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Fluoride content of infant formulas: soy-based formulas as a potential factor in dental fluorosis

M. Carole McKnight-Hanes, DMD Dennis H. Leverett, DDS, MPH
Steven M. Adair, DDS, MS Carol P. Shields, MS

Abstract

Recent reports of an increased prevalence of dental fluorosis in fluoridated and nonfluoridated communities have led to a reassessment of the amount of fluoride (F) being ingested by infants and young children. Manufacturers of milk-based formulas have taken steps to reduce the F concentration to negligible levels. Reduction of F concentration in soy-based formulas is more difficult because of F binding to phytate and tricalcium phosphate. This study assessed the F content of 3 milk-based and 4 soy-based infant formulas.

Three types of preparations in each brand were tested: ready-to-feed, liquid concentrate, and powdered concentrate. Concentrates were diluted according to the manufacturers' recommendations with water containing various concentrations of F. The ionic F was measured using an ion-specific electrode. Acid-diffusable F was measured after separation by the Taves method.

Soy-based formulas contained higher levels of F than their milk-based counterparts. In the case of ready-to-feed and liquid preparations the differences were statistically significant. The mean F concentrations for soy-based products were: ready-to-feed, 0.30 mg/l; liquid concentrate diluted with deionized water, 0.24 mg/l; and powdered concentrate diluted with deionized water, 0.08 mg/l. Both soy-based ready-to-feed and diluted liquid concentrate formulas provide daily F dosages which, in combination with supplemental dietary F (0.25 mg/day), exceed the currently defined norms for optimum daily F intake.

Recent reports have described an increased prevalence of dental fluorosis in children's teeth in both fluoridated and nonfluoridated communities (Aasenden and Peebles 1974; Forsman 1977; Messer and Walton 1980; Leverett 1982, 1986) greater than that reported in the early studies of Dean et al. (1942). Soparkar and DePaola (1985) reported finding an unexpectedly high number of school children with dental fluorosis residing in nonfluoridated areas of Massachusetts. Leverett and Levy (1983) reported similar findings in children of both fluoridated and nonfluoridated communities in an earlier study. Horowitz et al. (1984) speculated that the increased prevalence of dental fluorosis in younger children could be related to infant formulas and other foodstuffs processed with fluoridated water. Studies have indicated that in several species, including humans, a daily fluoride (F) intake of 0.1 mg/kg body weight during the period of enamel calcification is sufficient to cause mild dental fluorosis (Forsman 1977; Suttie et al. 1972). It should be emphasized that the levels of fluorosis reported by these investigators are in the very mild and mild categories described by Dean et al. (1942) and are, for the most part, not discernable by the layman.

Prior to 1978, Adair and Wei (1978), Stamm and Kuo (1977), and Singer and Ophaug (1979) found great variability in the F content of infant formulas. The concentrations ranged from 0.08 to 0.78 mg/l F for ready-to-feed milk-based formulas and from 0.31 to 0.92 mg/l in ready-to-feed soy-based formulas. Changes in the manufacturing process have subsequently led to a reduction in the amount of F in milk-based formulas to a considerably lower level. Because soy-based infant formulas contain phytates and tricalcium phosphates, both of which bind F, the potential for larger than optimum dosage of F for infants using soy-based formulas still exists.

A recently published study which evaluated the F content of infant formulas purchased in various geographic regions of the United States (Johnson and

Bawden 1987) indicates that the F concentration of infant formulas has been reduced from that reported for some products prior to 1980. This study reported higher F concentrations in all the groups of soy-based formulas that were tested compared to the milk-based formulas tested. Several studies have evaluated the dietary F intake of infants (Stamm and Kuo 1977; Adair and Wei 1978; Singer and Ophaug 1979; Ophaug et al. 1985). Most recently, Ophaug et al. (1985) reported findings based on the analysis of market basket food collections in 4 dietary regions of the United States. Their data indicated that the average dietary F intake of 6-month-old infants did not exceed 0.52 mg/kg, however. This study did not include soy-based formulas in the composite groups analyzed.

