International Journal of Pharmaceutics, 29 (1986) 191–193
Elsevier

IJP 00979

Effect of a Non-European (Nigerian) meal on the bioavailability of nitrofurantoin in man

F.A. Ogunbona and O.O. Oluwatudimu

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Ife, Ile-Ife (Nigeria)

(Received November 4th, 1985)
(Accepted November 14th, 1985)

Key words: nitrofurantoin – bioavailability – Non-European diet – Nigerian food – fatty meal

Summary

The effect of a Non-European (Nigerian) meal on the bioavailability of nitrofurantoin was investigated in man. In the study 8 healthy volunteers received each a single 100 mg dose of the drug orally after an overnight fast on one occasion and on another occasion immediately following a fatty meal of fried plantains and egg stew. Urine was collected before and for 24 h after drug administration. The bioavailability of the drug was evaluated from the urinary excretion data of the unchanged drug. It was found that the meal significantly increased ($P < 0.05$) only the extent of absorption of nitrofurantoin, while the rate of absorption of the drug caused by the meal was not significantly increased. It is suggested that fatty meals may enhance the therapeutic efficacy of nitrofurantoin in man.

Introduction

Nitrofurantoin (NF), a broad spectrum antibacterial drug indicated in genito-urinary tract infections, has been the subject of various bioavailability studies because of its poor water solubility. The cumulative amount of NF excreted in urine over a 24 h period has been shown to be a good estimate of the bioavailability of the drug by McGilveray et al. (1971) and Maier-Lenz et al. (1979). Bates et al. (1974), in a single dose study with 4 volunteers, showed that a standard European breakfast of cornflakes with sugar, buttered toast and milk significantly increased ($P < 0.05$) the bioavailability of NF by about 30%. Further work in the same laboratory revealed that the meal had the greatest absorption-enhancing effect with those formulations exhibiting the poorest dissolution characteristics (Rosenberg and Bates, 1976). These workers determined the bioavailability parameters of the drug from the measurement of urinary levels of the unchanged drug. They also reported a significant increase in the period of maintenance of the minimum effective urinary concentration (MEUC) of NF in the non-fasting compared to the fasting state. There is little information in the literature on the effect of a Non-European diet on drug bioavailability; we therefore thought it of interest and importance to report the effect of a Nigerian fatty meal on the bioavailability of nitrofurantoin.

Correspondence: F.A. Ogunbona, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Ife, Ile-Ife, Nigeria.

Experimental

Materials

Nitrofurantoin was obtained from Sigma

Chemicals and dimethylformamide from Hopkin and Williams. Varian 687 UV-VIS spectrophotometer and Corning pH meter Model 7 was used for the absorbance and pH determinations, respectively.

Drug administration and collection of urine

Eight healthy male volunteers aged 25 ± 1.5 years and weighing 65 ± 5.8 kg were each given one 100 mg nitrofurantoin tablet (SK & F) after an overnight fast. Blank urine samples were collected from the volunteers just before drug administration. Thereafter, total urine voided was collected hourly for the first 6 h, two-hourly up to the 12th hour and then at the 24th hour. In the second stage of the crossover one week later, ingestion of the drug by the volunteers followed immediately after eating equal portions of a meal of fried plantains and egg stew. Urine samples were collected as in the first stage. The volume and pH of the samples were measured as soon as possible after collection. Aliquots of the samples were either analyzed immediately or kept frozen in tubes wrapped in foil.

Determination of NF in urine

A modification of the spectrophotometric method described for the drug in the British Pharmacopoeia (1980) was adopted for the analysis of the drug in urine. 200 μl of urine was diluted to 10 ml with acetate buffer (pH 5.5) containing 1% dimethylformamide (DMF). The absorbance of the solution was read at 367 nm against a reference solution containing the same volume of blank urine in the buffer. In the case of urine samples with very low drug concentration, 1 ml of urine was used for the above process.

A calibration curve was plotted by spiking blank urine with varying amounts of NF solution (1 mg/ml) so as to give after dilution (with the buffer) 2–10 μg/ml of the drug. The absorbance was read at 367 nm as described above. Replicate analyses were carried out on spiked urine (100–400 μg/ml) to determine the precision of the method. All operations (except the absorbance measurement) were carried out in a dark room to prevent possible photodegradation of NF. The solutions were well wrapped in foil during the transfer from the dark room to the instrument room for the absorbance measurement. The results were subjected to statistical analysis using the Student's *t*-test.

Results and Discussion

A straight line calibration curve ($r > 0.99$) was obtained in the concentration range tested. The precision of the analytical method as measured by the coefficient of variation was less than 5%. In every subject, the cumulative amount of nitrofurantoin excreted in 24 h in the non-fasting condition was greater than the same value obtained in the fasting condition. The mean cumulative amount excreted in 24 h urine in the non-fasting state (Fig. 1) is significantly greater than the same value found for the fasting state ($P < 0.05$). In fact, the ingestion of the fatty meal gave rise to about 40% increase in the bioavailability of the

