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References

Andén, N.-E., Dahlström, A., Fuxe, K., Larsson, K., Olson, L. & Ungerstedt, U. (1966). *Acta physiol. scand.*, **67**, 313–326.
Andén, N.-E., Magnusson, T. & Rosengren, E. (1965). *Ibid.*, **64**, 127–135.
Carlsson, A., Fuxe, K., Hamberger, B. & Lindqvist, M. (1966). *Ibid.*, **67**, 481–497.
Carlsson, A. & Waldeck, B. (1965). *J. Pharm. Pharmac.*, **17**, 243–244.
Creveling, C. R., Daly, J. W., Witkop, B. & Udenfriend, S. (1962). *Biochim. biophys. Acta*, **64**, 125–134.
Hamberger, B. (1968). *Acta physiol. scand.*, in the press.
Heller, A., Seiden, L. S., Porcher, W. & Moore, R. Y. (1965). *Science, N.Y.*, **147**, 887–888.
Malmfors, T. (1965). *Acta physiol. scand.*, **64**, Suppl. 248.
Nybäck, H. & Sedvall, G. (1968). *Br. J. Pharmac. Chemother.* **32**, Proceedings, p. 38.
Owman, Ch. & Rosengren, E. (1967). *J. Neurochem.*, **14**, 547–550.
Persson, T. & Waldeck, B. (1968). *Acta pharmac. tox.*, **26**, 363–372.

The effect of methylcellulose on the absorption of nitrofurantoin from the gastrointestinal tract

SIR,—Although many pharmaceutical suspensions are viscous, little attention has been paid to the relation between viscosity and the absorption of insoluble drugs from the gastrointestinal tract.

The relation has already been noted with soluble drugs. Malone, Gibson & Miya (1960), for example, noted that an increase in the concentration of sucrose in aqueous solutions of sodium phenobarbitone considerably lengthened the induction time for narcosis. Davison, Guy & others (1961) found that the plasma and brain salicylate levels after the oral administration of sodium salicylate solutions were significantly reduced when methylcellulose was added to the formulation. Recently, Levy & Jusko (1965) showed that methylcellulose reduced the uptake of salicylic acid from ethanol–water mixtures by the ligated rat stomach.

I have found that the insoluble urinary antiseptic nitrofurantoin when dispersed in therapeutically realistic volumes in methylcellulose and taken by mouth, is not excreted as rapidly in the urine as the drug in water suspension.

Freshly prepared suspensions of 0·5% w/v nitrofurantoin in water were administered (1·5 mg/kg) to 9 healthy male volunteers after an overnight fast. This was followed by 100 ml water. The bladder was emptied and urine was collected at hourly intervals. The procedure was repeated with 0·5% w/v nitrofurantoin suspensions in 5% w/v methylcellulose solutions. All urine samples were assayed immediately after collection by a polarographic method described by Jones, Ratcliffe & Stevens (1965).

The effect of methylcellulose on the excretion rate of nitrofurantoin is shown in Fig. 1. In the presence of methylcellulose, the concentration of nitrofurantoin in urine rises less rapidly and the peak concentration is delayed by 1 hr. The

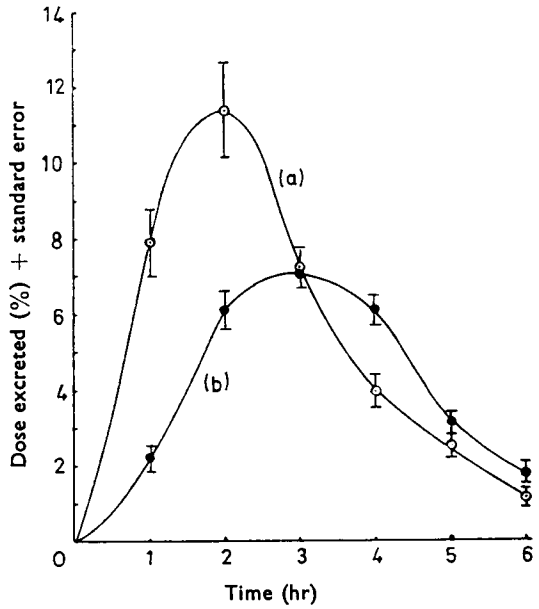

FIG. 1. Excretion rate of nitrofurantoin after oral ingestion of nitrofurantoin suspended in (a) water, and (b) methylcellulose solution.

amount of drug excreted in 6 hr is significantly reduced ($P < 0.01$) and the biological availability of the drug is impaired.

The effect of methylcellulose as suggested by Levy & Jusko (1965) may be due to a modification of the gastric emptying or intestinal transit rates. Alternatively, the movement of drug molecules in the gastrointestinal fluids might be affected. Possible complex formation would reduce the availability of the drug and the presence of methylcellulose would markedly affect the dissolution rate.

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References

Davison, C., Guy, J. L., Levitt, M. & Smith, P. K. (1961). *J. Pharmac. exp. Ther.*, **134**, 176–183.
Jones, B. M., Ratcliffe, R. J. M. & Stevens, S. G. E. (1965). *J. Pharm. Pharmac.*, **17**, *Suppl.*, 52S–55S.
Levy, G. & Jusko, J. (1965). *J. pharm. Sci.*, **54**, 219–225.
Malone, M. H., Gibson, R. D. & Miya, T. S. (1960). *Ibid.*, **49**, 529–534.