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Discussion

Methodological commentary on the analysis of metrifonate and dichlorvos in biological samples

Yakoub Aden Abdi, Tomas Villén and Lars L. Gustafsson

Unit of Tropical Pharmacology and Department of Clinical Pharmacology, Huddinge University Hospital, S-141 86 Huddinge (Sweden)

Örjan Ericsson

Unit of Tropical Pharmacology and Hospital Pharmacy, Huddinge University Hospital, S-141 86 Huddinge (Sweden)

F. Sjöqvist

Department of Clinical Pharmacology, Huddinge University Hospital, S-141 86 Huddinge (Sweden)

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In a recent article in this journal, Unni *et al.* [1] presented a new high-performance liquid chromatographic method for the analysis of metrifonate and its active metabolite, dichlorvos, in plasma. In view of our experience from pharmacokinetic studies of metrifonate and dichlorvos [2–4] we would like to discuss some important methodological problems inherent in the assaying of these two compounds in biological samples.

The most important factors in the analysis of metrifonate and dichlorvos are the degradation, and the conversion of metrifonate to dichlorvos. The concentrations of metrifonate decrease by approximately 20% during plasma sample preparation, *i.e.* during blood collection, centrifugation and pipetting. During the same period, the concentration of dichlorvos increases fifteen-fold [5] (see Fig. 1).The transformation of metrifonate to dichlorvos is base-catalysed, while dichlorvos is largely degraded by blood cholinesterases [6]. In order to obtain reliable concentrations of the compounds, the degradation processes and the formation of dichlorvos from metrifonate have to be prevented during blood collection. We have found direct acidification of the sample with phosphoric acid immediately upon collection to be an efficient way to overcome this problem [2].

Unni *et al.* [1] reported high concentrations of dichlorvos after metrifonate administration to patients. We believe that this is due to the transformation of metrifonate to dichlorvos during plasma sample preparation. In our studies the concentration of dichlorvos in whole blood was

Correspondence to: Dr. Yakoub Aden Abdi, Unit of Tropical Pharmacology and Department of Clinical Pharmacology, Huddinge University Hospital, S-141 86 Huddinge, Sweden.

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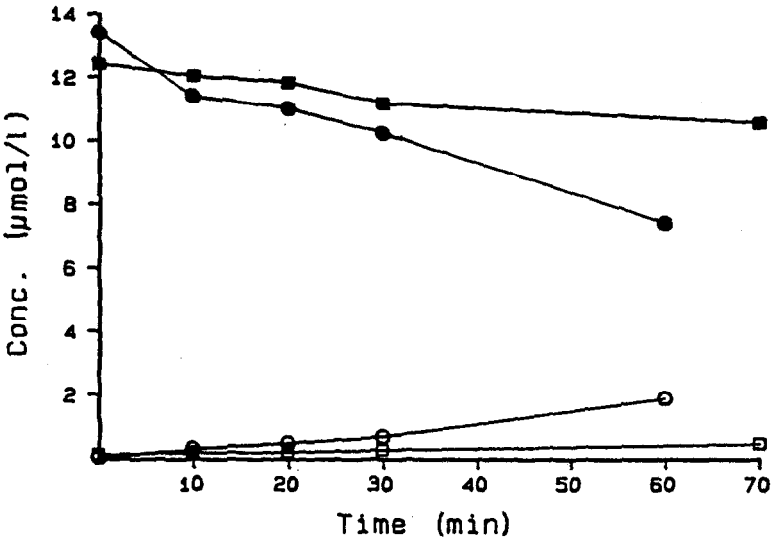

Fig. 1. Incubation of metrifonate in plasma (●) and in buffer (■) at room temperature (upper curves) and formation of dichlorvos in plasma (○) and in buffer (□) (lower curves).

always around 1% of that of metrifonate when we used acidified samples [2,4]. Plasma and urine samples will obviously give erroneous concentrations if used, because of this degradation.

Reliable pharmacokinetic data require accurate analytical methods and adequate sample handling, particularly when dealing with unstable substances like metrifonate and dichlorvos. Other examples of drugs requiring strict sample handling are ciclosporine [7], chloroquine [8] and reversible quaternary cholinesterase inhibitors [9].

REFERENCES

1 L. K. Unni, M. E. Hannant and R. E. Becker, *J. Chromatogr.*, 573 (1992) 99–103.
2 T. Villén, Y. Aden Abdi, Ö. Ericsson, L. L. Gustafsson and F. Sjöqvist, *J. Chromatogr.*, 529 (1991) 309–317.
3 Y. Aden Abdi, T. Villén, Ö. Ericsson, L. L. Gustafsson and M.-L. Dhal-Puustinen, *Bull. WHO*, 68 (1991) 731–736.
4 Y. Aden Abdi and T. Villén, *Pharmacol. Toxicol.*, 68 (1991) 137–139.
5 Y. Aden Abdi *et al.*, unpublished results.
6 B. Holmstedt, I. Nordgren, M. Sandoz and A. Sundwall, *Arch. Toxicol.*, 41 (1978) 3–29.
7 A. Lindholm, *Eur. J. Clin. Pharmacol.*, 41 (1991) 273–283.
8 L. Rombo, Ö. Ericsson, G. Alvan, B. Lindström and F. Sjöqvist, *Ther. Drug Monit.*, 7 (1985) 211–215.
9 S. M. Aquilonius and P. Hartvig, *Clin. Pharmacokin.*, 11 (1986) 236–249.