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TOXIC EFFECTS OF FLUORIDE ON HUMAN HEALTH

Nidhi Sharma Department of chemistry Government college, Kota

ABSTRACT

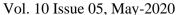
While certain creatures require it for survival, fluoride is not required for human development or the survival of most other organisms. The concentration of fluoride in drinking water varies widely throughout EU Member States, from 0.1 mg/L to 8.0 mg/L. Some EU Member States advocate for fluoridating drinking water; the most prevalent fluoridating chemicals are hexafluorosilicic acid and hexafluorosilicates. Hydrolysis of these compounds to the fluoride ion occurs swiftly and completely. It has been stated that there are no lingering fluorosilicate intermediates. As a result, fluoride ions are the primary material of interest (F-). There is no discernible threshold at which the risk of dental and bone fluorosis increases after systemic exposure to fluoride through drinking water. Other adverse health effects following systemic fluoride exposure, such as carcinogenicity, developmental neurotoxicity, and reproductive toxicity, have been suggested by limited epidemiological evidence; however, applying the general rules of the weight-of-evidence approach indicates that these observations cannot be unequivocally substantiated. For the purpose of this study, we assessed the total fluoride exposure of babies, children, and adults from all sources of fluoride, including water-based drinks, food, dietary supplements, and the use of toothpaste. Only occupational exposure to dust from fluoride-containing minerals contributes significantly.

Keywords: fluoridation of drinking water is not expected to lead to unacceptable risks to the environment.

INTRODUCTION

Although fluoride is not absolutely necessary for human development, it is helpful in warding against tooth decay (tooth decay). Therefore, since the early 20th century, public health protective measures against tooth decay have included the intentional fluoridation of drinking water and the development of fluoride-containing oral care products (toothpastes and mouth rinses), foods (fluoridated salts), and supplements (fluoride tablets) in a number of different parts of the world. Naturally occurring fluoride is found in both tap and mineral water, as well as drinks, foods, and other, less significant environmental sources. There's some evidence in the scientific literature to show that consuming fluoride can have some unfavourable impacts on

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health. Well-documented negative consequences of fluoride use include dental fluorosis and effects on bones (increased fragility and skeletal fluorosis).

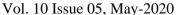
It has been claimed that fluoride can have systemic effects with prolonged or high exposure; these include effects on the thyroid, the developing brain, and other organs, as well as a link with some kinds of osteosarcoma (bone cancer). The high variability in fluoride levels found in tap (whether naturally occurring or the result of intentional fluoridation of drinking water) and mineral waters, as well as individual dietary and oral hygiene habits and practises, contribute significantly to the wide range in fluoride exposures both within and between populations.

All fluoride risk evaluations paint a similar picture: there's barely any wiggle room between the recommended intakes for cavity prevention and the maximum exposure levels. All previous evaluations have agreed that further monitoring of human exposure to fluoride from all sources and an assessment of new scientific findings on its danger profile are essential. The European Food Safety Authority (EFSA) and the Commission Scientific Committee on Consumer Products (fluoride in dental care products (SCCP 2009)) have both conducted exposure assessments in their most recent reviews, setting upper tolerable intake levels (UL) related to concentration limits for fluoride in natural mineral waters (EFSA 2005) and on calcium fluoride and sodium monofluorophosphate as a source of fluoride (EFSA 2008a, EFSA 2008b).

The US National Academies of Sciences adopted a same methodology in their 2006 evaluation of the EPA's fluoride water regulation (NRC 2006). The effectiveness of fluoride and, more specifically, the use of fluoridated water to prevent tooth decay, remains a contentious topic of debate. Due to this, some nations have stopped fluoridating their water supply while others have increased their intake. Opponents of water fluoridation have pointed to reports showing the health and environmental risks of the most commonly used fluoridating agents, silicofluorides (such as (hydro)fluorosilicic acid, sodium silicofluoride, disodium hexafluorosilicate or hexafluorosilicate, and hexafluorosilicic acid), as reasons to question the practise of intentional water fluoridation. Further, results imply that these compounds' presence in drinking water may have detrimental impacts on human health and may have amplifying effects on fluoride disposition in bone.