Recent surveys conducted at the Eastman Dental Center of parents of 6- and 7-year-old children indicate that approximately 15% of the children were fed soy-based formula as infants. The current philosophy regarding choice of formula for infants seems to support changing an infant to soy-based formula at the first indication of any problem with feeding (Hill et al. 1984; Gillooly et al. 1984; American Academy of Pediatrics Committee on Nutrition 1983). If a familial history of food allergies exists, infants sometimes are started out on soy-based formulas. In light of this information and as a part of a larger study evaluating the prevalence of, and possible explanations for, dental fluorosis, the aim of the present study was to evaluate and compare the F content of several milk-based and soy-based infant formulas.

Materials and Methods

Three types of milk-based and soy-based infant formulas were analyzed: ready-to-feed — canned liquid formula ready for direct feeding without dilution; diluted liquid concentrate — canned liquid formula diluted 1:1 with water prior to feeding; and diluted powder concentrate — dry formula prepared with a standard dilution of 1 scoop powder for each 2 ounces of water. The formulas were prepared according to manufacturers' recommendations prior to analysis and were diluted with water containing various concentrations of F, depending on the purpose of the analysis. The six types of formulas tested were:

Ready-to-feed, milk base (RF-M)
Ready-to-feed, soy base (RF-S)
Liquid concentrate, milk base (LC-M)
Liquid concentrate, soy base (LC-S)
Powder, milk base (P-M)
Powder, soy base (P-S).

The specific brand of each type of formula was selected on the basis of its availability in a variety of grocery stores and pharmacies in the Rochester, New York area. The brands of milk-based formula tested were: RF-M — Similac® (3 samples), SMA + iron® (2 samples), and Enfamil® (3 samples); LC-M: SMA + iron (2 samples) and Enfamil (3 samples); P-M: Enfamil (3 samples).

The brands of soy-based formulas tested were: RF-S: Prosobee® (6 samples), Nutrimigen® (4 samples), and Isomil® (6 samples); LC-S: Prosobee (5 samples), Isomil (3 samples), and Nursoy® (3 samples); P-S: Prosobee (3 samples) and Isomil (3 samples).

Fluoride was separated from 3 ml of the prepared infant formulas as hydrofluoric acid (HF), appropriately buffered, and analyzed directly using a fluoride combination electrode (Model 96-09 — Orion Research Inc; Orion, MA). The Taves (1968) separation method was employed to separate the acid-diffusable F from the sample.

A calibration curve was constructed of standards (dilutions from NaF primary standards) and the reagent blank, all of which had undergone sample separation. The reagent blank was low, 0.02 μg F (± .005 SE), and was subtracted from all standards and unknowns.

Each of the samples was analyzed in triplicate, with results presented as mg F/l of sample (weight/volume). Student's *t*-test was used to determine statistical significance of the findings.

Results

Table 1 shows the results of the F analyses of 3 milk-based and 4 soy-based formulas for F, after the formulas had been prepared according to manufacturers' directions using deionized water. Each cell represents at least 3 replications. Table 2 shows the mean concentrations of F in the formulas tested (mg/l), according to formula type and diluent. The mean F levels for the milk-based formulas tested were 0.127 ± 0.029 for RF-M, 0.121 ± 0.018 for LC-M, and 0.055 ± 0.009 for PC-M when the latter 2 were diluted with deionized water. The mean F levels of the soy-based formulas were 0.305 ± 0.083 mg/l for RF-S, 0.242 ± 0.078 mg/l for LC-S and 0.084 ± 0.021 mg/l for P-S, when the latter 2 were diluted with deionized water. There was a significantly greater amount of acid-diffusable F in both RF-S ($t = 3.3$, $P < 0.01$) and LC-S ($t = 2.9$, $P < 0.02$) than in the corresponding M preparations. The P-S also had more F than the P-M, although the difference was not statistically significant ($t = 1.4$, NS).

Based on the amount of F found in the various formulas, the average daily F intake from each of the formula types was calculated for a 3-month-old male and a 6-month-old male. The National Research Council's 1980 monograph on recommended dietary allowances shows the 50th percentile weight for 3-

TABLE 1. Fluoride Content of Tested Formulas (Mean mg/1 ± S.E.)

