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Ethanol and age enhances fluoride toxicity through oxidative stress and mitochondrial dysfunctions in rat intestine

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Abstract Fluoride toxicity and alcohol abuse are the two serious public health problems in many parts of the world. The current study was an attempt to investigate the effect of alcohol administration and age on fluoride toxicity in rat intestine. Six and 18 months old female Sprague Dawley rats were exposed to sodium fluoride (NaF, 25 mg/kg), 30 % ethanol (EtOH, 1 ml/kg), and NaF+EtOH (25 mg/kg+1 ml/kg) for a period of 20, 40, and 90 days. The levels of lipid peroxidation were increased, while the content of reduced glutathione, total, and protein thiol was decreased with NaF treatment. Under these conditions, animals showed an age-related decline in the activities of superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione-*S*-transferase which were further aggravated upon NaF or/and EtOH treatment. Mitochondrial respiration rate and the activities of complexes I, II, and IV enzymes of electron transport chain were decreased, while the levels of nitric oxide and citrulline were increased with age and NaF or/and EtOH treatment. Histological examination revealed large reactive lymphoid follicles, excess of lymphocytes in lamina propria of villi, villous edema, focal ileitis, necrosis of villi, and ulceration in NaF- or/and EtOH-treated animals in both the age groups. These findings suggest that fluoride mediate its toxic effects on intestine through oxidative stress and mitochondrial dysfunctions which are further augmented with alcohol consumption and advancing age.

Keywords Ethanol · Fluoride · Oxidative stress · Mitochondrial functions

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Introduction

Humans are exposed to fluoride inevitably because it is a ubiquitous contaminant of the environment. Among various sources, drinking water is the highest contributor of fluoride to humans [1]. The toxic effects of fluoride are not restricted to bone and teeth, but it also targets soft tissues, including gastrointestinal tract [2]. The mammalian small intestine is exposed to fluoride concentrations several times higher than those attained in other tissues. In addition, concurrent exposures to fluoride and other xenobiotics may further influence their toxic effects on intestine by undergoing some antagonistic or synergistic interactions. Alcohol consumption is common among human population across the globe, but little attention has been paid to evaluate toxic effects of fluoride together with ethanol ingestion. Interactions between fluoride and ethanol are an important problem in modern toxicology since both pose a risk to human and animal health. Co-exposures to fluoride and ethanol are common among alcoholics residing in high fluoride endemic areas.

A growing body of evidences suggests that exposure to fluoride or ethanol cause toxic effects by generating reactive oxygen species [3–5]. Free radical generation, lipid peroxidation, and changes in the antioxidants have been reported in the intestine of animals treated with fluoride [6] or ethanol [7]. Inkielewicz et al. [8] showed that fluoride-induced lipid peroxidation in liver, kidney, brain, and serum of male rats is