

XII. BIOLOGICAL AND HEALTH EFFECTS

Combined Summary and Conclusions

Toxicology of Atmospheric Degradation Products of Selected Hydrochlorofluorocarbons

Laurence S. Kaminsky
Department of Environmental Health & Toxicology
School of Public Health
State University of New York at Albany
Empire State Plaza
Albany, NY

*Assessment of Effects on Vegetation of Degradation Products from Alternative
Fluorocarbons*

D. C. McCune and L. H. Weinstein
Boyce Thompson Institute for Plant Research
Ithaca, NY

COMBINED SUMMARY AND CONCLUSIONS

There is a need for more information on exposure, especially to organic breakdown products. This should include estimates of ground level concentrations, modes of deposition (wet & dry) and should extend to identification of half-lives in soil and water, and the products of microbial transformation.

Nothing is known of the toxicology to humans, animals or plants of any of the organic breakdown products other than trifluoroacetic acid. It was considered dubious to extrapolate from analogous compounds (e.g. trichloroacetic acid). The limited work on toxicology of TFA was with very high concentrations compared with those potentially arising from HCFC's and CFC's. Studies should aim to determine the long-term threshold level for toxicological effects.

One of the major uncertainties is the fate of $-CF_3$ as there is conflict of opinion about the stability of the C-F bond. The biological evidence (from toxicology and pesticide biochemistry) indicates that $-CF_3$ is recalcitrant and may persist in the environment but an opinion was expressed that there may be significant chemical defluorination at room temperature. Because of the mammalian toxicity of monofluoroacetate, the possibility of defluorination of trifluoro- to monofluoro- needs to be firmly clarified.

In contrast with position regards organic products, and notwithstanding uncertainties about rates of deposition, it can be stated with a high degree of confidence that inorganic fluoride (HF) does not present a significant risk to human, animals, plants, or soil.

Likewise HCl is of no direct risk to humans, animals or plants. Acidity from inorganic acids or as a result of mineralization of organic products does not add any significant burden to the environment in the form of acide deposition.

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**TOXICOLOGY OF ATMOSPHERIC DEGRADATION PRODUCTS
OF SELECTED HYDROCHLOROFLUOROCARBONS**

Laurence S. Kaminsky

**Department of Environmental Health & Toxicology
School of Public Health
State University of New York at Albany
Empire State Plaza
Albany, NY 12201**

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EXECUTIVE SUMMARY

The potential environmental degradation products of the hydrochlorofluorocarbons are trifluoroacetic acid (TFA), mixed fluorochloroacetic acids, and hydrofluoric acid. There is no available toxicologic data on mixed fluorochloroacetic acids. The additional fluoride burden, arising from environmental degradation of hydrochlorofluorocarbons, (1 to 3 ppb) in rainwater is trivial compared to levels in fluoridated drinking water (1 ppm), and would provide an insignificant risk to humans.

Overall there is sparse available toxicologic data on TFA. The acute lethality of TFA in mice suggests that it is only slightly toxic, and that its lethal effects at high doses are not dependent on its metabolism.

While a no adverse effect level has not been determined, 240 mg TFA/kg in rats produced no bone marrow or small intestinal effects, 25 mg TFA/kg produced no body weight gains, relative testis weight gains, or testicular histologic changes in rats, and 2000 mg/kg every second day for 14 days in mice produced no hepatic necrosis, or heart and kidney histological changes.

TFA at 2000 mg/kg in mice significantly decreased hepatic NADPH and reduced glutathione levels, but after 24-hr both levels returned to normal. Administration of 150 mg TFA/kg/day for 5-6 days to rats decreased the hepatic glycogen content by 24%, the percent liver/body weight by 43%, hepatic pyruvate kinase activity by 42%, and increased hepatic glycerol 1-phosphate oxidase activity by 125%. Thus the lowest dose at which effects have been reported is 150 mg/day for 5-6 days.

TFA is not mutagenic, but no carcinogenicity data is available. However, trichloroacetic acid is hepatocarcinogenic in mice, although it is also not mutagenic in the Ames assay. While no chronic toxicity data on TFA is available it appears likely that on the basis of its resistance to metabolism, rapid clearance, lack of mutagenic potential, and low acute toxicity TFA is unlikely to exhibit significant chronic toxic effects. For a more complete assessment of TFA toxicity chronic studies are required, as well as acute studies in species other than the mouse. The potential for TFA to act as a peroxisome proliferator should be investigated, to gain insight into its hepatocarcinogenic potential.

