Fluoride

Introduction

Most fluoride in the body is found in bones and teeth, due to its high affinity for calcium and calcium phosphate. Ingestion of and topical treatment with fluoride is effective in inhibiting or partly reversing dental caries. Fluoride deposition into the dental enamel in the form of acid-resistant fluoroapatite crystals, especially during pre-eruptive tooth development, has been a critical factor in reducing the incidence of dental caries during the last few decades. And because it can stimulate growth of new bone, fluoride has been used experimentally to treat osteoporosis (Institute of Medicine [IOM] 1997). Despite these well-documented beneficial effects, there is no scientific agreement that fluoride should be considered an essential element—in other words, necessary for the life of the individual and continuation of the species. Despite these limitations, fluoride clearly is a beneficial nutrient.

Safety Considerations

Fluoride toxicity is well known and has been extensively reviewed (Department of Health and Human Services [DHHS], Public Health Service 1991; IOM 1997; Environmental Protection Agency [EPA] 1987; European Food Safety Authority [EFSA] 2005). The critical adverse effects (i.e., those of significant adverse consequences and occurring at the lowest intakes) are dental fluorosis in children and skeletal fluorosis in adults. Excessive intake in children before their permanent teeth are fully formed can result in dental fluorosis that manifests mainly as mottled brown discoloration and some increase in fragility. Dental fluorosis has been studied in relation to both municipal drinking water fluoridation (for the anticariogenic effect) and naturally occurring high-fluoride water supplies. The maximum fluoride intakes by children that will safely avoid dental fluorosis depend on age and body size, as well as intakes of calcium and other nutrients.

Excessive intake of fluoride by adults results in skeletal fluorosis, which carries an increased risk of bone fracture. The IOM, however, may have somewhat underestimated the potential for fluoride to increase bone fracture risk—8 mg/day. Some epidemiological data suggest that an increased rate of bone fracture is associated with drinking water containing high fluoride concentrations (4 mg per L) and low drinking water calcium concentrations (15 mg per L) (DHHS 1991).

The epidemiological data do not present any clear pattern of association of fluoride intake with cancer risk (DHHS 1991; EFSA 2005). Animal studies are almost all negative for carcinogenicity of fluoride compounds found in water and food. The sole exception is the finding of "equivocal evidence" of carcinogenicity of sodium fluoride in the male Fisher 344/N rat based on an increased incidence of osteosarcomas (DHHS, National Toxicity Program [NTP] 1990). With the large number of studies performed, a single study that suggests possible significant effects is not surprising. No other data suggest an increased cancer risk related to fluoride consumption.

Official Reviews

IOM (1997). The IOM UL for adults, representing the level at which skeletal fluorosis may be avoided, is 10 mg per day, based on an adult NOAEL of 10 mg and an UF of 1.0. Such a UL was justified by the lack of change in skeletal density found at higher intakes. For younger age groups with incomplete dental enamel development and maturation, the IOM selected dental fluorosis as the critical endpoint. On the basis of dose-response relationship data that indicated lower NOAEL and LOAEL values for these younger age groups, the IOM identified correspondingly lower UL values (0.7 mg per day for infants 0 to 6 months; 0.9 mg for 7 to 12 months; 1.5 mg for 1 to 3 years; and 2.2 mg for 4 to 8 years).

Expert Group on Vitamins and Minerals (EVM 2003). The UK's EVM considered fluoride for evaluation but declined to review it or offer an opinion because "it is inappropriate to comment on fluoride with regard to food fortification since this [the fluoridation of drinking water] is carried out as a public health measure."

EFSA (2005). The EFSA opinion on fluoride safety was published in 2005, with different UL values for different age groups. For younger children, the critical endpoint for the derivation of the UL was moderate enamel fluorosis, which occurred in less than 5 percent of populations at fluoride intakes of 0.1 mg per kg per day. No UF was applied as the intake was derived from population studies in the susceptible group. Calculated on a body weight basis, the UL was 1.5 mg per day for children ages 1 to 3 years and 2.5 mg per day for children ages 4 to 8 years. For children older than 8 years and adults, the UL was derived from therapeutic studies suggesting an increased risk for skeletal fractures at or above fluoride intakes of 0.6 mg per kg per day. With the application of a UF of 5 to account for the short duration and design of the studies, the UL was determined to be 5 mg per day for children 9 to 14 years and 7 mg per day for individuals 15 years and older.

CRN Recommendations

High intakes of fluoride can have adverse effects on the kidneys and the immune, gastrointestinal, genitourinary and respiratory systems. All of these effects occur at intakes higher than those that may cause skeletal fluorosis and possibly increase bone fracture risk. Thus, none can be considered the critical effect for identifying an UL. Instead, CRN, in agreement with the IOM and EFSA, identifies skeletal fluorosis as the critical effect in the evaluation of fluoride safety for adults.

The data associated with a daily intake of 1.5 L of fluoridated drinking water suggest that an increased risk of fracture related to skeletal fluorosis might occur with intakes of 6 mg of fluoride or more per day from this source. Thus, if the fluoride intake from foods and nonfluoridated water is approximately 1 mg per day, and the intake from fluoridated toothpaste is approximately 1 mg per day, the addition of these quantities to the 6 mg per day for high-fluoride water suggests that a total intake of 8 mg per day increases the risk of bone fracture in persons whose drinking water has low calcium concentrations. The adult LOAEL, then, is 8 mg per day. This contrasts with the IOM adult NOAEL of 10 mg per day. A UF of 1.3 is adequate for application to a conservative LOAEL, particularly given the IOM's selection of an UF of 1.0

for a NOAEL of 10 mg (producing a calculated UL of 10 mg). Therefore, CRN's calculated UL is 6 mg. CRN does not identify a ULS for adult fluoride supplementation.

Quantitative Summary for Fluoride

CRN UL, total intake	6 mg/day
IOM UL, total intake	10 mg/day
EFSA UL, total intake	7 mg/day
EC supplement maximum	Not determined
EVM SUL and guidance level	Not determined

References

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