Formulas	Ready-to-Feed (RF)	Diluted* Liquid Conc. (LC)	Diluted* Powder Conc. (P)
Milk-Based (M)			
Similac®	.122 ± .027	–	–
SMA (+ iron)	.094 ± .0005	.139 ± .009	–
Enfamil®	.166 ± .077	.103 ± .024	.055 ± .009
Soy-Based (S)			
ProSobee®	.345 ± .070	.152 ± .042	.104 ± .028
Nutramigen®	.381 ± .092	–	–
Isomil®	.190 ± .037	.231 ± .017	.063 ± .017
Nursoy®	–	.344 ± .045	–

* Formulas were prepared according to manufacturers' directions using deionized H_2O.

TABLE 2. Mean Fluoride Concentrations of Formulas Tested (mg/1) According to Formula Type and Diluent

Formula Type	Deionized Water	0.15 ppm F Water	1.0 ppm F Water	Student's t-Test
RF-M	0.127*	–	–	$t = 3.3$
RF-S	0.305*	–	–	$P < 0.01$
LC-M	0.121	0.196	0.621	$t = 2.9$
LC-S	0.242	0.317	0.742	$P < 0.02$
P-M	0.055	0.170	0.825	$t = 1.4$
P-S	0.084	0.200	0.854	N.S.

* Undiluted.

month old males to be 5.98 kg and for 6-month-old males to be 7.85 kg. Energy intakes have been surveyed in the United States, United Kingdom, Canada, and Sweden, for infants growing along the 50th percentile World Health Organization reference standard (WHO 1985). The daily intake of infants 2-4 months of age averaged 104 kcal/kg body weight, while the average daily intake of 5-7 month olds was 92 kcal/kg. We have chosen to use 100 kcal/kg as the basis for our intake estimates. Thus, a 3-month-old male is estimated to consume 598.0 kcal per day, or about 30 ounces (0.89 l) of formula. The corresponding intake for 6-month-old infants is 785 kcal per day, or about 32 ounces (0.95 l).

Based on the calculations of mean daily formula intake and F concentrations of the formulas, Figure 1 shows the mean daily F intake for a 3-month-old male. The optimum daily dosage of F generally is considered to be 0.05-0.07 mg F/kg of body weight (Farkas and Farkas 1974; Toth 1975). For the average 3-month-old male, this would be the equivalent of 0.30-0.42 mg of F per day, and is shown between two horizontal lines in Figure 1. Because both the American Dental Association (ADA) and the American Academy of Pediatrics (AAP) recommend dietary F supplementation of 0.25 mg daily at this age in communities with < 0.3 ppm F in the