A German Senate Commission for the Evaluation of Health Hazards in the Work Environment has recommended that a blood TFA level of 2.5 µg/ml is risk-free. However, the assessment has no experimental or epidemiologic basis.

BIOLOGICAL AND HEALTH EFFECTS

1. INTRODUCTION

Trifluoroacetic acid (TFA) is a liquid bp 72.4°C, mp 15.4°C, with a sharp biting odor. It has been proposed as the product of environmental degradation of the hydrochlorofluorocarbons HCFC-123, HCFC-124, HFC-134a, and HFC-125. Compounds HCFC-141b and HCFC-142b could yield mixed fluorochloroacetic acids, for which there is no available toxicologic data. The release of hydrochlorofluorocarbons into the environment could also give rise to HF, but the additional fluoride burden (1 to 3 ppb) in rainwater is trivial compared to levels in fluoridated drinking water (1 ppm), and would provide an insignificant risk to humans (Murray, 1986; World Health Organization, 1984; US EPA, 1986). Thus, in this paper only the toxicologic data on TFA is reviewed to assess the potential risks of environmental exposure.

Pharmacokinetics

There is little or no available data on the absorption, disposition, and elimination of TFA. In healthy human volunteers the half-life for renal excretion of TFA administered intravenously is 16 hr (Holaday and Cummah, 1976). In patients receiving halothane anesthesia the resultant metabolically-formed TFA had a half-life in the blood of 52-60 hr (Dallmeier and Henschler, 1977).

For rats (200-260 g) administered 1.3 mmol TFA/kg/day (150 mg TFA/kg/day) for 5 days the plasma TFA levels ($\mu\text{mol/ml}$ blood) were 0.7 and 0.75 after 1 day, 0.8 and 1.0 after 2 days, 1.1 and 1.25 after 3 days, 1.06 and 0.6 after 4 days, and 1.3 and 1.1 after 5 days. Each value represents a single estimation and results are for two different animals at each time point (Stier et al., 1972). The average TFA concentration in the livers of these animals was 1.1 $\mu\text{mol/g}$ liver. These values represent approximately 10% of the administered dose of TFA in the liver and 10% in the plasma (Stier et al., 1972).

TFA is not metabolized to any significant extent by rats (Fraser and Kaminsky, 1988). In humans TFA is not metabolized and is quantitatively excreted in urine (D.A. Holaday and R. Cummah, personal communication reported in Fiserova-Bergerova, 1977). Fluoro substituents, when constituents of a trifluoromethyl group, are metabolically stable relative to monofluoro substituents. Thus TFA is not metabolically defluorinated, in contrast to fluoroacetic acid, which has been demonstrated to be defluorinated by the rat hepatic microsomal system (Smith et al., 1977; Kostyniak et al., 1978).

Acute Toxicity

The majority of studies on TFA toxicity involve acute administration. Several LD₅₀ values have been reported. For male Swiss-Webster, albino mice administered sodium trifluoroacetate intraperitoneally, values of > 400 mg/kg (> 2.9 mmol/kg) (Rosenberg, 1971), > 2000 mg/kg (> 14.7 mmol/kg) (Airaksinen and Tammisto, 1968), > 5000 mg/kg (> 37 mmol/kg) (Blake et al., 1969), and > 2000 mg/kg (> 14.7 mmol/kg) (Airaksinen et al., 1970) were obtained. TFA itself produced death in two of five mice treated intraperitoneally at 150 mg/kg (1.1 mmol/kg), probably as a consequence of its acidity (Blake et al., 1969). The LD₅₀ of sodium trifluoroacetate when administered intravenously to mice was 1,200 mg/kg (10.5 mmol/kg) (Airaksinen and Tammisto, 1968). Preadministration of phenobarbital (40 mg/kg/day) for three days, or L-cysteine, isoniazid, ethanol, 4-iodopyrazole, or allopurinol administration 10 min before and 3 hr after sodium trifluoroacetate administration did not affect its LD₅₀, suggesting that the acetate was not being metabolized to toxic products (Airaksinen et al., 1970). Acute lethalties of the ord-

er reported for TFA, categorize it as a "slightly toxic" substance (Klaasen et al., 1986). Other toxic endpoints, primarily involving effects on metabolic activity, have also been investigated. Sodium trifluoroacetate in saline was administered by a single injection intraperitoneally to Swiss, albino, male mice (17-20 g) (Rosenberg, 1971). By 12-hr after administration of 2000 mg/kg (14.7 mmol/kg) the concentration of the coenzyme NADPH in the liver was statistically significantly decreased from 0.44 to 0.25 $\mu\text{mol/g}$. The decreased levels returned to normal by 24-hr after administration (Rosenberg, 1971). Reduced glutathione levels in the livers were also statistically significantly decreased from 4.33 to 3.94 $\mu\text{mol}/100\text{ mg}$ at 12-hr after administration and by 24-hr these levels had also returned to normal (Rosenberg, 1971).

