Review Article

Impacts of Fluoridation in Context

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Abstract *This review article is written from a food chemistry perspective. It focuses on the systemic effects of fluoride (rather than the effects of fluoride on the teeth) since fluoride research concentrates largely on the teeth to the virtual exclusion of systemic effects. This is surprising given that fluoride is a known systemic toxin. About 400 million people (~6% of the world's population) drink fluoridated water. The effect of fluoride on the teeth is topical (directly on the teeth) and not systemic, so drinking fluoridated water has no benefit. Fluoride is a lipid soluble neurotoxin and enzyme poison. Fluoride accumulates in the pineal gland (average 9000 ppm in calcium hydroxy apatite crystals) and bone. Dental fluorosis is a marker for skeletal fluorosis. At 1 ppm 32 % of US children have dental fluorosis. At 1 ppm some sections of the population (e.g. infants) will ingest too much fluoride. Unfluoridated and fluoridated countries have similar rates of tooth decay. Given that fluoridation of water supplies is not necessary to maintain a reduction in tooth decay and that the side effects of ingestion are undesirable, the practice is likely to come under increasing scrutiny. More studies on the systemic effects of fluoride are urgently required.*

Introduction

Fluoride is added to water to protect teeth against decay,[1] yet it is considered a neurotoxin in the laboratory.[2] Research about fluoride is primarily focussed on teeth with little examination of other systemic effects (i.e., upon enzymes, bone, brain, thyroid, pineal gland, etc). Maximum toxic dosages are unclear, as are maximum cumulative dosages. Adding to the confusion, fluoride is considered non-toxic when added to water, but toothpaste tubes have warnings to seek medical help if you swallow even small amounts. Identifying fluorosis is difficult and its symptoms can easily be mistaken for arthritis or possibly chronic fatigue syndrome. Fluoride can be considered a food safety issue since it is primarily ingested from water, and to a lesser extent, foods.

Fluorine Chemistry

Fluorine (F) is element number 9 on the periodic table of elements and has a atomic weight of 18.998 g/mol. Fluorine gas (F_2) is yellow but does not exist in nature as it is too reactive. Fluorine is the most electronegative and reactive element in the periodic table. However as the fluoride ion (F^-) it is much less reactive.

Fluoride (Figure 1) can be added to the water supply as hexafluorosilicic acid (H_2SiF_6), sodium fluorosilicate (Na_2SiF_6 - a powder) or sodium fluoride (NaF - a powder). However, water fluoridation is usually carried out using hexafluorosilicic acid (~23% in water), which is a by-product of the aluminum and phosphate industries.

Toothpastes most commonly contain fluoride as sodium fluoride but also use stannous fluoride, sodium monofluorophosphate or olaflur/dectaflur. As they are not normally ingested they are not a significant consideration when reviewing the systemic effects of fluoride.

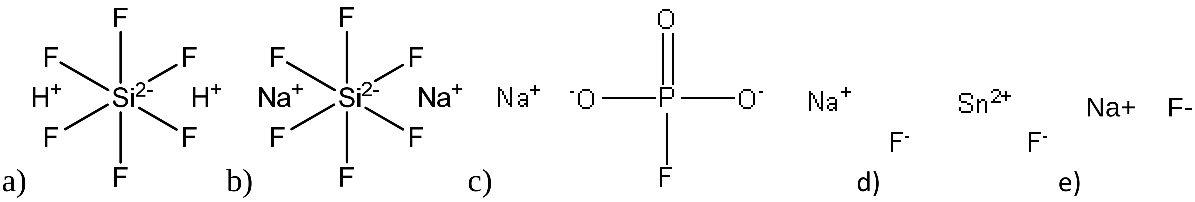

Figure 1. a)Hexafluorosilicic acid (H_2SiF_6), b)Sodium fluorosilicate (Na_2SiF_6), c) Sodium monofluorophosphate (Na_2PO_3F), d) Stannous fluoride (SnF_2) and e) Sodium fluoride (NaF).

