

## Preliminary Note

### Fluorinated surfactants in blood

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#### Abstract

An anionic fluorinated surfactant,  $C_nF_{2n+1}CH_2CH_2SO_3M$  ( $M=NH_4$  or  $H$ ,  $n=6-16$ ), was administered orally 10-times to three groups of rats at levels of either 0, 10, 100 or 1000  $mg\ kg^{-1}$ . Organic fluorine in rat blood increased linearly with the square root of increasing dose of the surfactant. For the 1–100  $mg\ kg^{-1}$  dose range, the average concentration of fluorine measured in rat blood ranged from 0 to 80 ppm after dosing, and 0–25 ppm after a 14-d recovery period. The data for the 1000  $mg\ kg^{-1}$  doses were obscured by 5/10 mortality.

Taves and co-workers [1, 2] found organic fluorine in human blood serum, in addition to inorganic fluoride normally present. The origin of the organic fluorine was attributed to volatile fluorinated substances absorbed in the body by inhalation. The blood of workers handling ammonium perfluoro-octanoate was found to contain from 1 to 71 ppm organic fluorine [3]. The retention mechanism of perfluoro-octanoic acid has been described as adsorption on protein in blood [4, 5].

The sorption and elimination kinetics of fluorine in blood for a fluorinated surfactant have been investigated by Kissa and Kinney [6] and Kissa [7]. An inhalation subchronic study on Zonyl®TBS, a partially neutralized ammonium salt of telomer sulfonic acids, used CrI/CD/BR male rats as the test animals. Airborne Zonyl®TBS was formed using two-stage dust generators and swept through the elutriators into the rat exposure chambers. The total fluorine content of rat blood was determined by combustion in an oxyhydrogen torch and analysis of the combusted analyte by the fluoride ion-selective electrode [8–10]. Inorganic fluoride in blood was determined by an analyte addition method using a fluoride ion-selective electrode [11]. The difference between total fluorine and a very small (<0.1 ppm) inorganic fluoride content was reported as organic fluorine. The

inorganic fluoride content of blood increased very little even for the largest surfactant doses and returned to normal values in a short time.

The concentration of organic fluorine in blood,  $C_b$ , increases linearly with the square root of the concentration,  $C_a$ , of the fluorinated surfactant in the air inhaled [6, 7]:

$$C_b = K_s \sqrt{C_a} \quad (1)$$

where  $K_s$  is a sorption coefficient.

We have found that the same relationship holds for a fluorinated surfactant ingested orally. To determine subacute oral toxicity, the partially neutralized ammonium salt of perfluoroalkylethanesulfonic acid,  $C_nF_{2n+1}CH_2CH_2SO_3M$  ( $M=NH_4$  or  $H$ ,  $n=6-16$ ), was administered in the Haskell Laboratory by intragastric intubation to three groups of CrI\CD male rats, 10 rats per group, 10 times at dose levels of either 10  $mg\ kg^{-1}$ , 100  $mg\ kg^{-1}$  or 1000  $mg\ kg^{-1}$ . Half of the rats were sacrificed after the last dose, the other half after a 14-d recovery period. For the 10 and 100  $mg\ kg^{-1}$  dose, the mortality rate was 0/10. However, five of the test rats dosed at 1000  $mg\ kg^{-1}$  died and the organic fluorine in the blood of the surviving rats was highly variable (172–213 ppm, avg. 197 ppm before recovery). Because of the mortality and variance, useful fluorine data for this extremely high dose could not be obtained.

We determined the organic fluorine content of blood by the same procedures used for the inhalation test. The data were analyzed statistically and the standard

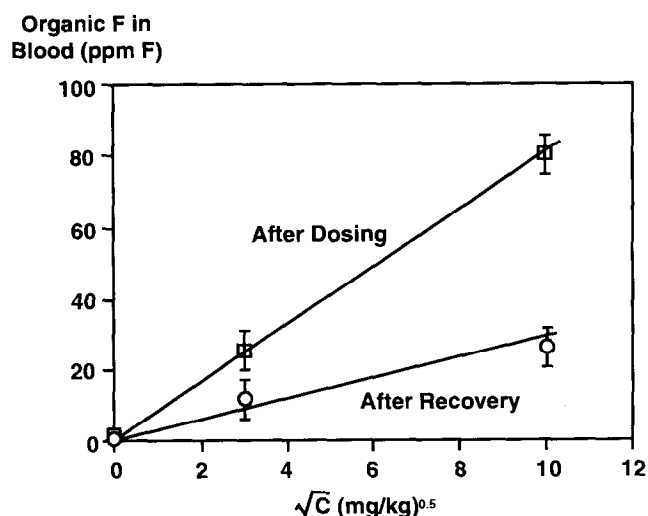


Fig. 1. Average values of organic fluorine in rat blood as a function of the fluorinated surfactant dose,  $C$ .

deviations calculated for each group average. The blood of the rats in the control group contained as an average 0.9 ppm (standard deviation 0.46 ppm) organic fluorine initially and 0.5 ppm (standard deviation 0.30 ppm) after 14 d. The inorganic fluoride content of blood (less than 0.1 ppm) was insignificant relative to the organic fluorine values.

Dosing with the fluorinated surfactant increased the organofluorine content of the blood linearly with the square root of the dose level (Fig. 1). Thus, the dose dependence of the fluorinated surfactant concentration in blood is the same for sorption via oral and inhalational pathways. Substantial amounts of organofluorine remained in the blood during the 14-d recovery period, indicating a slow elimination rate, typical of anionic fluorinated surfactants.

## References

- 1 D.R. Taves, *Nature (London)*, 217 (1968) 1050.
- 2 W.S. Guy, D.R. Taves and W.S. Brey, Jr., *ACS Symp. Ser.*, 28 (1976) 117.
- 3 F.A. Ubel, S.D. Sorenson and D.E. Roach, *Am. Ind. Hyg. Assoc., J.*, 41 (1980) 584.
- 4 R.H. Ophaug and L. Singer, *Proc. Soc. Exp. Biol. Med.*, 163 (1980) 19.
- 5 J. Belisle and D.F. Hagen, *Anal. Biochem.*, 101 (1980) 369.
- 6 E. Kissa and L.A. Kinney, *Tenside*, 26 (1989) 372.
- 7 E. Kissa, *Fluorinated Surfactants, Surfactant Science Series*, Marcel Dekker, New York, 1993.
- 8 R. Wickbold, *Angew. Chem.*, 64 (1952) 133.
- 9 P.B. Sweetser, *Anal. Chem.*, 28 (1956) 1766.
- 10 E. Kissa, *Anal. Chem.*, 55 (1983) 1545.
- 11 E. Kissa, *Clin. Chem. (N.Y.)*, 33 (1987) 253.