Male Wistar rats (200-260 g) were administered TFA in the drinking water for 5-6 days, equivalent to a dose of 150 mg TFA/kg body weight/day (1.3 mmol TFA/kg body weight/day) (Stier et al., 1972). In TFA-treated rat liver relative to untreated rat liver, the soluble protein increased by 6%, the glycogen content decreased by 24%, the neutral fat increased by 10% and the percent liver weight to body weight by 43%. None of these effects were evaluated for statistical significance. A number of enzyme activities in liver of TFA-treated animals was altered relative to control rat livers: pyruvate kinase decreased by 42%, phosphoglycerate kinase decreased by 10%, glycerol 1-phosphate oxidase increased by 125%, glycerol-phosphate dehydrogenase decreased by 4%, malic enzyme increased by 4%, glucose 6-phosphate dehydrogenase decreased by 17%, glyceraldehyde 3-phosphate dehydrogenase decreased by 4%, enolase decreased by 7%, malate dehydrogenase decreased by 10%, isocitrate dehydrogenase decreased by 10% and NADPH-oxidase increased by 7%. Again differences were not evaluated for statistical significance and it is doubtful whether any of the activities, with the possible exception of pyruvate kinase and glycerol 1-phosphate oxidase, were significantly affected.

In several studies TFA has been administered to animals, but without producing the certain specific effects which were sought. However, there has been no systematic attempt made to determine a no adverse effect level for TFA. TFA was neutralized in water and administered orally in a single dose to ten-week-old male Alpk/AP strain rats (Lloyd et al., 1988; Lloyd et al., 1986). At doses of 10 or 25 mg/kg (0.09 or 0.22 mmol/kg) body weight gains and relative testis weight were not affected, and no histological changes were noted in the testes relative to untreated controls (Lloyd et al., 1988; Lloyd et al., 1986). Equivalent doses of 2,2,2-trifluoroacetaldehyde and 2,2,2-trifluoroethanol significantly reduced body weight gain and relative testis weight, and produced histologically-detectable testicular damage.

When TFA (240 mg/kg, 2.1 mmol/kg) was administered intravenously to male Wistar rats no bone marrow or small intestinal toxicity was detected (Fraser and Kaminsky, 1988). The metabolic precursors of TFA, 2,2,2-trifluoroethanol and 2,2,2-trifluoroacetaldehyde, at equimolar doses produced significant decreases in intestinal dry weight and leukocyte counts (Fraser and Kaminsky, 1988).

Swiss male mice (17-20 g) were injected intraperitoneally with sodium trifluoroacetate at 1000 mg/kg (7.4 mmol/kg) and killed 24 hr later, at 2000 mg/kg (14.7 mmol/kg) and killed at 12 or 24 hr later, at 2000 mg/kg (14.7 mmol/kg) every second day for 14 days and killed on the 14th day (Rosenberg and Wahlstrom, 1971). There were no TFA-induced histological changes in hearts or kidneys of any of the treated mice. At the lowest dose of sodium trifluoroacetate (1000 mg/kg) histological changes in the liver were noted including a cloudy swelling of the hepatocytes with a slight fat accumulation. At the higher dose (2000 mg/kg) vacuolization of the hepatocytes was detected at all time periods (Rosenberg and Wahlstrom, 1971). However, even after multiple doses no hepatic necrosis was detected.