Intentional water fluoridation is still in use in the UK and Ireland, thus their representatives in the European Parliament have a lot of concerns about the topic of water fluoridation. The Commission believes it is necessary to consult its Scientific Committee on Health and Environmental Risks (SCHER), which should coordinate its efforts with those of the Scientific Committee on Consumer Products (SCCP), the EFSA Panel on Dietetic Products, Nutrition, and

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Allergies (EFSA NDA), and the EFSA Panel on Contaminants in the Food Chain (EFSA CONTAM), all of which have previously issued opinions on fluoride.

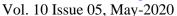
SCHER considered all papers submitted by various stakeholders in response to an open call on the internet for submission of relevant scientific information, including research articles and reviews published in peer-reviewed journals, reports from regulatory agencies and other organisations, and so on. Following three months of public input, a hearing was held, and new information was obtained, the court issued its preliminary opinion. The EU Scientific Committee on Emerging and Newly Identified Health Risks used a weight-of-evidence method to analyse the scientific data at hand (SCENIHR). Epidemiological research, laboratory studies on humans and animals, and laboratory studies on cells have all looked at the potential dangers of fluoridated water. Evidence from each of these categories is considered in a health risk assessment, with a final score based on a weighted average. A weight-of-evidence analysis was performed on the supporting documents.

Terms Of Reference

Please have the SCHER (Scientific Committee on Health and Environmental Risks):

- a. Critically review any information that is available in the public domain on the hazard profile and epidemiological evidence of adverse and/or beneficial health effects of fluoride, keeping in mind the SCCP opinion of 20.09.05 (SCCP 2005) on the safety of fluorine compounds in oral hygiene products, the EFSA NDA opinion of 22.2.05 on the Tolerable Upper Intake Level of Fluoride, and the EFSA CONTAM panel opinion of 22.06.05 In particular, the Committee should take into account material that has emerged since 2005, as well as evidence that has been provided before to that date but was ignored by the SCCP and EFSA committees.
- b. Carry out a comprehensive risk assessment for fluoride exposure that takes into account any and all potential exposure routes (both anthropogenic and natural). To do this, and in the event of uncertainties or a lack of actual exposure data, the SCHER is asked to conduct a sensitivity analysis that considers a variety of exposure scenarios (e.g., sources, age group), and to describe using appropriate quantitative or qualitative means the weight-of-evidence behind each scenario, the uncertainties surrounding each scenario, and the likelihood of it occurring in real life.

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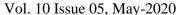
Scientific Rationale

Intentionally or naturally occurring fluoride in water, food, consumer, and medicinal items is effective in preventing dental cavities (tooth decay). However, there are a number of factors that contribute to dental caries, such as microorganisms in dental plaque, fermentable carbohydrates (especially sucrose), time, the individual's health status and level of oral hygiene, which are in turn influenced by their socioeconomic status and level of education. Fluorides may be found everywhere there is air, water, or rock. As a fluoride, for example cryolite, fluorine makes up 0.06 to 0.09% of the Earth's crust, placing it sixth in terms of the elements' relative abundance (Na3AlF6). The fluoride concentration of cryolite (used to make aluminium) and rock phosphates (used to make fertilisers) can reach as high as 54%. This fluoride, unfortunately, is mostly insoluble and so useless to living organisms. Solubility, soil acidity, and water availability all have a role in how readily available fluoride is in soil.

Although fluoride was found in the Icelandic volcano's ash, EFSA determined that there is insufficient evidence to warrant worry that it may adversely affect human or animal health if it were to be consumed in food or feed. Although fluoride levels in EU ground water are typically low, there are significant regional variances due to changes in geological conditions. Fluoride levels in surface water are typically lower than those in ground water (typically below 0.5 mg/L) and sea water (often between 1.2 and 1.5 mg/L).

