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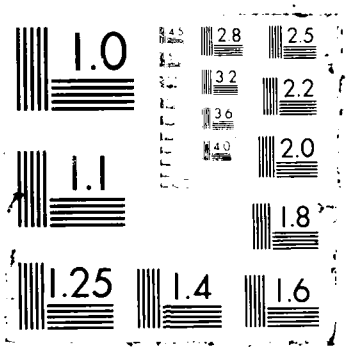
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CHEMOTHERAPY OF RODENT MALARIA

FINAL REPORT

WALLACE PETERS MD DSc

JULY 1985

Supported by

US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND

Fort Detrick, Frederick, Maryland 21701-5012

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London, WCIE 7HT, UK

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1. INTRODUCTION

During the first half of the period since the submission of the Final Report for DAMD-17-83-G-9518, the emphasis of our studies was on vector orientated investigations of causal prophylactic, gametocytocidal and sporontocidal activity. However, in August 1984, it became necessary to close the Winches Farm insectaries as the Anopheles stephensi colony had become infected with a microsporidian parasite Pleistophora (Vavraia) culicis. Since there is no practical way of eliminating this organism from an infected colony, it was decided that this essential closure should be used as an opportunity to refurbish the insectaries and install an effective environmental control system. During the course of this work, it was found that a considerable amount of building repair was needed as the roof timbers were affected by dry rot. This work is now complete and it is anticipated that mosquito linked studies will recommence within the next two months.

The latter part of the contract period and the three months between the conclusion of the extension period and the commencement of the new contract has been concerned primarily with blood schizontocidal activity and in particular with studies on the development of resistant strains. Rodent malaria strains resistant to Halofantrine and to quinine have been developed and these will be included in future blood schizontocidal activity tests.

2. ADMINISTRATIVE EVENTS

Staff employed on US Army funds are as follows:

Senior Technologist/ Research Assistant	- Mr B L Robinson	50 % time
Junior technician	- Ms A West	100 % time
Junior technician	- Ms J R Cox	100 % time
Secretary	- Mrs T Sargeaunt	25 % time

Other staff associated with the project but paid from from London School sources are:

Professor W Peters (Principal Investigator)	20% time
Dr D C Warhurst (Biologist)	20% time
Dr D S Ellis (Electron Microscopist)	10% time
Dr W E Ormerod (Biologist-Pharmacologist)	20% time

In the period covered by the contract we have received seven compounds from WRAIR (including an additional supply of Halofantrine for resistance studies).

The collection of cryopreserved strains of rodent malaria continues to expand with the inclusion of strains resistant to Halofantrine, quinine and artemisinin. In addition, we are producing clones of our standard strains which are being included. Lysates have now been prepared from many of the stabilates for use in isoenzyme characterization studies. When ccompleted, these studies will allow us to use defined cloned strains in our test systems.

Currently we have a battery of thirteen strains (derived from Plasmodium berghei or P.yoelii), which are resistant to

standard antimalarials, and one drug-sensitive P.berghei available for use in blood schizontocidal tests. Studies involving mosquito and exo-erythrocytic stages will in future employ P.yoelii 17X as well as P.y.nigeriensis.

An official visit was made to the School and Field Station by Dr Ho Chung and Ms Maxine Losee of USAMRDC in June 1984.

A close liaison has been maintained between the Principal Investigator and Colonel Davidson of WRAIR.

3. CHEMOTHERAPY STUDIES

3.1 Blood schizontocides

Data are summarised in Table 15 and detailed report sheets are appended as Tables 16 through 21.

3.1.1 WR 251855 AA

This lepidine, an analogue of primaquine, is very active against the drug-sensitive N strain of P.berghei possessing an ED_{90} of 0.67 mg/kg X 4 sc. Further studies ,involving our full battery of resistant lines, are to be carried out and results will be included in a subsequent report.