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Mutagenicity

TFA has been tested for mutagenicity in the Ames bacterial assay using two histidine-dependent strains of *Salmonella typhimurium*, TA98 and TA100 (Baden et al., 1976). TFA (150 mg/plate, 1.32 mmol/plate) was incubated in an agar-overlay assay at 37°C for 2 days without a microsomal activating system. No indication of mutagenicity was obtained under conditions where a positive control (N-methyl-N'-nitro-N-nitrosoguanidine) was highly mutagenic. This lack of mutagenicity of TFA was confirmed under similar conditions (Waskell, 1978). In a third study sodium trifluoroacetate was not mutagenic with *Salmonella typhimurium* TA98, TA100, and TA1535 at all concentrations used up to 35.7 mg/ml (0.26 mmol/ml), in the presence or absence of polychlorinated biphenyl (Aroclor 1254)-induced rat liver or testes post mitochondrial supernatants (Blake et al., 1981). The concentration of TFA in these assays was the maximum non-toxic concentration for the bacteria.

It is important to note that while trichloroacetic acid has also been found to be nonmutagenic in the Ames assay (Rapson et al., 1980; Waskell, 1978), it is a hepatocarcinogen in mice (Herren-Freund, 1987). Trichloroacetic acid has been demonstrated to produce peroxisome proliferation in mice (DeAngelo et al., 1986), which has been proposed as one of the mechanisms of hepatocarcinogenesis (Reddy et al., 1980), although it is questionable whether this mechanism applies in humans (Elcombe et al., 1985). Based on these reports the potential of TFA to act as a peroxisome proliferator should be investigated to gain insight into its potential as a hepatocarcinogen.

In Vitro Toxicology

TFA at 4 mM (450 mg/l) reduced the binding of the drugs warfarin and phenytoin to human serum albumin to 56% and 85% of controls, respectively. TFA at 10 mM (1140 mg/l) correspondingly reduced the binding to 44% and 77% (Dale, 1986). The results suggest that TFA generally affects the conformation of the albumin. The potential of TFA to produce metabolic disturbances was tested in vitro in cultured Morris rat hepatoma 7288C cells (Ishii and Corbascio, 1971). TFA (2.0 mM, 230 mg/l) did not affect uridine or thymidine uptake, while at 10 mM (1140 mg/l) leucine and acetate uptake by the cells was not affected. Thus at these concentrations DNA, RNA, protein and lipid synthesis by the cells was not affected.

When TFA was infused at 200 μ mol/hr into 100 ml of perfusion medium for an isolated perfused rat liver the levels of lactate and pyruvate decreased after 10 min (Stier et al., 1972). TFA produced a higher uptake and turnover of lactate and pyruvate. This result is unusual in that fluorinated compounds usually inhibit rather than accelerate metabolic processes.

Antigenicity

Aqueous solutions of chicken serum globin (10-15 mg/ml) and TFA (1.2 M) were mixed in a ratio of 1 to 1.5 at 4°C for 15 min. The mixture was dialyzed against water and lyophilized to produce a complex of TFA and chicken serum globin, which was used to immunize rabbits (Rosenberg and Wahlstrom, 1973). Under these conditions TFA acted as a hapten and elicited antibodies. The clinical significance of this observation is unknown.

Analysis

Several methods are available for the analysis of TFA in biological material. In urine or serum TFA is quantitated by neutralizing with sodium hydroxide, esterifying with 2,2,2-trichloroethanol, and gas chromatographic analysis with a nickel-63 electron-capture detector (Witte et al., 1977). The detection limit is 1 μg TFA/ml body fluid. Another method uses isotachopheresis to quantitate urinary or blood TFA (Mario et al., 1980). In serum TFA has been methylated and the head space vapor phase analyzed by gas chromatography on Poropak Q (Fraser and Kaminsky, 1987).

2. CONCLUSIONS

Overall there is sparse available toxicologic data on TFA. The acute lethality of TFA in mice suggests that it is only slightly toxic, and that its lethal effects at high doses are not dependent on its metabolism.

While a no adverse effect level has not been determined, 240 mg TFA/kg in rats produced no bone marrow or small intestinal effects, 25 mg TFA/kg produced no body weight gains, relative testis weight gains, or testicular histologic changes in rats, and 2000 mg/kg every second day for 14 days in mice produced no hepatic necrosis, or heart and kidney histological changes.

TFA at 2000 mg/kg in mice significantly decreased hepatic NADPH and reduced glutathione levels, but after 24-hr both levels returned to normal. Administration of 150 mg TFA/kg/day for 5-6 days to rats decreased the hepatic glycogen content by 24%, the percent liver/body weight by 43%, hepatic pyruvate kinase activity by 42%, and increased hepatic glycerol 1-phosphate oxidase activity by 125%. Thus the lowest dose at which effects have been reported is 150 mg/day for 5-6 days.