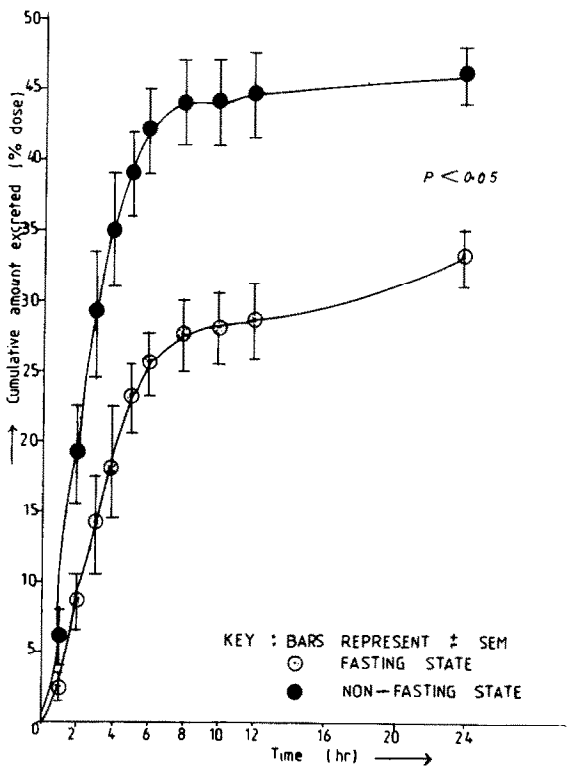

Fig. 1.

TABLE 1

BIOAVAILABILITY DATA FOR NITROFURANTOIN AFTER THE ADMINISTRATION OF 100 mg NITROFURANTOIN TO 8 VOLUNTEERS UNDER FASTING AND NON-FASTING CONDITIONS

	Fasting	Non-fasting	Significance
Cumulative amount excreted in 24 h (% dose) ± S.E.M.	33.0 ±1.7 * (36.08 ± 1.53) **	46.2 ±2.1 (44.35 ± 2.43)	$P < 0.05$ ($P < 0.5$)
Maximum excretion rate (V_{max}) ($mg \cdot h^{-1}$) ± S.D.	10.2 ±3.49 (10.9 ±0.76)	14.7 ±3.58 (14.4 ±1.63)	n.s. (n.s.)
Time of V_{ma} (h) ± S.D.x	3.3 ±1.28 (2.6 ±0.41)	2.5 ±0.93 (4.5 ±0.71)	n.s. (n.s.)
Period of MEUC (h) ± S.D.	4 ±2.0 (5.8 ±0.83)	5 ±1.0 (7.9 ±0.43)	n.s. ($P < 0.025$)

* n = 8.

** Literature values from Bates et al. are in brackets. N.S. = not significant ($P > 0.05$).

drug (Table 1). The meal also increased, although not significantly, the maximum excretion rate (V_{max} of the drug (Table 1). These findings are in agreement with the results of Bates et al. (1974) who studied the effect of a European meal on NF absorption.

The increase in the rate of absorption of nitrofurantoin caused by the Nigerian meal, as indicated by the shortening of the time required to attain V_{max} (Table 1), although non-significant, is contrary to the slowing down of the rate of absorption (also non-significant) observed for the European meal tested by the previous workers. Similarly, the period of maintenance of the MEUC of NF in man appeared unaltered by the Nigerian meal in contrast to the significant increase ($P < 0.025$) caused by the European meal.

We have recently shown that both the rate and extent of absorption of griseofulvia in man were increased by fatty contents of meals (Ogunbona et al., 1985). In this study, the Nigerian meal caused a significant increase only in the extent of absorption of nitrofurantoin in the volunteers. Recently, the reduced bioavailability of the drug in the rabbit has been ascribed to the decomposition of the drug in the stomach (Watari et al., 1983). Thus, delayed gastric emptying in the presence of food may result in reduced rather than increased bioavailability. The faster absorption rate observed in this study (Table 1) seems incongruent with an effective prolongation of residence time of the drug in the stomach due to the meal. Since the meals used in this study and the other two reported studies are fatty in composition it is possible that, like griseofulvin, the enhancement of the bioavailability of nitrofurantoin is due to accelerated dissolution of the drug in the gastrointestinal tract caused directly by the fat content of the food.

References

Bates, T.R., Sequeira, J.A. and Tembo, A.V., Effect of food on nitrofurantoin absorption. Clin. Pharmacol. Ther., 16 (1974) 63–68.

British Pharmacopoeia, British Pharmacopocia Commission, London, 1980, pp. 306–307.

McGilveray, I.J., Mattok, G.L. and Hossie, R.D., A study of bioavailabilities and dissolution rates of commercial tablets of nitrofurantoin. J. Pharm. Pharmacol., 23 (1971) 246S.

Maier-Lenz, H., Ringwelski, L. and Windorfer, A., Comparative pharmacokinetics and relative bioavailability for different preparations of nitrofurantoin. Arzneim. Forsch., 29 (1979) 1898–1901.

Ogunbona, F.A., Smith, I.F. and Olawoye, O.S., Fat contents of meals and bioavailability of griseofulvia in man. J. Pharm. Pharmacol., 37 (1985) 283–284.

Rosenberg, H.A. and Bates, T.R., The influence of food on nitrofurantoin bioavailability. Clin. Pharmacol. Ther., 20 (1976) 227–232.

Watari, N., Funaki, T., Alizawa, K. and Kaneniwa, N., Nonlinear assessment of nitrofurantoin bioavailability in rabbits. J. Pharmacokin. Biopharm., 11 (1983) 529–545.