The sources, hazards, and reduction of Fluoride- An Overview

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Abstract: Due to fluoride's (F) adverse impacts, Fluorosis on creatures of all kinds is now anticipated to become an enormous global concern. Geological natural resources combined with growing industrialization have made a significant contribution to the rising prevalence of fluoride-related health problems in both humans and animals. It mostly has detrimental impacts on humans and animals via weakening antioxidant defense systems and enzymatic cofactor chelation. It then results in metabolic problems, by influencing some biological functions, including metabolism, cell cycle, gene expression, oxidative stress, endocytosis, apoptosis, necrosis, ion transport, and hormone release.

Bone loss, dental mottling, skeletal dysfunctions including abnormalities that are incapacitating, and other essential organs not functioning properly. It was discovered that plants mostly absorb fluoride from water. Animals may subsequently enter the human food chain by consuming large fluoride cuisine with both plant and animal origins. Numerous safeguards and mitigation strategies have been devised to reduce the toxicity of fluoride, such as by using artificial compounds, and bioactive substances found in plants, and plant goods include things like pulpy fruit, grain mixes, and plant buckles.

Therefore, this article offers up-to-date information on the origins, toxicity, and different amelioration methods for reducing fluoride levels in the water. It also discusses the usage of different synthetic and natural chemicals and compounds to decrease fluoride's detrimental effects in vivo models.

Keywords: Amelioration methods, antioxidant defense system, Fluoride toxicity, health problems, organ abnormalities.

INTRODUCTION

Fluoride (F) is a key element in the periodic table's halides group because of its tiny size and high electronegative properties. Even though fluoride's mechanisms in lifeforms are still unknown, its chemical size and reactivity are distinctive in terms of biological traits. It's pervasively found in plants, water, soil, and air. Within the creature's body, fluoride manifests itself in food and drink. According to current studies, the majority of fluoride originates from pharmaceuticals (20%) and agricultural chemicals (30-40%).

The location affects both the presence and fluctuation of fluoride. It was discovered that the amount of fluoride in the soil ranges from 10 to 1000 parts per million. Still, it varies from 0.5 to 2200 parts per million in water. This event depends on water sources.

The World Health Organization (WHO) defines chronic fluoride toxicity as exposure to levels more than 1.5 ppm in animals. Most nations experience endemic levels of toxicity after being in the water. In the United States, 4mg/L of water is the recommended daily intake of fluoride. It is 0.8 in European countries. The drinking water quality in most Indian states shows higher levels of fluoride.

It inhibits both metabolism and reproduction at the same time, which results in decreased photosynthesis, and the channels for breathing. In the end, fluoride even damaged plant's demise. Fluoride poisoning in an animal's skeleton is a condition known as skeletal fluorosis. Lately, elevated fluoride consumption has been linked to oral cancer and tumors of additional organs. Early clinical signs included diminished food consumption and weight reduction. Following the attenuation of the antioxidant defense system. Fluoride also has an impact on the stomach, the brain, the muscles, etc. To mitigate these repercussions, numerous kinds of synthetic chemicals, herbal remedies, and plant molecules that are bioactive have been manufactured and included in the documentary about health. For example, research has shown that a substance known as melatonin, flavonoids, lipoic acid, etc. significantly reduces the risk of fluoride intoxication.

This paper critically examines the origin of fluoride levels all over the World and its harmful impacts on both plants and animals. Additionally, the piece addresses the recent ameliorative procedures created

using artificial chemicals, plant-based bioactive molecules as well as natural plant products.

Biochemistry of fluoride

Because of its smallest size and highest electric negativity, fluoride is the most important molecule within the Halides group (group VII) among the periodic tables, relative to every other molecule. It is element 13's most plentiful and extensively dispersed in soil, water, and other materials around the food. It is inclined to exist as diatomic in the state molecules and its atomic number is 9, and atomic weight is 18.9984. their electromobility traits allow them to react with fewer electromotive components or chemical groups. However, fluoride has numerous distinct chemical characteristics. These characteristics significantly affected the unique physiological and metabolic impacts.

Fluoride sources

The two primary routes by which fluoride entered the environment were through natural and human sources.

Natural assets

The Soil: Soil typically contains 150-400 mg/kg of total fluoride. The clay soil has a fluoride level of 1,000 mg/kg fluoride pollution of soil results from using fertilizers high in phosphorous with a total fluorine content of 1-1.5%. after inhalation, contaminated soil with fluoride demonstrated its toxicity of pollutants from the soil that has evaporated or through the tainted groundwater following the soil's fluoride-leaching.

Water: It is safe to drink water with a fluoride concentration of up to 1.0mg/L. however, the fluoride levels that range from 1.1 to 2.5 mg/L are just slightly polluted. On the other hand, a level over 2.6mg/L fluoride is considered highly polluted. Because of the leaching process, which transfers fluoride from the soil to the groundwater, it was discovered that the level of fluoride in groundwater is higher than that in surface water. The presence of fluoride in naturally occurring groundwater from the earth is caused by several processes.