TFA is not mutagenic, but no carcinogenicity data is available. However, trichloroacetic acid is hepatocarcinogenic in mice, although it is also not mutagenic in the Ames assay. While no chronic toxicity data on TFA is available it appears likely that on the basis of its resistance to metabolism, rapid clearance, lack of mutagenic potential, and low acute toxicity TFA is unlikely to exhibit significant chronic toxic effects. For a more complete assessment of TFA toxicity chronic studies are required, as well as acute studies in species other than the mouse. The potential for TFA to act as a peroxisome proliferator should be investigated, to gain insight into its hepatocarcinogenic potential.

A German Senate Commission for the Evaluation of Health Hazards in the Work Environment has recommended that a blood TFA level of 2.5 $\mu\text{g}/\text{ml}$ is risk-free (Dallmeier and Henschler, 1981). However, the assessment has no experimental or epidemiologic basis.

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**ASSESSMENT OF EFFECTS ON VEGETATION
OF DEGRADATION PRODUCTS FROM ALTERNATIVE FLUOROCARBONS**

**D.C. McCune and L.H. Weinstein
Boyce Thompson Institute for Plant Research
Ithaca, New York**

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EXECUTIVE SUMMARY

If one assumes that the mass of fluorine (F) deposited under steady-state conditions will have an upper limit of 1.5×10^9 per year and all F returns as hydrogen fluoride (HF) that is uniformly dispersed into global rainfall and is deposited by wet deposition, an upper limit for the concentration of F in precipitation would be about $3 \mu\text{g}$ per liter (3 ppb).

This quantity of F, with reference to concentration or rate of deposition, is well below that heretofore considered to be of significance with respect to the direct effects on plants of air-borne F from industrial operations. It also represents a 30 to 100% increase in what would be estimated to be natural background (3 to 10 ppb). Moreover, F at this concentration would be passively transported as a complex with essentially no capacity to modify the chemical speciation of elements in rain. The activity of F in rain is principally determined by Ca or Al, and pH and concentration of sulfate ions in precipitation could affect the potential of these elements to alter the activity of F. Nevertheless, Al concentrations in rain at the lower range of pH should be sufficient to complex F derived from the degradation of fluorocarbons.

The wet deposition of 3 ppb HF in rain and a total precipitation of 1000 mm per year would constitute a negligible enrichment of the soil in terms of its normal contents or in comparison to that from perhaps the lowest detectable atmospheric concentration of gaseous F. Nor would this deposition of HF affect the chemistry of acidic soils, and rain with a concentration of HF at least 10^3 greater would be needed to affect the chemistry of alkaline soils.

If one assumes that any or all F returns as a fluorinated acetic acid, the effects cannot be estimated because no data are presently available on the effects or degradation of trifluoroacetic acid in plants. Nevertheless, some species of plants can synthesize monofluoroacetate and omega-fluorooleate and -fluoropalmitate. Despite the great chemical stability of the methylene carbon-fluorine bond, plants can metabolize monofluoroacetate and enzymes capable of degrading it occur in soil microorganisms. This leads to the question of the ultimate fate of trifluoroacetic acid with reference to the possible mechanisms for biological dehalogenation and what end products could occur.

It is recommended that research be directed to: (1) metabolism of trifluoro- and other halidoacetates by plants and microorganisms; (2) phytotoxicity of perchloroacetate and alkylhydroperoxides; (3) bioaccumulation and toxicology of these compounds in components of terrestrial and aquatic ecosystems; (4) further quantitative knowledge of the biogeochemistry of F in natural systems.

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1. ASSUMPTIONS

The interaction of the degradation products of fluorocarbons with vegetation could occur in several modes: by direct effects on the plant; by changes mediated by the plant; or indirectly, by an affect on the immediate environment of the plant. For an assessment of any of these, certain assumptions are necessary as to the nature of the environmental exposures that could be expected. Ours will be based upon an envelope with the following boundaries.

Firstly, we shall assume that the mass of fluorine deposited globally per annum under steady-state conditions will have upper and lower limits of 1.5×10^9 and 0.5×10^9 kg, respectively. These values are based on another assumption that upper and lower annual rates for global emissions of fluorocarbons are, respectively, 3×10^9 and 1×10^9 kg with fluorine constituting an average of 50% of the mass of the fluorocarbons.

