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Determination of Toxicity and Hazard Levels of Fluorides in Laboratory Animals

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Abstract: This scientific article presents the determination of toxicity and hazard levels resulting from the chronic exposure of white mice to sodium fluoride solutions of varying concentrations over a period of three months. Based on the analysis of experimental data, it was established that sodium fluoride exhibits a high level of toxicity in the organism of white mice.

Keywords: Sodium Fluoride, White Mice, Intoxication, Pathoanatomical Changes, Parenchymatous, Mg/L, Gram

Introduction

In recent decades, the rapid expansion of industrialization, urbanization, and agricultural intensification has significantly increased the level of environmental pollution worldwide. Among the numerous contaminants released into ecosystems, particular attention has been given to toxic chemical compounds such as heavy metal salts (mercury, lead, cadmium, arsenic), industrial by-products, pesticides, pharmaceuticals, and various inorganic elements. One of the most widely and environmentally persistent elements among them is fluorine, which predominantly occurs in nature in the form of fluoride compounds [1].

Fluorides are naturally present in soil, water, air, and biological systems. However, anthropogenic activities—such as aluminum production, phosphate fertilizer manufacturing, coal combustion, and chemical industries—have considerably increased fluoride concentrations in the environment. As a result, fluoride contamination has become a global ecological and public health concern. In many regions, elevated fluoride levels in drinking water have been associated with adverse biological effects in both humans and animals [2].

Although fluoride is recognized as an essential trace element at low concentrations, playing a role in the mineralization of bones and teeth, excessive intake leads to toxic effects known as fluorosis. Chronic exposure to high levels of fluoride can result in dental fluorosis, skeletal deformities, metabolic disturbances, and dysfunction of vital organs such as the liver, kidneys, and endocrine glands. In addition, fluoride toxicity has been linked to enzymatic inhibition, oxidative stress, and disruption of cellular metabolism [3]. Laboratory animals, particularly white mice, are widely used as experimental models in toxicological research due to their physiological and genetic similarities to higher mammals, short life cycles, and sensitivity to environmental toxins. Studies on white mice provide valuable insights into the mechanisms of toxicity, dose-response relationships, and pathological changes associated with chemical exposure. Such

experimental models are crucial for evaluating the safety and hazard levels of chemical compounds before their broader environmental and biological impact is assessed. Despite extensive research on fluoride toxicity, there remain gaps in understanding the long-term effects of chronic exposure to varying concentrations of sodium fluoride, especially under controlled laboratory conditions. Determining threshold levels between safe, toxic, and lethal doses is essential for establishing regulatory standards and preventing adverse health outcomes [4].

Therefore, the present study is aimed at investigating the toxicity and hazard levels of sodium fluoride through chronic exposure experiments in white mice. By administering different concentrations of sodium fluoride over an extended period and evaluating clinical, physiological, and pathomorphological changes, this research seeks to provide a comprehensive assessment of fluoride-induced toxicity. The findings of this study contribute to a better understanding of the biological effects of fluoride compounds and may serve as a scientific basis for environmental monitoring, veterinary toxicology, and public health risk assessment [5].

Materials and Methods

In this context, we conducted experimental studies to determine the toxicity and hazard levels of sodium fluoride, a fluorine-containing compound, by administering aqueous solutions of different concentrations to white mice under chronic exposure conditions.

The laboratory studies on toxicity assessment of sodium fluoride solutions of varying doses were carried out in accordance with the guidelines: “Instructions for the Toxicological Evaluation of Chemical Substances and Pharmacological Preparations Used in Veterinary Medicine” [6]

Pathoanatomical changes in mice that died from sodium fluoride intoxication were examined using the evisceration method, followed by microscopic analysis.

For the purpose of this study, 35 white mice were selected and divided into experimental and control groups, with 5 animals in each group. The average body weight of the mice was 48.5 grams. All animals were active and demonstrated good feed intake.

Under laboratory conditions, aqueous solutions of sodium fluoride at different concentrations were prepared and administered orally to the experimental animals daily over a period of three months. Both control and experimental groups were monitored daily. The daily intake of sodium fluoride solution, the general physiological condition of the organism based on clinical examinations, as well as changes observed in the gastrointestinal and central nervous systems were systematically monitored. The body weight of the white mice was measured at both the beginning and the end of the experiment [7]. At the conclusion of the study, white mice that had received different doses of sodium fluoride solution were subjected to pathological and anatomical examinations.

In order to determine the toxicity and hazard level of sodium fluoride in white mice, the experimental design included several groups. The control group received drinking water containing 0.02 mg/L of sodium fluoride. The first experimental group received 1.5 mg/L, the second group 15 mg/L, the third group 50 mg/L, the fourth group 150 mg/L, the fifth group 300 mg/L, and the sixth experimental group received 450 mg/L of sodium fluoride in their drinking water. The experiment was conducted over a period of three months [8].