Almost all fluoride research has been conducted on NaF (which dissociates into Na^+ and F^-). The assumption has been that H_2SiF_6 and Na_2SiF_6 dissociate into their component ions (eg. H^+, F^-, Na^+ and Si^{+4}) when diluted and raised to a pH of 7. If this happened, the effects of NaF and other complexes would be comparable. However, at pH 3 the majority of the F is complexed with Si. The effects of NaF are different than those of the Si complexes: no effect was noticed with NaF, but with Si-fluoride complexes lead levels in the blood increased three times in rats.[3] This is because the pH of stomach acid is around 2: the ions recombine and Si-fluoride complexes, as well as other complexes, are produced.

What levels are permitted in foods?

Food Standards Australia and New Zealand (ANZ) do not list fluoride as a recognized food additive. However, in July 2009 the ANZ food standards code was changed to permit the voluntary addition of fluoride to bottled water at levels of 0.6–1.0 mg/L. Nutrient reference values for ANZ populations have been established for different age groups (Table 1).

Table 1. Fluoride Nutrient Reference Values for Australian and New Zealand Populations[4]

Population Subgroup	Adequate Intake/AI (mg/day)		Upper Limit/UL (mg/day)	
Infants 0-6 months	0.01		0.7	
Infants 7-12 months	0.5		0.9	
1-3 years	0.7		1.3	
4-8 years	1.0		2.2	
9-13 years	2.0		10.0	
14-18 years	3.0		10.0	
	Males	**Females**	**Males**	**Females**
Adults 19+ years (including pregnant/lactating women)	4.0	3.0	10.0	10.0

Does fluoride occur naturally?

Fluoride occurs naturally in some foods and in water. The fluoride levels in water of most countries are low. Countries like China and India, on the other hand, have many areas where the natural levels of fluoride in water are high enough to cause crippling skeletal fluorosis. The levels in breast milk average only 0.033 ppm even when fluoride intake is high.[5] Levels in fresh food are rarely a consideration, except in tea which can add between 1-9 mg/day of fluoride.[5-7]

How much fluoride is in water?

In Australian water, fluoride is permitted at up to 2 ppm although it is normally maintained at around 0.9–1.0 ppm. Using the UL of 0.7 mg/day (Table 1) it can be seen that any bottle-fed infant will surpass the UL for fluoride every day. The National Health and Research Council Dietary Guidelines recommends against this practice.[8] Other countries also warn against the use of fluoridated water for bottle fed infants and other high risk groups (e.g., dialysis patients),[9] yet ANZ food standards consider this practice to be safe and have stated on their website: "Bottled water with added fluoride is safe for everyone and can be used to make up infant formula."[10]

How is fluoride increased in foods?
Boiling water concentrates fluoride (by evaporation).[11] Processing foods often increase the amount of fluoride (e.g., adding fluoridated water to a soup or reconstituting fruit juice using fluoridated water).

Can fluoride be removed?
The simplest method of removing fluoride is distillation.[11] Reverse osmosis is also highly effective.[11] Both these methods remove all other minerals from the water as well which may not be desirable. Activated alumina (Al_2O_3) cartridges are an alternative method.[11] Cartridges require regular changing but there is no easy way to tell when this should occur.

At what dose does fluoride have undesirable physiological effects?
The National Health and Medical Research Council of Australia has deemed 10 mg/day of fluoride as the UL,[8] but few toxicological studies have been carried out to prove this. Most studies have concentrated on the teeth and fewer studies on rest of the body. The organs mostly affected by fluoride include the brain,[12,13] thyroid, parathyroid and adrenal glands,[14] and the pineal gland.[15] However, fluoride concentrates in the bones (i.e., about 50% of ingested fluoride is retained, but young children may retain up to 80%).[8] Many enzymes are affected by fluoride (e.g., Judd lists 66 enzymes which includes P450 oxidases and enzymes involved in neurotransmitter synthesis[16]). When 2-10 mg/day of fluoride was administered to 15 individuals with hyperthyroidism (over a period of 20-245 days), 6 individuals had significant clinical improvements marked by an amelioration of tachycardia and tremor, and a ceasing of their weight loss.[17] The reduction in basal metabolic rates was attributed to fluoride inhibiting the thyroid iodide-concentrating mechanism.[17] Similar daily intakes of fluoride might also have adverse effects upon the basal metabolic rates of euthyroid (i.e., normal thyroid function) individuals.