Secondly, we shall assume that all fluorine (F) returns either as hydrogen fluoride (HF) or as a fluorinated acetic acid. A subsidiary assumption is that the latter occurs as the trifluoro-form although the occurrence of difluoromonochloro- and monofluorodichloro-forms are possibilities and the partitioning of fluorine among them could be considered.

Thirdly, we shall assume that fluorine is deposited by the mode of wet deposition, i.e., by rainout in precipitation. Concomitant assumptions are that this is uniformly dispersed into an average global rainfall of 4.9×10^{17} liters per year (Erchel, 1975). Consequently, upper and lower limits for the concentration of fluorine in precipitation would be, respectively, 3 and 1 μg per liter (3 and 1 ppb).

2. INORGANIC FLUORINE

Concern with the effects of fluorides on plants has been devoted to that resulting from dry deposition (mainly with reference to gaseous HF and secondarily with particulate forms). The occurrence of precipitation as rain or mist and the presence of dew or free water on the foliage has mainly been considered with respect to their effects on the accumulation of air-borne fluoride and not with fluoride in wet deposition. That is, precipitation has been viewed primarily with respect to its facilitation of the solution and subsequent absorption of deposits by the foliar tissues or its elution of deposited fluoride from foliage. (For example: the effects of mist on toxicity of HF and cryolite, McCune et al, 1977; models for the accumulation of fluoride by forage, Craggs and Davison, 1985).

Accordingly, our evaluation of inorganic fluoride from fluorocarbon degradation rests upon a comparison with what is known about the effects of industrial emissions and what could be considered the natural condition.

2.1. HF in precipitation

One problem is to what extent the concentration of fluoride in rain can be partitioned into natural and anthropogenic sources, and then to what extent the products from the atmospheric degradation of fluorocarbons represent an increased burden over that contributed by the other sources. In general, one can come to the conclusion that the assumed quantities of fluoride in rain due to the degradation of fluorocarbons

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may represent close to the detectable increment of present levels, be deposited as complexes, and have no effect on the chemistry of rain water or on the plant.

2.1.1. Quantity

In a metropolitan area (Yonkers, New York), fluoride concentrations never exceeded 100 ppb and infrequently were greater than 50 ppb in rainfall (Jacobson et al., 1976). In Newfoundland, rain and snow considered free of anthropogenic influence had fluoride averaging less than 10 ppb whereas precipitation enriched by a source (probably by washout) had average concentration of 280 ppb in rain (range of 110 to 580 ppb) and an average of 360 ppb in snow water (range of 110 to 1040 ppb) (Sidhu, 1982). Barnard and Nordstrom (1982) found a difference between coastal and inland sites in the distribution of values. Coastal values ranged from 2 to 24 ppb with a median of 4.2 ppb and were uncorrelated with sodium concentrations; inland values ranged up to 34 ppb with a median of 9.4 ppb. They further concluded, from mass balance considerations, that most of the fluoride in precipitation was anthropogenic in origin rather than from maritime aerosols, volcanic activity (2 to 3 ppb), or soil particles (ca 1 ppb).

2.1.2. Chemistry

Ares (unpublished) has concluded that at the concentrations present in rainfall, fluoride is passively transported as a complex with essentially no capacity to modify the chemical speciation of elements in rain water. Basically, the composition and form of minerals in dust determine, in addition to quantity, the activity of fluoride in rain.

Ares also concluded that the major ions determining the activity of fluoride in solution would be Ca or Al, depending upon the pH. Above pH 5.0, the solubility of Ca and other salts of fluoride limit its activity to a level no greater than 10^{-4} M. Below pH 4.5, hydrates of Al(III) regulate nearly all fluoride at molar ratios of Al:F of greater than 4 by the formation of Al-F complexes.

The solution of sulfate ions in precipitation will secondarily affect Ca and Al and thereby their potential to alter the activity of fluoride. Nevertheless, at the concentrations of fluoride assumed, HF derived from the degradation of fluorocarbons would not alter the acidity or composition of rain.

That Al concentrations in rain should be sufficient to complex fluoride at the lower pH range is deduced from limited data. In the vicinity of Göttingen, levels of Al ranged from 48 to 174 ppb with a mean of 89 ppb (Ruppert, 1975). In the vicinity of Solling, Ares (unpublished) found concentrations of Al in rain ranging from 10 to 1720 with a median of 100 ppb.