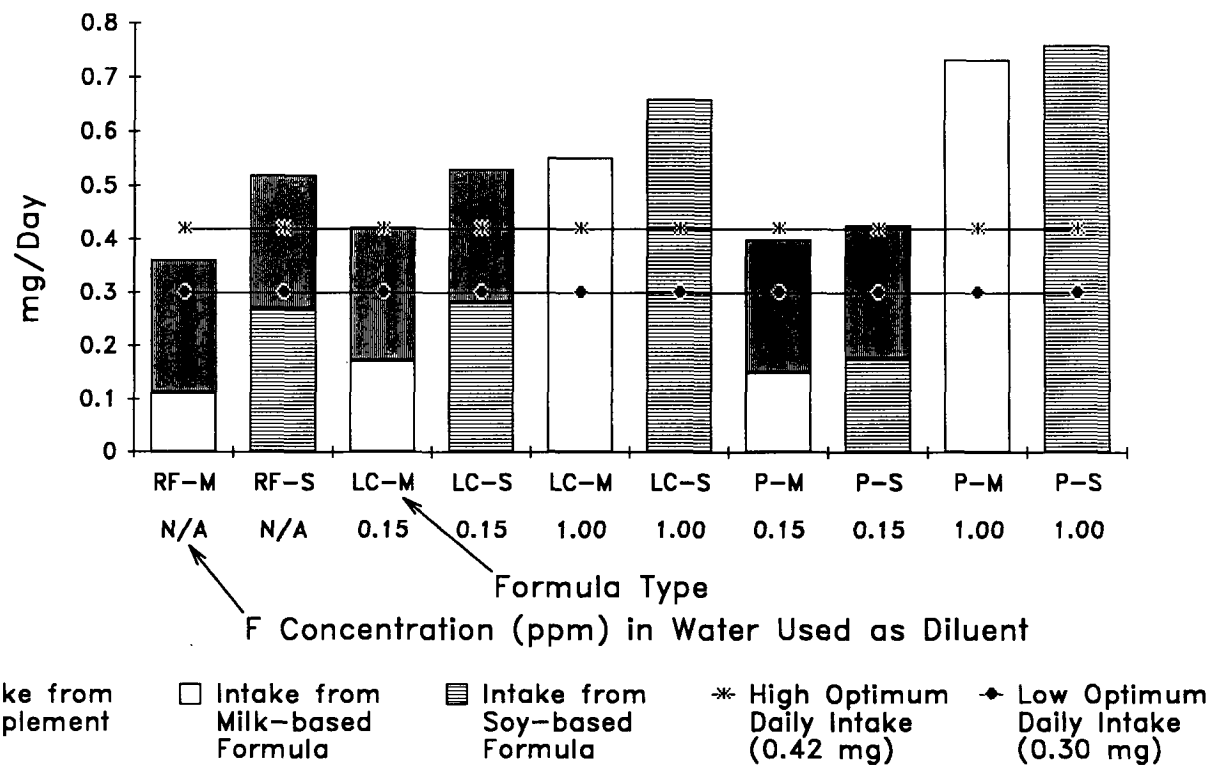

FIG 1. Mean daily fluoride intake — 3-month-old male.

drinking water, we have added that amount of additional F to all bars in Figure 1 except those with 1.0 ppm F in the water. As can be seen, optimum daily F consumption is exceeded with every type of formula tested except for RF-M and P-M with 0.15 ppm F in the water. S formulas always exceeded M formulas in F content. Although formulas diluted with optimally fluoridated water clearly provide the largest mean daily F intake, only the RF-M and the P-M diluted in 0.15 ppm F water provided nearly the optimum daily F intake when the 0.25 mg/day F supplement was added.

Figure 2 shows the mean daily F intake for a 6-month-old male. In this case the optimum F intake is 0.39-0.55 mg F per day. Again, the formulas mixed with optimally fluoridated water provide the highest mean daily F intake, almost double the optimum. Using water with low F content or using the RF formulas, both the M and S formulas tend to provide around the optimum amount of F, with the S formulas exceeding the M formulas.

Discussion

A degree of intra- and interbrand variability was found among the milk-based formulas. Variability of F content with milk-based formulas can be explained partially by the nature of the manufacturing process. Some milk-based formulas are prepared from nonfat dry milk, while others use liquid skim milk as their base (Adair and Wei 1978). The source of the milk base used in manufacturing results in differences in final F content.

Both inter- and intrabrand F content variability were greater among the soy-based formulas than among the milk-based formulas. The variability of the soy-based formulas probably relates to varying amounts of phytate and tricalcium phosphate (both of which bind F) used in the formulation (Adair and Wei 1978). It is important to note that all the S formulas had higher F levels than any of the M formulas (Table 2).

It should also be noted that LC-M and LC-S formulas contain higher levels of F than the P-M and P-S formulas (Table 2). This leads to speculation that liquid (presumably water) used to prepare the LC formulas contains F. As pointed out by Johnson and Bawden (1987), the F content of the water used in manufacturing this formula may vary from 0.2 to 0.4 ppm.