How does fluoride interfere with enzymes?
Fluoride can interfere by attaching itself to metal ions located at an enzyme`s active site or by forming competing hydrogen bonds at the active site. Energy production is affected when this occurs. Fluoride might, therefore, be a pathogenic factor in causing clinically significant problems, such as weakness, drowsiness, and cognitive impairment.[18]

Is dental fluorosis a marker for fluorosis?
It is also known that crippling skeletal fluorosis is caused by excessive fluoride ingestion (Figure 2). Thus, dental fluorosis is a marker for skeletal fluorosis and other serious physiological effects. Even at low levels of 1 ppm, 32% of US children are affected by dental fluorosis.[19] Crippling skeletal fluorosis may be produced by levels of 10-20 mg/day over 10-20 years.[20]

Figure 2. Severe dental fluorosis
(Photo provided by: Kennedy D: China's battle with crippling water. Corte Madera, CA. Green Planet Films. 2000. *Retrieved from: [**www.greenplanetfilms.org/product_info.php?products_id=176**].* Used with permission)

What about less serious fluorosis?
Fluoride levels of 0.9 ppm in naturally occurring water supplies (Xinjiang region of China, Hentian prefecture) may affect people who are iodine deficient, causing hearing loss, mental retardation and bone retardation.[21] It is likely that iodine and fluoride compete for similar binding sites in the human body. When iodine is low, as in this example, there would be less competitive inhibition, and more fluoride would be available to bind to various tissues within the human body. China has naturally occurring levels of fluoride, so the population consumes fluoride daily and their exposure varies according to how much they drink. In the Jiangsu Province of China, Sihong county, fluoride levels of 1.9 ppm (in naturally occurring water supplies) are associated with lowering population IQ (i.e., by 5-10 points).[22]

The pineal gland is the second most perfused organ in the body (after the kidneys) and studies show it contains fluoride levels ranging from 9,000-21,000 ppm (in calcium hydroxyl apatite crystals). The lower level approaches that of skeletal fluorosis and the upper level exceeds that of severe skeletal fluorosis.[14] Rat studies show that fluoride accumulates in the brain and is associated with both hyperactivity (when exposed before birth) and hypoactivity (when exposed after birth).[12]

What is the toxic/lethal level of fluoride?
Chronic toxic doses of fluoride can accumulate over a long period of time. It is difficult to prove chronic fluoride toxicity because this depends on the length of exposure, which may stretch many decades. Acute lethal doses can result from one significant exposure. A lethal dose for children is 5-15 mg/kg fluoride. Thus, as little as 35 mg can kill a 7 kg infant while 5-10 g (32-64 mg/kg) can kill a 70 kg adult.[24] Acute fluoride poisoning was found to have caused a fatality in a public water system in Alaska where the concentration was 150 ppm (i.e., about 17.9 mg/kg).[25]A chronic dose of 10 mg/day is often cited in the literature as the UL in adults.[8] More than this amount per day would put a person at risk of developing chronic fluoride toxicity over time. Individuals living in warmer climates, sports people and diabetics are likely to ingest more than 10 mg/day (i.e., equates to 10 L of water at 1 ppm), and are at risk of developing chronic fluoride toxicity, especially when all foods and beverages (e.g., tea) and non-food sources (e.g., toothpaste) are included in an individual's

calculated amount of ingested fluoride. It should be noted that toothbrushing does not by itself increase blood levels enough to negatively influence bone production.[26] However, when toothbrushing (i.e., provides 1,350-1,500 mg/L or 1.35-1.50 g/L of fluoride) is combined with increased fluid intake and the regular intake of beverages like tea (i.e., can add 1-9 mg/day of fluoride),[6,7] it is possible that individuals would be at risk of developing chronic fluoride toxicity since their daily consumption might be more than 10 mg for extended periods of time.