2.2. Effects on soil

The fluoride content of normal soils ranges from 20 to 1000 ppm depending upon minerals present, depth in the soil, and content of organic matter, with an average of about 200 ppm (see review by Davison, 1983). Assuming a concentration of 3 ppb in rain and a total precipitation of 1000 mm per year, about 30 g F ha^{-1} would be deposited per year, which is equivalent to an enrichment of about 0.04 ppm

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(using Davison's bulk density factor for soil). By comparison and using Davison's estimate of deposition velocity, exposure to air averaging $0.05 \mu\text{gF m}^{-3}$ would result in the deposition of about 380 gF ha^{-1} per year. Consequently, this wet deposition would constitute a negligible contribution to the soil in terms of normal contents or in comparison to that from perhaps the lowest detectable atmospheric concentration of gaseous fluoride.

The data of Ares (1986) would also indicate that wet deposition of HF in the assumed range of concentrations would not affect the soil solution in acidic forest soils. In these, it was estimated that 99.9% of fluoride was complexed with Al, and one could conclude that 3 ppb in rain would not affect the chemistry of the soil. Ares postulated that the solubility of fluoride in alkaline soils (pH 7.2 to 8.2) is controlled by ralstonite (NaMgAlF_6) at high Na levels or fluorite (CaF_2) at low Na levels and that rain with a concentration at least 10^3 greater than that assumed in this assessment would be needed to affect the soil chemistry.

In areas subject to airborne fluoride from industrial emissions, enrichment of fluoride and changes in soil chemistry have been observed (Ares, 1978; Fluhler et al., 1982; Polomski et al., 1982; Sidhu, 1982). Nevertheless, it has been concluded that the increased levels of fluoride found in foliage in these areas represents more the result of increased deposition directly to the plant than of uptake from an increased level of fluoride in soil (Braen and Weinstein, 1985; McClenahan, 1976).

2.3. Gaseous HF

By way of comparison, the effects of gaseous fluoride are relatively well known although knowledge is not as plentiful as would be desired for practical applications to environmental quality. Table 1 lists some values for different averaging times of what could be considered protective for three classes of vegetation. Some standards for fluoride are also based on the concentration present in foliar tissue, and Table 2 presents an example of this kind of standard.

The short-term (24-hour) value for highly sensitive plants is based upon the effects of HF on gladiolus or young foliage of conifers, such as spruce, fir, and pine (see reviews by McCune, 1969; Weinstein, 1977). The 1-month value for highly sensitive plants represents what could be protective for grapevines

Table 1. Possible acceptable limits for atmospheric concentrations of gaseous fluoride with reference to effects on vegetation.

Plant Sensitivity class	Concentration ($\mu\text{gF m}^{-3}$)		
	Averaging time		
	24 hours	1 month	7 months
High	1.6	0.4	0.25
Moderate	3.6	1.5	0.6
Low	10.0	2.5	1.2

Table 2. Standards of the State of Maryland for the concentration of fluoride in vegetation.

Class of vegetation	Concentration of fluoride (μgF per g dry mass)		
Forage for cattle ^a	80	60 ^b	35 ^c
Field crops	35 ^d		
Ornamental plants	40 ^d		
Conifers & evergreens (current)	50 ^d		
“ ” (older)	75 ^d		
Deciduous trees & shrubs	100 ^d		
Grasses & herbs (not grazed)	150 ^d		

- a) Unwashed samples
- b) Mean for two months
- c) Mean for 12 months
- d) Foliage washed before analysis

based on the work of Doley (1986) with the Chardonnay cultivar of *Vitis vinifera*. The 7-month concentration for highly sensitive plants is based in part on the results of MacLean et al. (1984) as related to the occurrence of suture red spot (SRS) on fruit of peach. This is one of the most sensitive responses of plants to HF and also an economically significant effect. If protection against the occurrence of SRS is not of concern, a higher value such as $0.4 \mu\text{gF m}^{-3}$ based upon Doley (1986) could be used.

The averaging periods above were chosen mainly because they represent the exposure regimes used to furnish the experimental data. However, they should also recognize what characteristics of exposure could be operationally significant in the vicinities of the sources and receptors. Given the variability observed in the concentrations of HF in quotidian or weekly cycles and the temporal variations in the susceptibility of plants under ambient conditions, one could propose periods shorter than 24 hours or greater than 24 hours and less than 30 days. With respect to a seven-month value, there is some question as to whether a mean value is appropriate when the median of the population of samples from which it is derived could be zero.

