stressors such as 2-deoxy-D-glucose is accompanied by an increase in DA turnover[21,22] while the normal behavioral response to such challenges is blocked by DA receptor antagonists[23,24]. Perhaps the persistent behavioral deficits seen in lesioned rats result because of an inability to provide sufficient DA in response to increased need.

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Effect of fluoride administration on renal glucose-6-phosphatase activity in rats[1]

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Summary. Renal glucose-6-phosphatase activity was found to be significantly elevated by fluoride administration (NaF 35 mg/kg, i.p.). The elevation of the enzyme activity was markedly suppressed by adrenalectomy.

Taylor et al[2]. reported an increase in urinary excretion of glucose after a dose of fluoride (NaF 20-30 mg/kg, i.v.). Shearer[3] found increases in kidney glucose in rats receiving 25 mg/kg NaF i.p. Net glucose liberation from gluconeogenic tissues of the liver and kidney was believed to be controlled through glucose-6-phosphatase[4]. The present study was designed to examine the effect of fluoride on the renal glucose-6-phosphatase activity in rats given a single dose of NaF (i.p.).

Materials and methods. Male Wistar albino rats weighing about 100 g were maintained on the MF basal diet (purchased from Oriental Yeast Ind., Japan) and water ad libitum. The animals were maintained at a temperature of 22 °C for a minimum of a week. All animals were fasted for 24 h before the experiments in order to minimize the effects of glucose absorption from the bowels and to stabilize the urinary excretion of glucose. The rats were sacrificed at various intervals after a single i.p. administration of NaF (0, 10, 20 or 35 mg/kg). NaF (35 mg/kg, i.p.) was injected into rats 2 days after adrenalectomy or parathyroidectomy. Microsomes were prepared according to the method of Jørgensen[5]. At the time of sacrifice, the rats were anesthetized with ether and killed by cardiac puncture. The kidneys were removed and the tissues (1 g) were immediately homogenized in a Potter-Elvehjem teflon-glass homogenizer with 5 ml of ice-cold 0.25 M sucrose-0.03 M histidine buffer (pH 7.2). Reproducible preparations of the heavy microsomal fraction were obtained by centrifugation (25,300 × g, 30 min) of supernatant after sedimentation of the mitochondria at 10,800 × g for 30 min. The preparations of the heavy microsomal fraction (1 mg of protein/ml of 0.25 M sucrose-0.03 M histidine buffer, pH 7.2) were stored in a refrigerator (−20 °C). Glucose-6-phosphatase activity was determined according to the method of Swanson[6]. Protein was determined by the method of Lowry et al.[7]. Glucose-6-phosphate (disodium salt) was obtained from the Sigma Chemical Co. (St. Louis, USA).

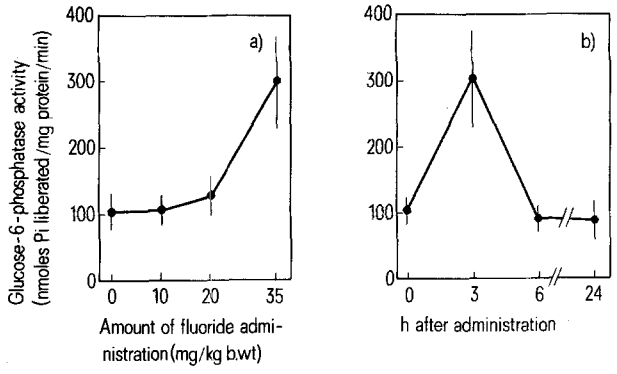
Results and discussion. The responses of renal glucose-6-phosphatase activity to different doses of fluoride were examined as shown in the figure, a). Increasing doses of fluoride caused a more pronounced increase in renal glucose-6-phosphatase activity. The changes in renal glucose-

Effect of fluoride administration on renal glucose-6-phosphatase activity in intact, adrenalectomized and parathyroidectomized rats

Treatment		Glucose-6-phosphatase activity (moles/mg protein/min)	T/N
Intact	None (normal)	102.1± 20.2	1
	Fluoride	300.3± 131.5	2.94*
PTX	None	36.4± 9.4	0.36* (1)
	Fluoride	105.7± 25.7	1.04 (2.90)
AX	None	60.7± 6.7	0.59* (1)
	Fluoride	46.0± 1.2	0.45* (0.76)

The animals were killed 3 h after the fluoride dose (35 mg/kg, i.p.). Values are averages obtained from 4-6 rats ± SE. T/N: ratio of treatment of fluoride or - ectomy against normal rats, *P < 0.01. Numbers in parentheses are relative values of respective controls. PTX: parathyroidectomized rats, AX: adrenalectomized rats.