There are no comprehensive data on the levels of fluoride in EU Member States' natural drinking water; however, even the most rudimentary data show wide variations both between and within countries, with concentrations ranging from 0.01 to 5.8 milligrammes per litre (mg/L) in Ireland, from 0.10 to 3.0 mg/L in Finland, and from 0.11 to 1.1 mg/L in Germany. These days, bottled natural mineral water often serves as people's primary water supply. Extreme fluoride concentration ranges, up to 8 mg/L, have been documented (EFSA 2005). Waters with a concentration of more than 1.5 mg/L must be labelled as not suitable for the regular consumption of infants and children under the age of 7 as per Commission Directive 2003/40/EC of 16th May 2003 establishing the list, concentration limits and labelling requirements for the constituents of natural mineral waters and the conditions for using ozone-enriched air for the treatment of natural mineral waters and spring waters. Using a daily consumption of 2 litres of water as a reference point, the World Health Organization (WHO) set a recommendation value for naturally occurring fluoride in drinking water of 1.5 mg/L and suggested that artificial fluoridation of water supplies not exceed 1.0 mg/L. (WHO 2006).

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Only a few areas in Ireland, the United Kingdom, and Spain fluoridate their drinking water, with values between 0.8 and 1.2 mg/L. (Mullen 2005). For human consumption, the maximum allowable level of fluoride (both naturally occurring and added by fluoridation) is set at 1.5 mg/L, as per Council Directive 98/83/EC on 3rd November 1998. Fluoride in water has recently been suggested by the US Department of Health and Human Services.

Dissociation of hexafluorosilicic acid in aqueous solution

It has been argued that human exposure to the compounds used in drinking water fluoridation, hexafluorosilicic acid and hexafluorosilicates, may occur due to inadequate dissociation of these agents in drinking water. There has been insufficient research on the toxicity of these substances. Fluoride ion and fluorosilicate species equilibrium in aqueous solutions throughout a broad concentration and pH range has been the subject of recent research. Hydrolysis of hexafluorosilicates to fluoride was quick and the release of the fluoride ion was almost complete throughout the pH-range and at the concentrations of hexafluorosilicates/fluoride important for drinking water. Sensitive 19F-NMR analysis failed to detect any lingering fluorosilicate intermediates. Colloidal silica is quickly generated from other hexafluorosilicate hydrolysis products such as Si(OH)4 (Finney et al. 2006). Natural occurrences of Si(OH)4 in drinking water are common and pose no health concerns. Because fluorosilicates in water are rapidly hydrolyzed to fluoride, these data imply that human exposure to fluorosilicates caused by the use of hexafluorosilicic acid or hexafluorosilicate for drinking water fluoridation is relatively minimal.

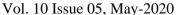
OBJECTIVE

- 1. To investigate the effects of fluoride and other water-fluoridation chemicals on human health
- 2. The second goal is research on water fluoridation and the toxicity of fluoride...

Fluoride distribution, metabolism and excretion

After entering the bloodstream, fluoride quickly travels to all parts of the body. In most cases, the plasma half-life is estimated to be between 3 and 10 hours in the short term. While both the plasma and the blood cells contain some fluoride, plasma concentrations are around twice as high as blood cell concentrations. The concentration of fluoride in saliva is around 65-75% that of plasma (Ekstrand 1977). Fluoride levels in the blood vary with the frequency and amount of fluoride consumed, rather than being maintained at a steady state. Fluoride exposure appears to have a direct effect on plasma fluoride levels in adults. Those who are exposed to water with a

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concentration of 0.1 mg/L or less typically have plasma fluoride levels of 9.5 g/L, whereas those who are exposed to water with a concentration of 1.0 mg/L have plasma fluoride levels of 19-28.5 g/L. Bone accretion and dissolution rates, as well as the renal clearance rate of fluoride, all have a role in determining the plasma fluoride concentration. The majority of fluoride leaves the body via the kidneys' elimination.

No tube secretion of fluoride occurs, although the glomerulus does perform some reabsorption of the fluoride ion after filtering it out of the plasma. Humans have a median renal clearance of fluoride of 50 mL/min. Urine fluoride excretion can be affected by a number of parameters, such as urinary pH, urinary flow, and glomerular filtration rate. Renal clearance rates (adjusted by body weight or surface area) do not appear to vary much with age. However, a considerable decrease in renal clearance of fluoride has been found in older persons (greater than 65 years of age), which is consistent with the age-related fall in glomerular filtration rates.

