OXAMNIQUINE PHARMACOKINETICS FOLLOWING ORAL ADMINISTRATION TO HEALTHY VOLUNTEERS

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Oxamniquine, 6-hydroxymethyl-2-isopropyl amino methyl-7-nitro- 1,2,3,4 - tetrahydroquinoline, is one of the newer drugs used to treat Schistosomiasis, a disease afflicting over 200 million people. Reports of the metabolism and urinary excretion of oxamniquine in man and animals have appeared in the literature (Kaye and Woolhouse, 1976; Kaye and Roberts, 1980), however little has appeared concerning detailed human pharmacokinetics.

Following approval by the local hospital ethics committee, five healthy volunteers (three females and two males) participated after giving informed consent. Oxamniquine (Vansil (Pfizer) capsules containing 250 mg oxamniquine base) was administered with 200 mls tap water following a 12 hour (overnight) fasting period, at a dose of 15 mg/kg. Serial blood samples (3 mls) were collected by separate venipuncture into heparinised tubes at 0, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0 and 7.0 hours post-administration. The plasma was separated and analysed for unchanged oxamniquine by a reverse-phase HPLC method using an acetonitrile : perchlorate-phosphate buffer pH 3.0 eluent with a Spherisorb-ODS column. The results are summarised in Table 1.

Table 1. Oxamniquine Pharmacokinetic Parameters

Subject	AUC(0-7hr) (ug.hr/ml)	AUC (0- ∞) (ug.hr/ml)	C_{max} (ug/ml)	t_{peak} (hr)	$t_{1/2,a}$ (hr)	t_{lag} (hr)	$t_{1/2}$ (hr)
1	5.42	8.52	1.2	4	1.05	0.71	3.14
2	3.88	4.39	0.97	4	1.04	0.29	1.48
3	8.74	10.14	2.21	2	1.43	0.47	1.49
4	10.98	12.07	4.34	1	0.10	0.35	1.23
5	11.82	20.37	2.68	4	1.01	0.43	3.86
Mean	8.17	11.1	2.28	3	0.93	0.45	2.24
SD	3.45	5.9	1.35	1.4	0.49	0.16	1.18

The mean post-peak half-life of oxamniquine found in the present study was approximately 2 hours. Previously (Kaye, 1984), a mean elimination half-life of 1.5 hours has been reported. Since the absorption of oxamniquine appears to be comparitively slow, especially in volunteers 2 and 3, the post-peak half-life may partly reflect the absorption kinetics.

The results also indicate wide interindividual variations in peak plasma concentrations (C_{max}), time to peak (t_{peak}) and total area under the curve (AUC). This could be attributed to interindividual variation in presystemic metabolism of oxamniquine as has been suggested previously from animal studies (Kaye and Roberts, 1980).

The large variability in plasma concentrations indicates that it would be expedient to monitor plasma levels of oxamniquine in addition to the routinely performed egg counts in patients receiving the drug for treatment of Schistosoma mansoni infestation.

Kaye, B., Woolhouse, N.M. (1976) Ann. Trop. Med. Parasitol. 70: 323-328
Kaye, B., Roberts, D.W. (1980) Xenobiotica 10: 97-101
Kaye, B. (1984) W.H.O. TDR/SCH-SWG(5)/84-1