemisphere (CH), cerebellum (CB), and medulla oblongata (MO) regions of the brain.

MATERIALS AND METHODS

The same eighty young adult inbred Swiss strain male albino mice (*Mus musculus*) employed in our earlier work[9] were used here. Twenty grams of black

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tea solids (Lipton Yellow Label from Hindustan Lever Limited, Mumbai, India) and 1000 mL deionized water were used to produce 2% tea infusion.[10]

On completion of the 30-days treatment period,[9] the animals were sacrificed by cervical dislocation. The brains were dissected carefully, blotted free of blood, and weighed to the nearest mg; different regions of the brains were separated carefully and utilized for study. The glycogen, cholesterol, and total lipid contents were estimated by colorimetric method of Seifter et al.,[11] Zlatkis et al.,[12] and Zollner and Kirsch,[13] respectively.

Statistical analysis: Results are expressed as standard error of the mean (± SEM). Data were analyzed statistically as in our previous investigation.[9]

RESULTS

As seen in Tables 1, 2, and 3, no significant differences in glycogen, cholesterol, and total lipid contents were observed among the different control groups in any region of the mice brain.

Table 1. Effect of black tea infusion on sodium fluoride-induced biochemical changes in the cerebral hemisphere in mice. Values are mean ± SEM (n=10 per group) (Values in parenthesis are % changes, as compared to control)

Parameters	Control		Treated	
	Group I	Group II	Group III	Group IV
	Control	Black tea infusion	Low dose NaF	High dose NaF
Glycogen (µg/100mg tissue weight)	1835.52 ± 33.16	1834.38 ± 17.04 (-0.06)	2005.91 ± 32.87^{abdfgh} (9.28)	2287.25 ± 35.80^{abcegh} (24.61)
Cholesterol (mg/100mg tissue weight)	2.70 ± 0.02	2.65 ± 0.10 (-1.71)	3.05 ± 0.12^{abdfg} (12.94)	3.63 ± 0.11^{abcegh} (34.59)
Total lipid (mg/100mg tissue weight)	13.01 ± 0.27	13.06 ± 0.32 (0.37)	15.23 ± 0.24^{abdgh} (17.04)	17.57 ± 0.26^{abcegh} (37.29)

	Treated + Withdrawal		Treated + Antidote	
	Group V	Group VI	Group VII	Group VIII
	Low dose NaF + Withdrawal	High dose NaF + Withdrawal	Low dose NaF + Antidote	High dose NaF + Antidote
Glycogen (µg/100mg tissue weight)	1991.44 ± 56.52^{abdfgh} (8.49)	2256.20 ± 37.93^{abcegh} (22.92)	1849.22 ± 27.67^{cdef} (0.75)	1884.92 ± 28.55^{cdef} (2.69)
Cholesterol (mg/100mg tissue weight)	2.95 ± 0.09^{abdfg} (9.45)	3.50 ± 0.11^{abcegh} (29.81)	2.70 ± 0.09^{cdef} (0.15)	2.93 ± 0.04^{df} (8.60)
Total lipid (mg/100mg tissue weight)	14.58 ± 0.21^{abdg} (12.05)	16.98 ± 0.22^{abgh} (30.49)	13.08 ± 0.27^{cdefh} (0.49)	14.02 ± 0.18^{abcdefg} (7.75)

[a] As compared to group I: p<0.05; [b] As compared to group II: p<0.05; [c] As compared to group III: p<0.05.
[d] As compared to group IV: p<0.05; [e] As compared to group V: p<0.05; [f] As compared to group VI: p<0.05;
[g] As compared to group VII: p<0.05; [h] As compared to group VIII: p<0.05.

Table 2. Effect of black tea infusion on sodium fluoride-induced biochemical changes in the cerebellum in mice. Values are mean ± SEM (n=10 per group) (Values in parenthesis are % changes, as compared to control)

Parameters	Control		Treated	
	Group I	Group II	Group III	Group IV
	Control	Black tea infusion	Low dose NaF	High dose NaF
Glycogen (µg/100mg tissue weight)	1767.44 ± 30.10	1753.97 ± 28.06 (-0.76)	1880.97 ± 34.26^{abdfg} (6.42)	2102.73 ± 25.74^{abcegh} (18.97)
Cholesterol (mg/100mg tissue weight)	2.61 ± 0.05	2.63 ± 0.02 (0.61)	3.04 ± 0.04^{abefgh} (16.32)	3.41 ± 0.029^{abcegh} (30.75)
Total lipid (mg/100mg tissue weight)	12.50 ± 0.16	12.40 ± 0.06 (0.83)	14.84 ± 0.20^{abdefgh} (18.68)	17.30 ± 0.26^{abcefgh} (38.39)

	Treated + Withdrawal		Treated + Antidote	
	Group V	Group VI	Group VII	Group VIII
	Low dose NaF + Withdrawal	High dose NaF + Withdrawal	Low dose NaF + Antidote	High dose NaF + Antidote
Glycogen (µg/100mg tissue weight)	1864.41 ± 20.29^{abdfg} (5.49)	2079.19 ± 37.55^{abcegh} (17.64)	1781.89 ± 35.03^{cdef} (0.82)	1815.29 ± 36.75^{df} (2.71)
Cholesterol (mg/100mg tissue weight)	2.95 ± 0.08^{abdf} (12.98)	3.34 ± 0.07^{abcegh} (27.96)	2.70 ± 0.07^{cdf} (3.33)	2.83 ± 0.05^{abcdf} (8.50)
Total lipid (mg/100mg tissue weight)	13.05 ± 0.31^{bcdf} (4.37)	16.40 ± 0.24^{abcdegh} (31.16)	12.55 ± 0.27^{cdfh} (0.37)	13.16 ± 0.22^{abcdfg} (5.25)

[a] As compared to group I: p<0.05; [b] As compared to group II: p<0.05; [c] As compared to group III: p<0.05. [d] As compared to group IV: p<0.05; [e] As compared to group V: p<0.05; [f] As compared to group VI: p<0.05; [g] As compared to group VII: p<0.05; [h] As compared to group VIII: p<0.05.

