Salivary excretion of paracetamol in man

The tacit assumption that drugs administered to man are excreted in the saliva has only been substantiated in a few cases. Bender, Pressman & Tashman (1953) indicated the presence in human saliva of the antibiotics penicillin and streptomycin after parental administration. Graham & Rowland (1972) reported the salivary excretion of salicylate in man. Salivary levels of *p*-aminosalicylic acid have been used by Krakowka, Izdebska-Makosa & Wareska (1966) as an index of genuine drug intake by patients, while the use of salivary excretion in the biochemical monitoring of industrial workers in hazardous environments has been proposed by Joselow, Ruiz & Goldwater (1969). We have examined the salivary excretion of paracetamol in man.

Eight males, 20 to 30 years and 65 to 75 kg, were selected. Each had undergone an extensive medical screening. No medication or ethanol was allowed for 48 h before the study. Saliva and plasma concentrations of paracetamol were measured by a modification of the method of Gwilt, Robertson & McChesney (1963). Four different formulations of paracetamol with varying amounts of the excipients: soluble starch, maize starch, magnesium stearate, talc and alginic acid were administered to the volunteers on a cross over basis. Tablets (2) each containing 0·5 g paracetamol were taken with 150 ml tap water on an empty stomach. The mouth was promptly rinsed with 10% ethanol solution. Saliva samples were collected by direct salivation into plain plastic vials. Blood samples were taken from the antecubital vein by venipuncture and transferred to heparinized containers. Plasma and saliva samples were stored at −20° until analysis.

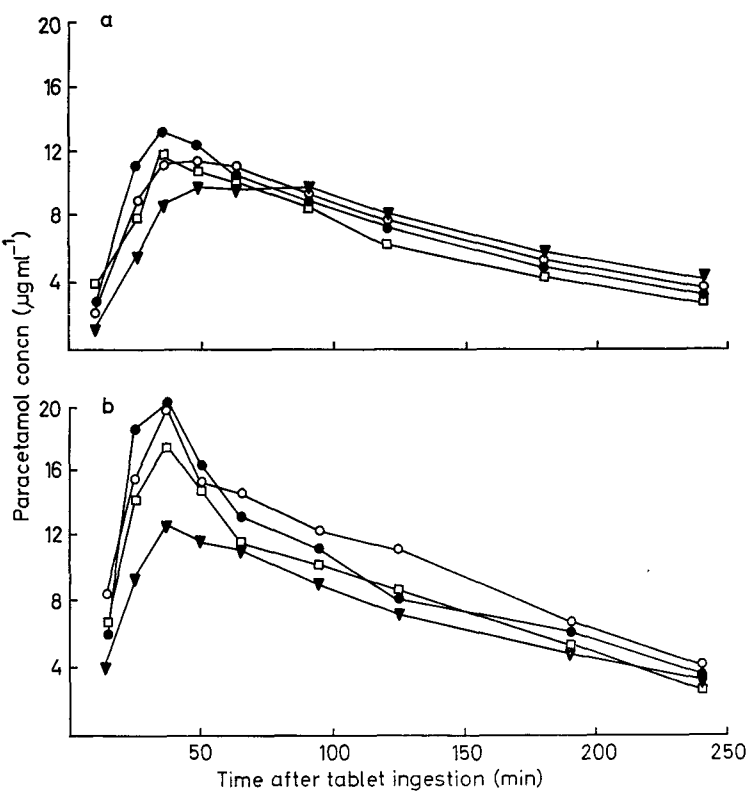

FIG. 1a. Mean plasma paracetamol concentrations in a panel of 8 subjects receiving 4 formulations.
b. Corresponding saliva paracetamol concentrations to plasma levels shown in Fig. 1a.

Table 1. *Correlation coefficients of plasma and saliva paracetamol levels.* All comparisons were made using 32 pairs of data. With 30 degrees of freedom the correlation coefficient should be >0·45 for significance at the $P=0{\cdot}01$ level. This condition was satisfied by all correlations except at 125 min after medication.

	Plasma and saliva parameters compared									
	AUC 240 min	C_{max}	Levels (μg ml^{-1}) post medication (min)							
			26	38	50	65	95	125	190	240
Correlation coefficient r	0·64	0·73	0·78	0·78	(0·77)	(0·56)	0·47	0·36	0·50	0·64

Two subjects ingested 2 g paracetamol (4 Panadol tablets) and saliva samples were collected at hourly intervals for 8 h. The samples were screened by t.l.c. (Cummings, King & Martin, 1967) and no evidence of paracetamol sulphate or glucuronide was found at any sampling time. A linear relation between dose and the area under the curve (AUC) of salivary excretion of paracetamol was found for one subject taking 0·5, 1·0, 1·5 and 2·0 g paracetamol as 0·5 g Panadol tablets. The mean plasma concentrations of paracetamol of 8 subjects receiving four formulations on separate occasions is shown in Fig. 1a and the corresponding saliva concentrations in Fig. 1b. The correlation coefficients of plasma and saliva paracetamol concentrations at various times, of AUC to 240 min and of C_{max} are shown in Table 1.

It was assumed that the varying amounts of excipients would affect the intestinal absorption of paracetamol, although from the plasma profiles there was no significant difference between the formulations. The excipients, however, should have no effect on the distribution of paracetamol between plasma and saliva and consequently the correlations were made using the pooled data from the formulations.

Having established the correlation, the saliva concentration of paracetamol could have two uses: Its specific identification and estimation in the saliva of patients suffering from paracetamol overdose may assist the clinician to decide further treatment; and the measurement of the biological or systemic availability (Barr, 1969) of paracetamol formulations could be achieved without the discomfort, possible hazard and necessary attendance of medical staff required for repeated venipunctures. A similar conclusion was arrived at by Graham & Rowland (1972) with reference to salivary excretion of salicylate.

We would like to acknowledge the assistance of Dr. R. S. Andrews in preparing paracetamol sulphate and glucuronide and the technical assistance of the staff of the Metabolic Studies Department.

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February 19, 1973

REFERENCES

BARR, W. H. (1969). *Drug Information Bull.*, **3**, 27–42.
BENDER, I. B., PRESSMAN, R. S. & TASHMAN, S. G. (1953). *J. Am. dent. Ass.*, **46**, 164–172.
CUMMINGS, A. J., KING, M. L. & MARTIN, B. K. (1967). *Br. J. Pharmac. Chemother.*, **29**, 150–155.
GRAHAM, G. & ROWLAND, M. (1972). *J. pharm. Sci.*, **61**, 8, 1219–1222.
GWILT, J. R., ROBERTSON, A. & MCCHESNEY, E. W. (1963). *J. Pharm. Pharmac.*, **15**, 440–444.
JOSELOW, M. M., RUIZ, R. & GOLDWATER, L. J. (1969). *Am. Ind. Hygiene Assoc. J.*, Jan–Feb.
KRAKOWKA, P., IZDEBSKA-MAKOSA, Z. & WARESKA, W. (1966). *Pol. med. J.*, **5**, 895–899.