Anthropogenic Sources: Human activities such as industrialization, motorization, fluoridating drinking water sources, fluoridating dental goods, refrigerants, and fire extinguishers, among others, can lead to anthropogenic fluoride contamination. There was also fluoride pollution from airborne sources. In normal locations that are neither industrialized or contaminated, the mean concentration of fluoride is often less than 0.1 ug/m^3. The levels in the industrial region may be somewhat greater, but they should stay within 2-3 ug/m^3. In multiple nations, the primary trigger of fluoride responsible for pandemic fluorosis is domestic coal burning. Animals such as cattle, buffaloes, sheep, goats, and camels have perished due to industry-released fumes and effluents heavy in fluoride. Numerous investigations show dietary supplements containing mineral mixtures are a significant cause of animal fluoride poisoning. Additionally, the integration of contemporary chemical production and use in various industries, such as sodium fluoride (NaF), calcium fluoride (CaF), hydrogen fluoride (HF), phosphate manures, and sulfur hexafluoride (SF) are the primary fluoride sources.

Global scenario of fluoride levels: Twenty-three Countries worldwide fall within the crucial area concerning fluoride levels. The impact on billions of individuals is because of fluoride exposure. Twenty million people in India are seriously in danger of developing fluorosis of widespread fluorosis. India's drinking water contains between 0.5 to 697 mg/L of fluoride.

Rajasthan's fluoride distribution: The largest state, Rajasthan, has 10% of the nation's land area yet only receives 1/100 of the nation's total rainfall. It merely has a share of 1/10 of the typical share of more water than the entire nation. The location and water quality decline are caused by geological configuration. The state is thus facing a serious water issue. The large portions are covered by the huge Indian Thar Desert impacted by fluoride. As a result, there is an exceptional lack of precipitation, with 5 to 20mm of rainfall in a year. Because groundwater is deeper and has more concentrated minerals, it is unsafe to drink. Due to its dry and semi-arid environment and scarcity of surface water resources, Rajasthan significantly depends on groundwater for agricultural and drinking purposes. The only state where high fluoride affects practically every district in Rajasthan. The fluorosis problem, which manifests in 23 districts at different intensities (dental, skeletal, nonskeletal, etc.), can be seen. According to research conducted in 1994 by the Rajasthan Voluntary Health Association, 2433 villages in Rajasthan- roughly 2.6 million people- have a fluoride problem. Furthermore, some 30,000 people consume water with a fluoride dosage of 10mg/L.

Impacts of fluoride

Fluoride's impact on human health: Around the world, fluoride contamination poses a serious risk to public health. If fluoride intake is kept to a minimum (0.5-1.5 mg/L), it is thought to be healthy for humans. Fluoride works to stop tooth decay by helping damaged enamel to remineralize and by preventing the microorganisms that cause decay in dental plaque from producing acid. Additionally, fluoride is a regular component of enamel itself. Sources: Hussain et, al. (2002) and the Public Health Engineering Department, Rajasthan, (1991). However, it is also known to have impacts on the immune system, the molecular level of development, the teeth, osteosclerosis, skeletal fluorosis, kidney alterations, and the endocrine system if the content in drinking water exceeds 1.5mg/L (WHO,1996). Fluoride and its biological effects have been linked, as demonstrated by Smith and Hodge in 1959. Only reports of the neurological symptoms that have come from India are reported by Short et, al. 1937, on the neurological problems in fluorosis. There have been theories put up regarding a mechanism for fluoride effects on the central nervous system because of how much the central nervous system depends on this energy source. Youth in China's high-fluoride drinking water regions were found to have lower IQs than a matched group of children in low-fluoride drinking water regions (Li de, al. 1995; Lu et, al. 2000).

Carcinogenic Consequences: Effects that cause cancer, it can be challenging for epidemiologists to identify the carcinogenic effects of long-term exposure to fluoride ions. Fluoride ion ingestion is known to increase the risk of both bladder and kidney cancer. This is because it contains hydrogen fluoride, an acidic and potentially fatal substance created in urine in an acidic environment (T. Kamal, 2023). An examination of the excessive fluoride ion pollution of groundwater samples from open and bore wells was conducted in the Tiruvannamalai region. (Chicas et al., 2022).

Effects on Neurons: In addition to its effects on learning and memory, excessive fluoride consumption in humans can cause neurotoxicity. A study by Choi et al. (2012) found that fluoride concentrations more than 1 mg/l can cause neurotoxicity. Compared to the mature brain, the developing brain exposed to fluoride ions is far more vulnerable to toxicants, and this exposure could potentially cause irreversible harm to the growing brain.