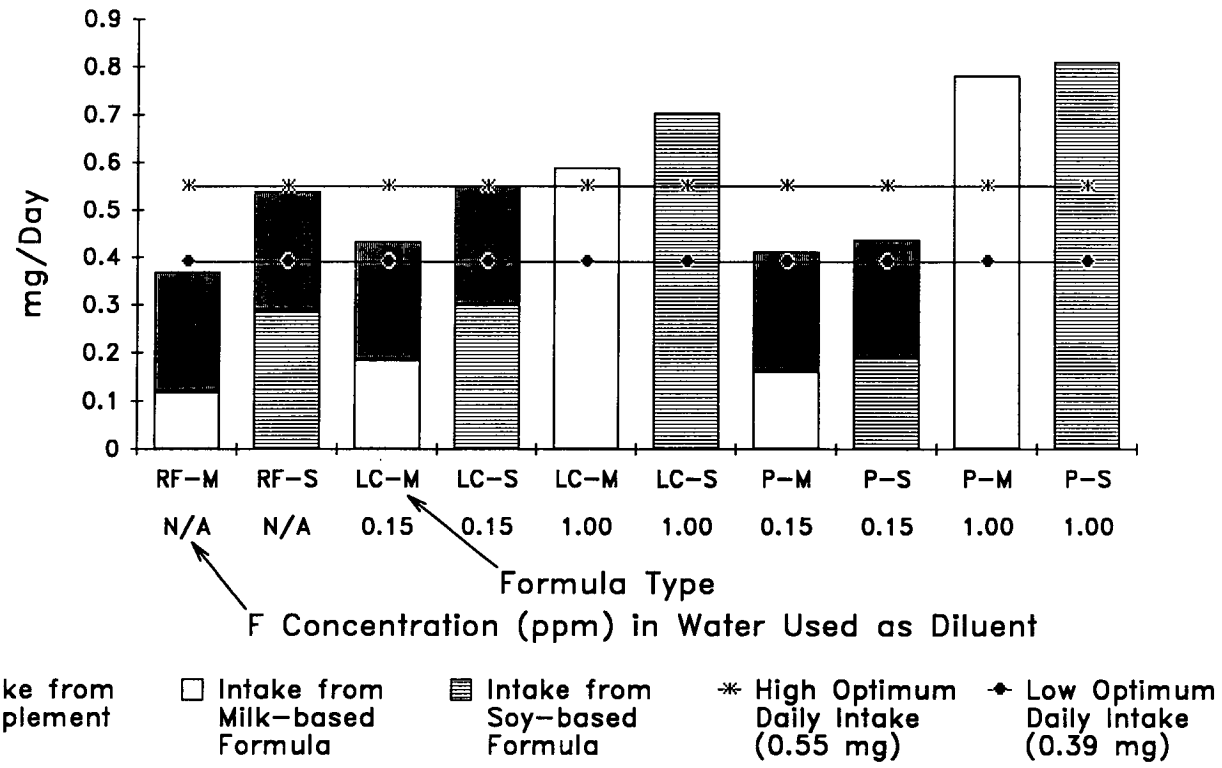

FIG 2. Mean daily fluoride intake — 6-month-old male.

The results of this study are consistent with those reported by Johnson and Bawden (1987) with the exception of one product (Nursoy-LC). The sample in this study was found to have considerably more F (0.344 mg/l) than the highest F concentration found for Nursoy-LC (0.15 mg/l) by Johnson and Bawden. Due to this discrepancy, another Nursoy-LC sample was purchased in Augusta, Georgia, and analyzed for F content in the same laboratory and in the same manner as the other samples. The mean F concentration for this sample was 0.36 mg/l F.

The bioavailability of F is more important in considering fluorosis than the amount of F in the infant formula. Studies have been done with M infant formulas to assess the bioavailability of the F content (Spak et al. 1982; Ekstrand et al. 1984). Fluoride diffuses out of the stomach into the blood as a weak acid, HF, which has a pKa of 3.45 (Ekstrand 1984). The diffusion of HF is probably dependent upon access to the mucosal surface of the gastrointestinal tract (Toothaker 1980). Ericcson (1958) speculated that coagulation of milk in the stomach and formation of calcium F might decrease the absorption rate. Ekstrand et al. (1984) illustrated, by way of fecal output data (10% of ingested F found in feces), that the bioavailability of F from milk-based formula to young infants (2-4 months) was fairly high. From these studies one might speculate that the bioavailability of F from S formulas, when used as the sole source of nutrition, could be as high and possibly higher than the bioavailability of F from M formulas. S formula would have good access to the mucosal surfaces of the gastrointestinal tract, less tendency toward coagulation and, possibly, a consequently higher absorption rate. Further studies are needed to determine the actual bioavailability of S formulas.