Results and discussion

The analysis of the obtained results revealed that, over the three-month period, white mice in the experimental groups that consumed sodium fluoride solutions at varying doses exhibited notable changes in internal organs as well as in dental structures. It was observed that increasing doses of sodium fluoride had a progressively negative impact on the viability and survival of the animals [9].

Clinical observations of the control group did not reveal any significant adverse changes. The fur of the mice remained soft and glossy, food intake was normal, and no pathological alterations were detected in the gastrointestinal or central nervous systems [10].

Experimental Study on the Toxic Effects of Sodium Fluoride in White Mice (n = 35)

Group	Dose and Administration Method	Number of White Mice (Beginning of Experiment)	Number of White Mice (End of Experiment)
Control (Group 1)	0.02 mg/L	5	5
Experimental Group 1	1.5 mg/L	5	5

Experimental Group 2	15 mg/L	5	5
Experimental Group 3	50 mg/L	5	4
Experimental Group 4	150 mg/L	5	2
Experimental Group 5	300 mg/L	5	1
Experimental Group 6	450 mg/L	5	0

Results and Pathomorphological Findings

In the first experimental group, which received 1.5 mg/L of sodium fluoride, linear streaks were observed in the enamel layer of the teeth, along with a high accumulation of fluoride in tissues. In the second experimental group (15 mg/L), pathological and histological changes were observed in the thyroid gland, kidneys, and bones in approximately half of the animals [11].

Furthermore, when the fluoride concentration in drinking water reached 50 mg/L and 150 mg/L, in addition to dental alterations, significant pathohistological changes were detected in internal organs and bones. These changes were accompanied by decreased enzymatic activity and deterioration of the general condition of the animals. Mortality due to intoxication was recorded in one mouse at 50 mg/L, while in the 150 mg/L group, three mice died as a result of intoxication associated with cachexia [12].

At a concentration of 300 mg/L of fluoride in drinking water, acute intoxication symptoms were clearly manifested, resulting in four deaths among the experimental mice. In the sixth experimental group (450 mg/L), all mice died within a few days due to acute toxicity [13].

Analysis of Pathoanatomical Examination

External Examination of the Body

The examined white mouse had a body weight of 55 g and appeared emaciated. The dorsal fur was smooth, while the fur on the abdomen and chest appeared matted. The mucous membranes of the nasal and oral cavities were yellowish-reddish in color, and the teeth were discolored (yellowish). The body was not rigid, and no nasal discharge was observed. The eyes were open, with reddish mucous membranes; no discharge was detected from the ears. Blood vessels were engorged, and pinpoint hemorrhages were observed on the inner surfaces of the ears. The perianal region was dry.

Internal Examination

The thoracic and abdominal cavities were opened, and internal organs were extracted for examination. The size, shape, color, consistency, and cut surfaces of parenchymal organs were carefully evaluated. The thoracic and abdominal cavities were dry, and the anatomical positioning of internal organs was within normal limits. However, small pinpoint hemorrhages were observed beneath the thoracic cage. The blood was dark red and non-coagulated, and subcutaneous muscles showed signs of atrophy [14].

The lungs appeared bright red, with areas of hemorrhage and hyperemia. The heart exhibited vascular hyperemia in the epicardium. The liver was enlarged, with a nutmeg appearance, and hemorrhhages were present in the hepatic capsule; blood was visible on the cut surface. The spleen was moderately enlarged. The kidneys showed small pinpoint hemorrhages in the cortex, with a soft consistency and non-coagulated blood visible on the cut surface. Signs of inflammation were observed in the thyroid gland.

Gastrointestinal Findings

The stomach cavity contained foamy, whitish-gray contents. The mucous membrane was hyperemic, with dilated blood vessels and areas of hemorrhage [15]. The small intestine was filled with yellowish contents, and the mucosa appeared pale pink. The large intestine contained partial fecal masses, with pale reddish mucosa. The cecum was filled with dark reddish contents, and its mucous membrane appeared pale reddish with vascular hyperemia.

Conclusion

The administration of sodium fluoride solutions at various concentrations in drinking water to laboratory animals demonstrated significant adverse effects on their organism. The acute toxic dose for white mice was determined to be 50 mg/L, while the lethal dose reached 450 mg/L.

The main pathological changes observed in fluoride intoxication included pinpoint hemorrhages and hyperemia in the thoracic cavity and lungs, enlargement of the liver, spleen, and kidneys, as well as vascular hyperemia in the heart. Additionally, hyperemia and hemorrhages were detected in the gastric mucosa. Dental examination revealed yellowish-brown spotted lesions in the enamel layer, while skeletal changes were characterized by increased bone fragility.

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