Effects on development: According to several studies, the placenta allows fluoride ions to diffuse inactively from the mother's womb to the fetus (Malhotra et al., 1993; Gupta et al., 1993). This suggests that the fluoride ion concentration in the umbilical cord and the mother's blood plasma have a positive correlation. Higher fluoride intake during pregnancy can disrupt a woman's iodine level, which can negatively impact thyroid function during a crucial intrauterine stage of brain development, according to a recent study (Griebel-Thompson et al., 2023).

Dental concerns: A naturally occurring substance called fluoride makes teeth stronger and keeps them from deteriorating. Blotching of the tooth surface or enamel is a symptom of dental fluorosis, which provides insight into the connection between fluoride consumption and human health. Early in the tooth's development, there is a significant increase in mineralization and damage to matrix proteins during enamel growth. A particular condition known as the dose-related disorder of large gaps in crystalline structure, enamel mineralization, excessive retention of enamel proteins, and a rise in porosity is brought on by exposure to F^- content during the mineralization of teeth (Aoba and Fejerskova, 2002).

Fig,1: Depicts the various impacts of fluoride on human health.

Fig.1.1: Carcinogenic consequences

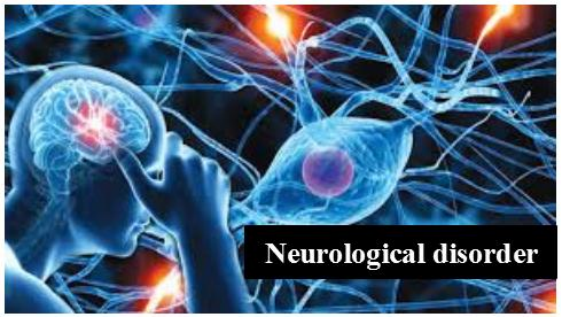

Fig.1.2: Effects on Neurons

Fig.1.3: Effects on Development

Fig.1.4: Dental cares

Humans, livestock, and animals used for research are all at risk for several adverse effects that result from extended exposition to fluoride (F). animals suffering from chronic food-borne illness first exhibited lower body and consumption of feed, which led to weight gain (BWG). Extended exposure to fluoride results in fluorosis, which causes a degenerative condition that progresses, dental mottling, and a variety of skeletal disorders. Experimental data show that fluoride exposure causes oxidative stress in soft tissues such as the liver, kidney, brain, and lungs both in vitro and in vivo. Fluoride suppresses the actions of antioxidant enzymes such as catalase, glutathione peroxidase, and superoxide dismutase lowering glutathione levels. A decrease in glutathione results in surplus oxidative damage of membrane phospholipids and macromolecules: disintegration, mitochondrial membrane, lipid peroxidation, apoptosis, and depolarization. Determination of the nervous system also happened as a result of the fluoride exposure. According to several studies, the rat's hippocampus can result in degeneration because of the unbalanced oxidant-antioxidant system. Fluoride quickly passed through the blood-brain barrier and led to cell deterioration in the nervous system. Every one of the fluoride impacts is condensed in Tbale1,2.

The Toxicity of Fluoride:

Table 1: Excessive fluoride exposure causes the multiple oxidative biomarkers involved in hepatic oxidative damage to change.

Study type, model, and dosage		Outcome	References
In-vitro (animal cells)	1.35- and 2.5-mM mouse pancreatic beta-cells (BTC-6) for 12 hours	+O^2 generation$^-$, -SOD activity, -Δψm	5
	Primary rat, its hippocampus neurons at concentrations of 20,40, and 80 mg/L, or 1.05, 2.1, and 4.2mM for 24 hours.	+ROS generation, -GSH levels, and – GSH-Px activity, as well as SOD, +Lipid peroxidation	6
	Murine hepatocytes for an hour at a concentration of 100 mM	+The production of reactive oxygen species (ROS), -GSH level, -GSH: GSSG ratio, -Catalase and SOD activity, +lipid peroxidation, and protein oxidation	13
Using human cells in (in-vitro study)	Neuroblastoma (SH-SY5Y) cells were	+ lipid peroxidation + protein oxidation	22

	treated for twenty-four hours at 0.05-5 mM		
	Eight hours after being subcutaneously treated with 250 mg of NaF/kg, male albino guinea pigs were slaughtered.	+generation of NO in blood	12
in-vivo (animals)	For eight weeks, male Wistar rats were treated orally to 5 mg/kg body mass/day.	+O^2 generation -SOD activity, -Δψm	32
	Male Swiss albino mice were subjected to 50mg/L of drinking water for a while.	+ Production of ROS, -GSH concentration, -the SOD activity in βλοο$^{\delta}$, The liver's catalase activity	38
Sign indicate increased (+) and decreased (-) gene regulation			

Table 2: Regulation of gene expression linked to cytokines and apoptosis through fluoride exposure