As previously stated, the optimum daily intake of F is approximately 0.05-0.07 mg F/kg of body weight (Farkas and Farkas 1974; Toth 1975). For a 3-month-old male weighing 5.98 kg, the optimum F dosage would be between 0.30 and 0.42 mg/day. For a 6-month-old male weighing 7.85 kg the optimum daily F ranges between 0.39 and 0.55 mg/day. This has important implications when the F content of the drinking water is considered together with infant formulas and dietary F supplements.

In areas with low levels of F in the drinking water, dietary F supplementation is frequently recommended. The daily dietary F supplementation level recommended by the ADA Council on Dental Therapeutics (1984) for infants younger than 2 years of age is 0.25 mg F. This schedule is also recommended by the AAP (1979). As a result, infants receiving daily dietary F supplementation and almost any one of the formulas tested could be receiving higher than optimum dosages of F. Based on mean F levels, the dosage for either a 3- or 6-month-old male residing in a nonfluoridated community could be as high as 0.55 mg/day. This dosage exceeds the optimum daily F dosage based on weight (0.30-0.42 mg) for a 3 month old. For a 6 month old the intake falls at the high end of the range of optimum F dosage (0.39-0.55 mg). In fluoridated communities, without dietary F supplementation, the F dosage is even higher, up to 0.81 mg for a 6-month-old male.

By 6 months of age many infants are receiving more nutrition from sources other than formula, with a concomitant decrease in formula intake. At that age the solid diet may be contributing more or less F per day than the formula, depending upon the types and quantities of infant foods and water being consumed. Ophaug et al. (1985) found F intake for 6-month olds to range from a minimum of 0.097 mg/day to a maximum of 0.65 mg/day. Again, infants at the higher end of the range are receiving larger than optimum daily F dosages.

Considering the significant differences found between the F content of S formulas (LC and RF) and that of M formulas (LC and RF), the type of formula consumed becomes a factor in recommending supplemental dietary F. Supplemental dietary F often is recommended from birth for fully breast-fed infants (Adair and Wei 1978), for infants fed only cow's milk (Stamm and Kuo 1977), and for infants in whom future delivery of dental care may be a problem, i.e., handicapped children (Nowak 1976). Infants in areas naturally low in water F also are given dietary F supplements, but due to the potential risk of dental fluorosis, the nature of the infant's diet (type of formula, amount of formula consumed daily, F level of the drinking water, etc.) should be ascertained before recommending dietary F supplementation. The findings of this study, if substantiated by other investigators, reinforce the suggestion (Leverett 1982; Cutress et al. 1985) that we need to reconsider our definition of optimum F ingestion and/or optimum concentrations of F in current modes of administration.

Summary

Soy-based ready-to-feed and diluted liquid concentrate formulas were found to contain significantly higher levels of F than milk-based formulas. These findings, coupled with the potential bioavailability of the F in soy-based formulas, suggest that infants consuming soy-based (and some milk-based) formulas, along with supplemental dietary F, are receiving larger than optimum daily dosages of F, given currently defined norms for F dosage.

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Dr. McKnight-Hanes is an assistant professor, pediatric dentistry, Medical College of Georgia. Dr. Leverett is chairman, community dentistry, Dr. Adair is chairman, pediatric dentistry, and Mrs. Shields is a research associate, oral biology, Eastman Dental Center, Rochester, New York. Reprint requests should be sent to: Dr. Dennis H. Leverett, Chairman, Dept. of Community Dentistry, Eastman Dental Center, 625 Elmwood Ave., Rochester, NY 14620.

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