Bio-mimetic molecules

Fluoride can form complexes and facilitate the uptake of every metal ion, such as aluminium (Al^{3+}) and lead (Pb^{2+}), except for the alkali metals (i.e., lithium, sodium and potassium).[3,27] For example (Figure 3), the fluoride-aluminum complex (AlF_4^-) has about the same size and shape as phosphate (PO_4^{3-}).

Figure 3. Tetra fluoroaluminate ion (AlF_4^-) and phosphate ion (PO_4^{3-})

Since energy production is partially dependent on having sufficient phosphate ions, it is conceivable that fluoride-metal complexes disrupt enzymatic function. For example, signalling G-proteins can become disrupted by AlF_4^- because this fluoride-metal complex can switch them on when no messenger has arrived.[28,29] Since fluoride can cause goitre,[30,31] AlF_4^- is implicated in inactivating deiodinases.[21,32] Fluoride interferes with the body's defence mechanisms against reactive oxygen species, leading to lipid peroxidation and inflammation, which suggests that fluoride might be implicated in a range of diseases characterized by increased oxidative damage.[33] Fluoride increases the uptake of aluminum into the brain in rat studies,[34] which might have etiologic implications in human neurodegenerative diseases.

Treating fluoride poisoning

Fluoride is a lipid soluble neurotoxin absorbed on contact. It is a substance that workers are usually discouraged from working with. Hydrofluoric acid (HF; Figure 4) is probably the best known source of fluoride poisoning.[35-37] Special training and extra protective equipment is required to work with HF. Following absorption, HF binds to calcium (CaF_2) and magnesium (MgF_2) ions in the body causing severe systemic effects. HF poisoning (including fluoride poisoning from any exposure) is treated with calcium gluconate ($C_{12}H_{22}CaO_{14}$) and calcium chloride ($CaCl_2$) intravenously to ameliorate hypocalcaemia, tetany, cardiac arrhythmias, and neurotoxicity resulting from fluoride excess.[36-38]

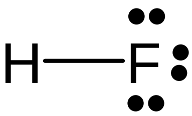

Figure 4. Hydrofluoric acid (showing lone pairs of electrons)

Does fluoride have to be ingested to work?

According to the National Research Council, “the major anticaries benefit of fluoride is topical and not systemic.”[9] Fluoride should therefore be placed directly on the teeth to exert its therapeutic effects and does not need to be ingested. Toothpaste usually has a concentration of 1,350-1,500 ppm (i.e., 1,350-1,500 mg/L or 1.35-1.50 g/L of fluoride). While toothpaste is not a food item, it is sometimes ingested accidently. Some toothpaste includes a warning to call a hospital if a small amount (pea sized amount ~0.25 mg) is ingested. In children under 7 years of age, parents should only apply a pea-sized amount of fluoride toothpaste on the toothbrush and discourage swallowing; otherwise, their children might ingest too much for their body weight.[39] Children should be encouraged to rinse and/or spit after brushing as this will significantly reduce fluoride ingestion from toothbrushing.[40]

Unfluoridated versus Fluoridated Countries

Only about 400 million people (~6%) worldwide (out of ~7 billion) drink fluoridated water and most fluoridated water is in the United States. Only 8 countries have more than 50% of their populations drinking fluoridated water.[41] The Centres for Disease Control and Prevention have stated that fluoridation was one of the ten most important public health measures of the 20th century.[42] On the other hand, many countries (i.e., East Germany, Finland, Cuba and the Province of British Columbia in Canada) have removed fluoride citing a wide range of health concerns. Furthermore, no unfluoridated countries have shown an increased incidence of dental caries (Figure 5).