6-phosphatase activity with time after the injection of a single dose of fluoride were examined (figure, b). The enzyme activity reached a maximum 3 h after the administration of fluoride. On the other hand, parathyroid hormone (PTH) is known to stimulate the production of the renal glucose-6-phosphatase[8]. Plasma PTH levels are significantly elevated in classical endemic fluoresis[9] and endemic fluorosis with Genu Valgum[10]. Therefore, the elevation of the renal enzyme activity induced by a fluoride dose was examined with adrenalectomized or parathyroidectomized rats in this study. The enzyme activities were suppressed to 0.36- and 0.59-times those in intact rats by parathyroidectomy and adrenalectomy, respectively. Adrenalectomy almost completely suppressed the elevation of the enzyme activity induced by fluoride, but parathyroidectomy partially suppressed it. The ratio of elevation of the enzyme activity induced by fluoride was not altered by parathyroidectomy (table). In this experiment, it was postulated that the elevation of the renal glucose-6-phosphatase activity in fluoride-intoxicated rats is probably due to stimulation of the adrenal function rather than to stimulation of the parathyroid function by fluoride dosage.



a) Effect of fluoride on glucose-6-phosphatase activities in rat kidney. The rats were killed 3 h after a single i.p. administration of NaF.
b) The changes in glucose-6-phosphatase activities in kidney after a single i.p. administration of fluoride. Dosage of NaF was 35 mg/kg b.wt. Each value represents the mean of 6 rats. SE indicated by vertical lines.

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Effects of lipid soluble antioxidants on cytotoxicity induced by photochemical products of cholesterol[1]

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Summary. Lipid soluble antioxidants, butylated hydroxytoluene and vitamin E, were shown to suppress cytotoxicity induced by cholesterol-derived photoproducts in Chinese hamster embryo cells. These cholesterol-derived photoproducts were rather toxic.

Photochemical conversion of cholesterol to certain carcinogenic substances was suggested as a possible mechanism for the tumorigenic effect of UV light on skin[3]. Exposure of human skin to UV light resulted in the formation of myriads of polar cholesterol photoproducts[4]. A mixture of water soluble and lipid soluble dietary antioxidants have been shown to suppress the formation of UV light-induced squamous cell carcinomas in hairless mice[5]. This same mixture of antioxidants was also effective in inhibiting the production of premalignant lesions and the development of tumors from pre-malignant lesions induced by 3-methylcholanthrene in the skin of hairless mice[6]. Hairless mice maintained on such antioxidant supplemented diet showed a rapid increase of liver weight, however, only small differences in body weight occurred and no distinct histological changes were observed in skin or liver under a light microscope[7].

In Chinese hamster embryo cells, antioxidants such as ascorbic acid, DL-α-tocopherol, butylated hydroxytoluene and reduced glutathione were shown to reverse UV light-induced cytotoxicity[8]. Recently, the toxicity of some cholesterol derived photoproducts on Chinese hamster embryo cells has been studied. It was demonstrated that the toxicity of cholestan-3β,5α,6β-triol and cholesterol derived polar photoproduct was greater than that of dimethylbenz-(α)anthracene - a known chemical carcinogen[9]. It was the purpose of the present study to determine whether lipid soluble antioxidants alone could be effective in reducing the detrimental effect of cholesterol derived lipid soluble toxic compounds on Chinese hamster embryo cells.

Materials and methods. Chinese hamster embryo cells were used in this study. The maintenance of cell culture has been described before[8]. Cells between the 4th and 7th passages were used. Falcon 60 mm plastic dishes were seeded with 1×10^3 cells in 2 ml of conditioned medium (1:1, centrifuged used medium/fresh medium). 2 h after plating, butylated hydroxytoluene (BHT) and DL-α-tocopherol (vitamin E) were added, so that each Petri dish contained 0.02 µM/ml BHT and 0.002 µM/ml vitamin E. 24 h after plating the cells, groups of 8 Petri dishes were treated with the respective sterol compounds which were dissolved in dimethylsulfoxide (DMSO) such that the final concentration of DMSO in the culture medium was less than 0.5%. At this concentration, DMSO has no influence on the plating efficiency of Chinese hamster embryo cells. 8 days after plating, all dishes were fixed with glacial acetic acid:metha-