$$AUC_{SP} = \frac{F.D}{CL_{SP}} \quad (4)$$

$$AUC_{ASP} = \frac{fm.\ F.D}{CL_{ASP}} \quad (5)$$

Combining equations (4) and (5) produces an alternative means of calculating R.

$$R = \frac{AUC_{ASP}}{AUC_{SP}} = \frac{fm.\ CL_{SP}}{CL_{ASP}} \quad (6)$$

Again R has been calculated from plasma and saliva data. Table 2 lists the R values for the five healthy volunteers and their acetylator status.

In summary, evidence is presented for the good correlation between saliva and plasma concentrations of SP and TSP following oral administration of sulphasalazine to healthy volunteers and patients with inflammatory bowel disease. Saliva data may be used with confidence to calculate certain pharmacokinetic parameters, to assess acetylator status and therefore to modify dosage regimens of sulphasalazine.

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AMILORIDE HANDLING IN RENAL FAILURE

Amiloride, an acylguanidine, is a potassium conserving diuretic with an action which is independent of aldosterone (Baba, Lant, Smith, Townshend & Wilson, 1968). Hyperkalaemia is a potential side-effect (Wilson, Richmond, Simmonds & North, 1966; Lundvall & Berlind, 1967; Bull & Laragh, 1968; Surveyor & Saunders, 1968), and occasional fatalities have been reported (McNay & Oran, 1970). Several of these patients were either seriously ill or had other causes of renal impairment and all received at least 20 mg per day. Since amiloride is highly charged at physiologic pH it was relevant to study its elimination in patients with renal disease.

Five patients with creatinine clearances ranging from 5-97 ml min^{-1}, who were attending the hypertension clinic at Hammersmith Hospital, London were studied. Four were male and their ages ranged from 43–66 years. All gave informed consent to entering the study which had been approved by the local ethical committee. After fasting, each patient took a 5 mg capsule of amiloride with a 15.75μCi ^{14}C label.

Table 1 Pharmacokinetic parameters in patients receiving amiloride 5 mg

Patient	% 15.75 μCi ^{14}C *received*		*Plasma* $T_{\frac{1}{2}}$ *(h)*	*Kel* (h^{-1})	*Creatinine clearance* $(ml\ min^{-1})$
	Urine	*Faeces*			
1	13.6	95.0	102.5	0.0055	6
2	43.5	29.1	21.4	0.0323	46
3	31.4	40.6	7.5	0.0924	97
4	31.2	5.8	143.5	0.0048	5
5	25.9	—	43.8	0.0158	17
Five normals studied by Weiss *et al.* (1969)	52.4	40.1	6	0.116	113

Blood samples (10 ml) were drawn at time zero and at 1, 2, 3, 4, 6, 8 and 24 h after dosing and thereafter at appropriate time intervals up to 9 days. Urine was collected for 72 h in 4 patients and for 7 days in the fifth. Faeces were collected for 72 h after dosing in three patients and for 4 days in a fourth.

After sampling, plasma was separated from blood by centrifugation and radioactivity measured by counting in either Bray's solution or Instagel in a Packard Tri-carb Liquid Scintillation Counter. Urine samples were treated in a similar fashion. Faeces were frozen, homogenized in water and later analysed for radioactivity by combustion according to the method of Gupta (1968). The half-life and rate constant for amiloride elimination were calculated for each patient from the regression of log radioactivity in plasma on time and the results compared with those obtained in normal subjects studies by Weiss, Hersey, Dujovne & Bianchine (1969).

The results are summarised in Table 1. There was a considerable prolongation of the half-life of amiloride in patients with diminished renal function. In addition, urinary excretion was delayed and continued for up to 7 days in the two patients with most severe renal damage. Cumulative urinary recovery varied between 13.6 and 43.5% of the dose. Overall there was a highly significant correlation between the Kel and creatinine clearance, $r=0.992$, $P<0.01$. Faecal recovery was slow and incomplete in most patients.

The present results show that the half-life of amiloride is prolonged and its excretion delayed in the presence of renal failure. This finding is not surprising in view of the highly charged nature of the molecule and the fact that previous studies by Weiss *et al.* (1969) have shown it to be excreted unchanged in the urine. Although previous reports of hyperkalaemia associated with the use of amiloride have concerned patients receiving 15 or 20 mg daily, it would appear from the present data that its use in smaller doses is potentially hazardous in those who are severely ill or who have renal failure.

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