In general one could conclude that atmospheric levels of gaseous fluoride below those considered protective for vegetation would result in greater accumulations of fluoride in foliage and soil than would the wet deposition of HF from fluorocarbon degradation.

3. HYDROGEN CHLORIDE

Although hydrogen chloride could also result from degradation of some compounds proposed as alternatives, it is much less toxic to plants than fluoride. For example, Guderian (1977) recommends a concen-

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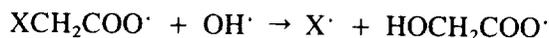
trations no greater than $50 \mu\text{g m}^{-3}$ as being protective of the most sensitive vegetation. In addition, concentrations of chloride in foliage associated with thresholds for foliar injury are in the range of 0.2 to 2% by dry weight.

4. FLUORO-ORGANIC COMPOUNDS

No data are presently available of the effect of trifluoroacetic acid on plants. Nevertheless, some plants do synthesize monofluoroacetate and some data is available on the degradation of this compound by plants and microbes.

The distribution of fluorine-containing organic molecules in nature appears to be limited to its occurrence as monofluoroacetate (Marais, 1944) and in omega-fluorine homologues, fluorooleate and fluoropalmitate (Peters et al. 1960; Ward et al., 1964). For more details on their distribution see Weinstein et al. (1972). The carbon-fluorine bond in these compounds has extraordinary stability and its slow release is accomplished by refluxing in 20 percent sodium hydroxide or heating at 100C in concentrated sulfuric acid. Complete release occurs only after refluxing in 30 percent sodium hydroxide or by sodium fusion at 400C.

Monofluoroacetate is a naturally-occurring compound in plants, and has been implicated in "lethal synthesis" in many mammals (Peters, 1952), i.e., the biosynthesis of monofluorocitrate from fluoroacetate, which blocks aconitic hydratase and can result in death. It seemed likely that, despite the great chemical stability of the methylene carbon-fluorine bond, there might be enzymes capable of degrading it. The cleavage of the carbon-fluorine bond of monofluoroacetate was first reported by Horiuchi (1962) using extracts from a pseudomonad isolated from soil. Although defluorination occurred, significant defluorination was not reported until Goldman (1965) isolated a pseudomonad from soil that grew on a medium containing monofluoroacetate as the sole carbon source. The results were quickly verified for other soil organisms (Tonomura et al., 1965; Kelly, 1965). The enzyme capable of cleaving the carbon-fluorine bond was a haloacetate halidohydrolase (Goldman and Milne, 1966; Goldman et al., 1968; Goldman, 1969) that catalyzes the reaction



where X = F, Cl, or I.

Preuss et al. (1968, 1969) first reported that higher plants can cleave the methylene carbon-fluorine bond. This was shown by the liberation of $^{14}\text{CO}_2$ following incubation with 2- ^{14}C -fluoroacetate in germinating seeds of peanut, castor bean, and *Acacia georginae*. Pinto bean seeds were not able to liberate $^{14}\text{CO}_2$. In peanut, inorganic fluoride was one product of the reaction. The other was postulated to be glycolic acid. The enzyme that accomplishes defluorination in plants has not been characterized.

The facility by which the carbon-fluorine bond can be cleaved by enzymes found in soil microorganisms and higher plants, leads to the question of the ultimate fate of trifluoroacetic acid (Pattison, 1959), one of the major products of photochemical oxidation of several of the alternative fluorocarbons. It is probable that plant and/or microbial enzymes can remove fluorine atoms from the molecule. Whether de-

halogenation will occur as it does with dichloroacetate (Goldman et al., 1968), i.e., removal of both halogen atoms together, or whether it might be a stepwise dehalogenation, with monohalidoacetate as the end product, is not known.

5. RECOMMENDATIONS

It is apparent that the quantities of inorganic fluoride assumed in this discussion are well below those heretofore considered to be of interest with respect to the environmental consequences of industrial operations. They could represent a doubling of what would be estimated to be natural background. Accordingly, research on their possible biogeochemical effects should be directed to the identification of natural systems presently uninfluenced by anthropogenic fluoride and a better understanding of pathways of transport and transformation for fluoride in them.

With reference to the effects of fluoro-organic compounds, it is recommended that research be directed to: (1) metabolism of trifluoro- and other halidoacetates by plants and microorganisms; (2) bioaccumulation and toxicology of these compounds in components of terrestrial and aquatic ecosystems; (3) phytotoxicity of perchloroacetate and alkylhydroperoxides.