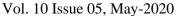
Dental fluorosis

There is widespread agreement that dental fluorosis in young children is a symptom of excessive fluoride intake from all sources. Fluorosis manifests as white, opaque striations across the enamel's surface at first, and as the condition worsens, the porous regions enlarge, pitting develops, and the surface takes on a discoloured brownish tint. The severity of the symptoms is proportional to the amount of exposure. Refer to Appendix I for a description of how fluorosis is categorised. There is a correlation between the amount of fluoride in drinking water and the prevalence and severity of dental fluorosis. Fluorosis is caused by consuming excessive amounts of fluoride over a lengthy period of time, but only when teeth are still developing.

When it comes to dental fluorosis, it's important to pay attention to the stages right before the eruption of both the baby teeth and the permanent teeth. Between the ages of four and six months in the womb, the jawbone begins to solidify and the first deciduous tooth buds begin to form. The permanent tooth buds begin mineralizing at birth and continue to do so over the course of the next 12–14 years. Dental fluorosis is the outcome of too much exposure to fluoride during tooth formation, as shown in a number of studies. The enamel of a developing tooth may be adversely affected if too much fluoride is absorbed. This won't be seen until the teeth come in, which can take up to five years after initial exposure.

When, how much, and how long a person is exposed to fluoride throughout the enamel-forming process all have a significant impact on the development and severity of fluorosis. The fluorosed enamel consists of a layer of wellmineralized enamel above a layer of hypomineralized enamel. Dental fluorosis is a condition for which the specific causes and triggers are unknown. It appears

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that at high fluoride levels, the ameloblasts are systemically affected by fluoride, but at lower fluoride levels, the ameloblasts may respond to fluoride's effects on the mineralizing matrix (Bronckers et al. 2009). According to the EFSA NDA panel, "moderate" fluorosis in permanent teeth is not commonly seen in children with daily intakes of less than 0.1 mg F/kg BW/day (EFSA 2005). Community fluorosis index vs daily fluoride exposure (in milligrammes per kilogramme of body weight) graph (see Figure 1). (Butler et al. 1985, Fejerskov et al. 1996, Richard et al. 1967). The dose-response curve is linear, suggesting that fluorosis can develop even with minimal exposure to fluoride in drinking water.

Skeletal fluorosis

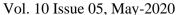
Fluoride's toxicity to bone is caused by a variety of different methods. By exchanging hydroxyl groups in the carbonate-apatite structure for fluoride ions, fluorohydroxyapatite is synthesised, which modifies the bone's mineral composition. When fluoride ions replace hydroxyl ions in a compound, the resultant structure is more compact and has greater electrostatic stability because the fluoride ions are located in the same plane as the calcium ions. According to Catanese and Keavney (1996), changes in mineralization have an effect on bone strength because the strength of bones is assumed to originate at the interface between collagen and the mineral. Long-term exposure to excessive amounts of fluoride causes a degenerative disease known as skeletal fluorosis.

Individuals in India, China, and Africa, where fluoride consumption is unusually high (e.g., due to high concentrations of fluoride in drinking water and indoor burning of fluoride-rich coal), have been documented to suffer from skeletal fluorosis, in some cases with severe paralysis. Workers in Europe's aluminium, fluorospar, and superphosphate industries have all reported symptoms of skeletal fluorosis (Hodge and Smith 1977). Most of the existing studies have an inadequate design for evaluating the dose-response relationship and creating a N/LOAEL for skeletal fluorosis because to confounding variables including nutritional status and climate, which affect how much water is affected by fluoride.

CONCLUSION

There have been several epidemiological studies examining the connection between fluoride consumption and reduced bone fractures. A person's bone fluorine uptake decreases as they become older. Up to 90% of ingested fluoride is deposited in the skeleton in the first year of life, with that number gradually decreasing to 50% in children older than 15 years of age. Fluoridation at levels of 0.6 to 1.1 mg/L may actually reduce total fracture risk, and there is no apparent link between water fluoridation and bone fracture risk (McDonagh et al., 2000). (AU-

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NHMRC 2007). Water with a content of 4 milligrammes per litre or more of fluoride per litre is thought to enhance the risk of bone fractures under specific circumstances (NRC 2006). SCHER agrees that youngsters in the European Union (EU) may be at risk for developing dental fluorosis. The existence of a threshold is undetectable. Skeletal fluorosis is not known to be endemic anywhere in the European Union. SCHER believes that there is not enough information to determine whether or not drinking water with elevated amounts of fluoride increases the risk of bone fracture.

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