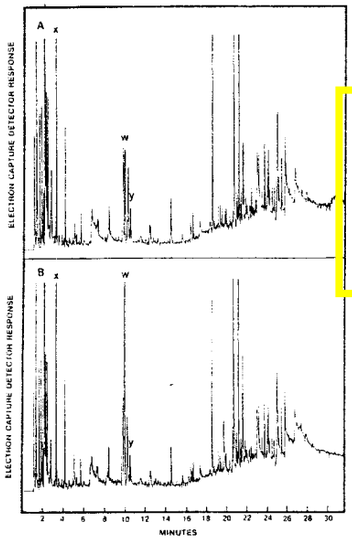

FIG. 5. GC/electron-capture detector of the pooled plasma (6 h postdosage); see Fig. 4A for the *same* sample on MPD and note the simplified chromatogram using the MPD-specific fluorine detector. (A) Rat plasma, 6 h postdosage; (B) A spiked with the unsaturate ($C_7F_{15}CF{=}CHCOO^-$). (w) 2-Hydroperfluoro-2-decenate ($C_7F_{15}CF{=}CHCOO^-$); (x) perfluorooctanoate ($C_7F_{15}COO^-$); (y) 2*H*,2*H*-perfluorodecanoate ($C_8F_{17}CH_2COO^-$). Note the unidentified fluorine containing metabolite (z) is not apparent with the electron-capture detector. Furthermore, while the MPD responds to the total fluorine content of a compound per the empirical formula, the electron-capture detector has different sensitivities for different compounds. In this series, the sensitivity is $C_7F_{15}CF{=}CHCOOCH_3 > C_7F_{15}CF_2CH_2COOCH_3 > C_7F_{15}CF_2CH_2CH_2OH$.

The fluorine-containing biotransformation product of the alcohol eluting at 10.0 min has not as yet been identified but it is speculated that it contains a carboxyl group since diazomethane renders it volatile for GC. The unsaturate has been identified (by GC retention data) and an additional metabolic derivative is possible in that the smallest molecular metabolite ($C_7F_{15}COO^-$) observed in this work has one less CF_2 group than the starting alcohol.

The metabolism of fluorine-containing and perfluoro long-chain acids has not been studied in great detail. It is known that the perfluoroheptyl chain (specifically perfluorooctanoate) is metabolically stable (14–16) while ω-fluorocarboxylic acids (17) undergo β oxidation. The high inorganic fluoride level in the plasma (Table 1) and formation of perfluorooctanoate suggest the overall reaction.

$$C_7F_{15}CF_2CH_2CH_2OH \rightarrow C_7F_{15}CO_2^- + 2\,HF.$$

1*H*,1*H*,2*H*,2*H*-perfluorodecanol — perfluorooctanoate

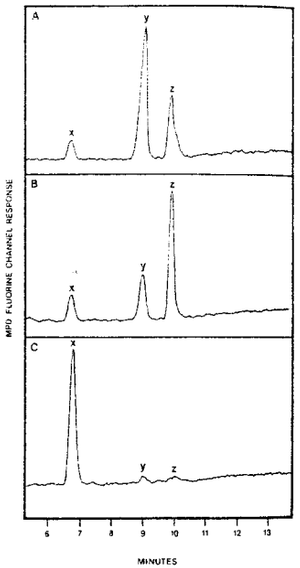

FIG. 6. Rat plasma extracts at various times, postdosage. (A) Rat 10 (2 h postdosage; (B) Rat 9 (6 h postdosage); (C) Rat 20 (48 h postdosage). (x) Perfluorooctanoate ($C_7F_{15}COO^-$); (y) 2*H*,2*H*-perfluorodecanoate ($C_8F_{17}CH_2COO^-$); (z) unidentified metabolite.

Figure 5 illustrates the electron capture response obtained for the esterified plasma extract on the capillary column system and shows the complex mixture which is simplified by monitoring only the fluorine content on the GC/MPD. It is obvious that an ideal system would combine the selectivity of the microwave-sustained helium plasma detector with the improved separation capabilities of a capillary system and this is under development at this time.

MPD plots of the fluorine channel response are shown for various rats (Fig. 6). Note that the 2*H*,2*H*-perfluorodecanoic acid ester is the predominant component in the 2-h-postdosage rat. The chromatograms in Fig. 6 illustrate the progressive biotransformation of the alcohol to perfluorooctanoate. Differences in the rate of biotransformation of the alcohol between rats were observed.

ACKNOWLEDGMENTS

We wish to acknowledge the contributions of Vicki Bunnelle, Richard A. Newmark, Robert A. Prokop, and Robert E. Ober.

REFERENCES

1. Taves, D. R. (1968) *Nature (London)* **217**, 1050–1051.
2. Taves, D. R. (1968) *Nature (London)* **220**, 582–583.
3. Venkateswarlu, P., Singer, L., and Armstrong, W. D. (1971) *Anal. Biochem.* **42**, 350–359.
4. Venkateswarlu, P. (1975) *Anal. Biochem.* **68**, 512–521.
5. Venkateswarlu, P. (1975) *Biochem. Med.* **14**, 368–377.
6. Belisle, J., and Hagen, D. F. (1978) *Anal. Biochem.* **87**, 545–555.
7. Guy, W. S., Taves, D. R., and Brey, W. S. (1976) Biochemistry Involving Carbon-Fluorine Bonds, pp. 117–134, Amer. Chem. Soc., Washington, D. C.
8. Guy, W. S. (1972) Fluorocompounds(s) of Human Plasma: Analysis, Prevalence, Purification and Characterization, Ph.D. thesis, University of Rochester, Rochester, N. Y.
9. Belisle, J., and Hagen, D. F. (1980) *Anal. Biochem.* **101**, 369–376.
10. Venkateswarlu, P. (1975) *Clin. Chim. Acta* **59**, 277–282.
11. Liggett, L. M. (1954) *Anal. Chem.* **26**, 748–750.
12. Clark, L. C., Wesseler, E. P., Miller, M. L., and Kaplan, S. (1974) *Microvasc. Res.* **8**, 320–340.
13. German Patent 27 42 685.
14. Ophaug, R. H., and Singer, L. (1980) *Proc. Soc. Exp. Biol. Med.* **163**, 19–23.
15. Griffith, F. D., and Long, J. E. (1980) *Amer. Ind. Hyg. Assoc. J.* **41**, 576–583.
16. Ubel, F. A., Sorenson, S. D., and Roach, D. E. (1980) *Amer. Ind. Hyg. Assoc. J.* **41**, 584–589.
17. Saunders, B. C. (1972) *in* Carbon-Fluorine Compounds—Chemistry, Biochemistry and Biological Activities, pp. 13–15, Elsevier, Amsterdam.