On the other hand, oral administration of low dosage (LD) and high dosage (HD) NaF (6 and 12 mg/kg-bw/day) for 30 days caused significant dose-dependent increases in the content of glycogen, cholesterol, and total lipid in the CH, CB, and MO regions of the mice brain. Withdrawal of the treatment for 30 days did not produce significant recovery except in the total lipid content of the CB and MO regions. However, treatment with black tea infusion along with NaF caused significant mitigation as compared to the respective NaF treatment alone and with NaF treatment plus withdrawal groups in all the three regions of mice brain.

DISCUSSION

The NaF-induced accumulation of glycogen content in CH, CB, and MO regions of the brain might be due to inhibition of glycolysis[14] caused by reduction of the activity of isocitrate dehydrogenase enzyme.[15] Accumulation of glycogen in brain from F exposure has also been reported by Chinoy et al.[16] Accumulation of cholesterol and total lipids was also reported previously in guinea pigs, fish, rats, and mice.[17,18] This effect might be due to inhibition of lipase by F, which reduces

the release of free fatty acids and glycerol as well as enhancing lipogenesis.[19] Hypercholesterolemic, hyperlipidemia, hyperphospholipidemia, and hypertriglyceridemia have been reported in previous studies, indicating excessive immobilization of fat.[20,21] The alteration in lipid and carbohydrate metabolism in the present study might also be due to increase in lipid peroxidation activity.[22]

Table 3. Effect of black tea infusion on sodium fluoride-induced biochemical changes in the medulla oblongata in mice. Values are mean ± SEM (n=10 per group) (Values in parenthesis are % changes, as compared to control)

Parameters	Control		Treated	
	Group I Control	Group II Black tea infusion	Group III Low dose NaF	Group IV High dose NaF
Glycogen (µg/100mg tissue weight)	1686.90 ± 29.57	1658.50 ± 15.92 (-1.68)	1830.50 ± 24.77 ^{abdfgh} (8.51)	2022.19 ± 25.95 ^{abcegh} (19.88)
Cholesterol (mg/100mg tissue weight)	2.19 ± 0.05	2.21 ± 0.07 (0.73)	2.52 ± 0.93 ^{abdfg} (14.91)	2.92 ± 0.04 ^{abcegh} (32.97)
Total lipid (mg/100mg tissue weight)	11.21± 0.14	11.21 ± 0.11 (-0.01)	13.85 ± 0.16 ^{abdfgh} (23.54)	15.86 ± 0.14 ^{abcefgh} (41.47)
	Treated + Withdrawal		Treated + Antidote	
	Group V Low dose NaF + Withdrawal	Group VI High dose NaF + Withdrawal	Group VII Low dose NaF + Antidote	Group VIII High dose NaF + Antidote
Glycogen (µg/100mg tissue weight)	1822.44 ± 18.42 ^{abdfgh} (8.03)	2007.66 ± 26.10 ^{abcegh} (19.02)	1697.65 ± 20.03 ^{cdefh} (0.64)	1759.85 ± 23.79 ^{abcdefg} (4.32)
Cholesterol (mg/100mg tissue weight)	2.43 ± 0.06 ^{abdf} (10.72)	2.84 ± 0.10 ^{abcegh} (29.27)	2.24 ± 0.10 ^{cdf} (2.01)	2.39 ± 0.03 ^{adf} (9.03)
Total lipid (mg/100mg tissue weight)	12.34 ± 0.08 ^{abcdfg} (10.07)	13.69 ± 0.08 ^{abdegh} (22.11)	11.26 ± 0.14 ^{cdefh} (0.44)	12.70 ± 0.20 ^{abcdfg} (13.28)

[a] As compared to group I: p<0.05; [b] As compared to group II: p<0.05; [c] As compared to group III: p<0.05.
[d] As compared to group IV: p<0.05; [e] As compared to group V: p<0.05; [f] As compared to group VI: p<0.05;
[g] As compared to group VII: p<0.05; [h] As compared to group VIII: p<0.05.

Mitigation of glycogen accumulation by administration of black tea infusion can be viewed as due to an increase in the utilization of glycogen by its conversion into glucose. Han[23] has suggested that epigallocatechin gallate (EGCG), an active compound of tea, can be used for the treatment of diabetes mellitus. Maron et al.[24] found that administration of black tea inhibited the synthesis of cholesterol and decreased its concentration in brain. Since the antilipogenic effect of black tea might be due to its radical scavenging activity,[25] the mitigation of F-induced alteration in brain by black tea infusion might be due to its potent antioxidative properties.[26]

In conclusion, the present investigation has shown that black tea infusion mitigates the F-induced accumulation in glycogen, cholesterol, and total lipids in the CH, CB, and MO regions of mice brain.

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