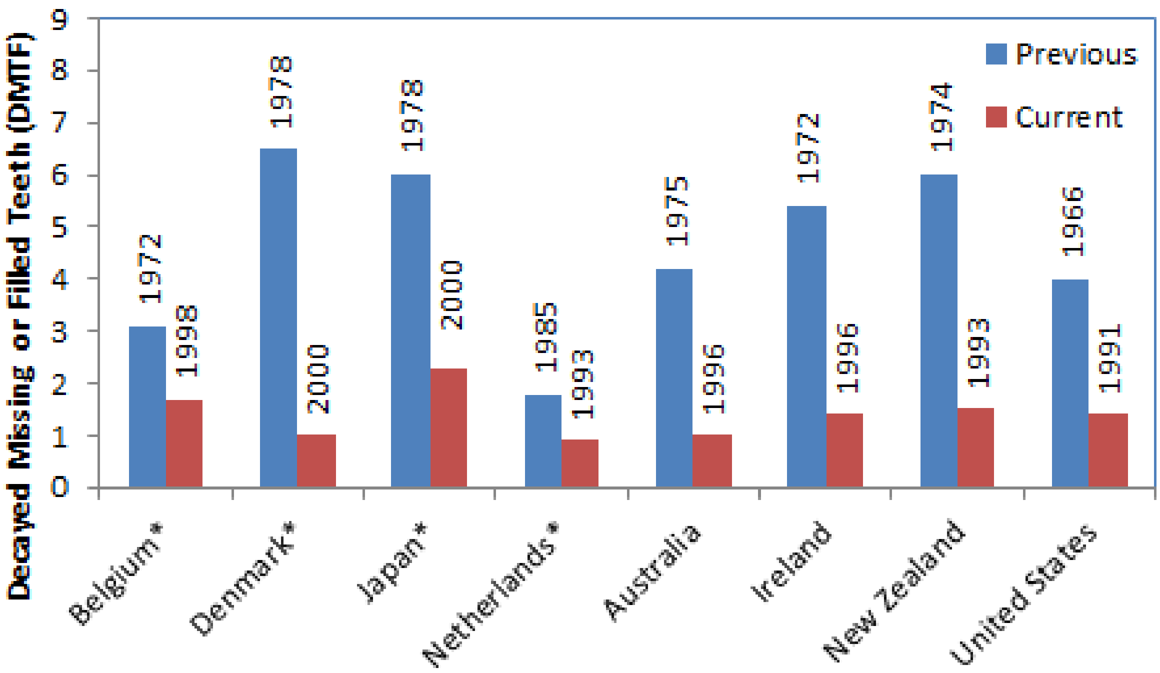

Figure 5. Tooth decay in 12 year olds: effects from four unfluoridated (left side)* and four fluoridated (right side) water supplies

(Adapted from: Connett P et al: The Case Against Fluoride. White River Junction, VT. Chelsea Green Publishing. 2010;38. Used with permission)

Conclusion

Key points in this fluoride review are that ~6% of the world’s population drinks fluoridated water. The action of fluoride is topical (directly on the teeth) not systemic (drinking it is not beneficial). Fluoride is a lipid soluble neurotoxin and enzyme poison. Fluoride accumulates in the pineal gland (average 9000 ppm in calcium hydroxy apatite crystals) and bone. Dental fluorosis is a marker for skeletal fluorosis. At 1 ppm, 32 % of US children have dental fluorosis. Even at 1 ppm some sections of the population (e.g. infants) will ingest too much fluoride. Unfluoridated and fluoridated countries have similar rates of tooth decay. Given that fluoridation of water supplies is not necessary (applying fluoride topically achieves the same effect) and since unfluoridated populations have roughly the same rate of tooth decay, it is no longer necessary to fluoridate water to maintain a reduction in tooth decay. It is also a matter of some urgency that better studies of the systemic effects of fluoride are carried out.

Competing Interests

The author declares that he has no competing interests.

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