Study Type	Type and amounts	Outcome	References
Using Human cells in (in-vitro study)	Neuroblastoma cells (SH-SY5Y) were treated for 24 hours at 40, 80 mg/L, or 2.1 and 4.2 mM.	+ compounds involved in apoptosis caspases 3 to 8, Fas, and Fas-L.	20
In-vivo (Humans)	Mononuclear cells in peripheral blood from Mexicans consuming water at concentrations between 1.9 and 4.02 mg/F/L.	-chemokines inflammatory (CCL1, CCL18, CCL19) -cytokines (IL-1L; IL-2).	30
Sign indicate increased (+) and decreased (-) gene regulation			

Reduction of fluoride poisoning through plant-based products:

Several recent years have seen research in several areas, including the development of different techniques to directly reduce the amount of fluoride present in water sources, the ingestion of numerous substances or molecules, and the application of plant metabolites (such as quercetin, pineal protein, and melatonin) on test animals. Because the plant products are rich in nutritional content, they exhibit mitigating effects on teratogenicity caused by fluoride it has a variety of proteins along with vitamins, minerals, and antioxidants.

Spirulina is a small, filamentous cyanobacterium that is a member of the Oscillatoriaceae family and has long been used as a food additive. Numerous beneficial qualities of Spirulina include its antimicrobial, antiviral, anti-inflammatory, anti-cancer, and antioxidant qualities.

Quinoa, a plant in the family Chenopodiaceae, is a superfood that is an excellent source of complete proteins, minerals, vitamins, antioxidants, fibers, and unsaturated fatty acids.

For thousands of years, traditional and folk treatments have employed aloe vera, a perennial succulent plant in the Asphodelaceae family, to treat and cure a wide range of ailments. It has been utilized in traditional medicine to treat skin conditions including burns and fractures, as well as asthma. Lately, its antioxidant properties have been investigated.

Prosopis cineraria, commonly referred to as Khejri, is the Leguminosae family tree that is the state tree of Rajasthan. Prosopis cineraria is frequently used as an antihyperlipidemic, antioxidant, antibacterial, antiviral, anticancer, and analgesic for the treatment of dysentery, bronchitis, and asthma.

However, additional methods of lessening the harmful effects of fluoride include the consumption of tamarind seeds, leaves, seeds, fruit pulp, and plant juices, of Azadirachta indica and others. These methods are included in Table 3. Furthermore, several man-made chemical compounds, such as quercetin, lycopene, melatonin, and pineal protein, are also very effective in lessening the damage caused by fluoride.

Table 3: Research on using natural plant-based to reduce the harmful effects of fluoride.

Serial no.	Animal species used in research	Fluoride dosage and delivery technique	Period of study	Plants for dosage and route	Impact on the factors under study	References
1	Male Wistar rats in adulthood	10.3mg/kg/b. w dose through oral gavage	35 days	Extract from blackberries, 1.6 g/kg b.w given orally	+Superoxide dismutase activity, overall antioxidant capacity. and glutathione level	37
2	Mature Swiss albino mice	600-ppm NaF, the dose given orally	45 days	Banaba extract- 50, 150, and 250 mg/kg b. w	+several TCA enzymes in brain areas, including aconitase, succinate dehydrogenase (SDH), and ICDH.	27
3	Swiss albino male mice	600-ppm NaF, the dose given orally	14 days	Fluid of ethanol from termination arjuna bark, 50mg/kg/b. w given orally through the oral gavage method	+glutathione peroxidase, +GSH, +catalase, -serum glutamic-oxaloacetic transaminase, -alkaline phosphatase.	3
4	Male Swiss albino mice bred in colonies	Sodium fluoride dose at 100ppm	30 days	Powder of tamarind leaf, 2.5-10 g% fed by diet	Improved antioxidant profiles in both hepatic and renal tissues, -plasma glucose, -lipid levels, -lipid peroxidation, +hepatic glycogen content, +hexokinase activity, and +cholesterol excretion.	31
Sign indicate increased (+) and decreased (-) gene regulation						

CONCLUSION

Based on this review, it can be concluded that fluoride is a common element in all settings due to its electronegativity. In certain nations, it falls within the range, in contrast, the majority of the reviewed countries revealed more than the recommended threshold. Approved by the WHO (World Health Organization). Water is the primary source of fluoride exposure among several sources. Thus, methods for purifying water should be created to provide a cost-effective and secure way to carry around water. High fluoride exposure has negative effects on immune system function, oxidative stress, apoptosis, and nutritional utilization in both humans and animals. Therefore, it's critical to implement corrective actions to stop the spread of the disease and its endemicity. Concurrently, some synthetic compounds, plant bioactive molecules, and secretions from the pineal gland have demonstrated a protective quality against the toxicity of fluoride. However, more thorough research is needed before these compounds may be widely used as medicinal medicines.

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