3.1.2 BK 74491 (WR number not known)

This compound has an ED_{90} of 3.4 mg/kg X 4 sc against P.berghei N strain, a level of activity comparable with that of primaquine. Further studies involving the resistant lines are scheduled.

3.1.3 BK 73127 (WR number not known)

BK 73127 is slightly more active than the preceding compound against the N strain with an ED_{90} of 2.1 mg/kg X 4 sc. Data from tests with resistant lines will be included in a later report.

3.1.4 Amodiaquine

In view of a recent resurgence of interest in this compound, it was decided to examine amodiaquine for activity against some of our resistant lines. In the drug sensitive N strain amodiaquine has an ED_{90} of 2.7 mg/kg X 4 sc, a value very similar to that of chloroquine.

When used against the moderately chloroquine-resistant NS line, the ED_{90} value increased significantly to 25.5 mg/kg - a resistance factor of 9.4. Our highly chloroquine-resistant RC strain was also highly resistant to amodiaquine, the resistance factor being considerably in excess of 22 (ED_{90} = >60 mg/kg). A similar result was obtained with the quinine-resistant N/1923 strain where the ED_{90} was also in excess of 60 mg/kg.

The mefloquine-resistant N/1100 line was also markedly insensitive to amodiaquine and the ED_{90} against this strain was 75 mg/kg X 4 sc. This represents a resistance factor of 27.8 for the N/1100 when compared with N strain.

3.2 Causal prophylaxis

Causal prophylactic test data for 8-aminoquinolines and quinine analogues are summarised in Tables 1 and 2, detailed results from all tests are included in Tables 22 through 34.

3.2.1 Putative metabolites and analogues of primaquine

Results of earlier studies on all of the above compounds, with the exception of RCGJM-97, have been reported previously and the current tests have been performed to confirm earlier conclusions or to extend the dose range. The results obtained with WR 6890 and 15081 confirm our earlier findings of activity and illustrate the slightly lower level of activity of WR6890.

TABLE 1 A summary of causal prophylactic activity in some 8-aminoquinolines.

LON	WR Number	MFED	Residual activity
1801	15081	10 - 30	Nil at 30
1802	6890	30 - 100	Nil at 100
1877	199508AD	> 100	Nil at 100
1783	ANC-IX-19	Inactive at 100	Nil at 100
1908	RCGJM-97	30 - 100	Present at 30

MFED = Minimum fully effective dose. All doses expressed in mg/kg.

WR 199508 AD and the McChesney compound, ANC-IX-19, have been examined at higher dose levels and slight activity at 100 mg/kg is demonstrable with WR 199508 AD. No evidence of activity was found at this dose with ANC-IX-19.

A further compound, RCGJM-97 (3-bromo-primaquine, received from Dr McChesney) was found to be fully active at 100 mg/kg but this activity is at least partially due to the residual action of the compound.

3.2.2 Quinine analogues

These four quinine analogues showed no significant activity at 100 mg/kg in our preliminary tests (previously reported). In the current studies at higher dosage, PH 4007 and pH 4901 show activity at 300 mg/kg associated with residual activity in the

case of Ph 4007. Neither Ph 4017 nor Ph 4900 show any activity at 300 mg/kg.

TABLE 2 A summary of causal prophylactic activity of four quinine analogues.

LON	WR Number	MFED	Residual activity
1884	Ph 4007	> 300	Nil at 300
1885	Ph 4017	Inactive at 300	Nil at 300
1886	Ph 4900	Inactive at 300	Nil at 300
1887	Ph 4901	> 300	Nil at 300

3.2.3 Floxacrine analogue

The floxacrine analogue, WR 250547 AA, had previously been reported to be fully active at 3 mg/kg with evidence of residual activity being present. From the new data presented here it is apparent that residual activity is the major component in the overall activity. At a dose of 1 mg/kg the residual element accounts for all the demonstrable activity. The minimum fully effective dose in the causal prophylaxis test is the same as that of floxacrine (1.0 - 3.0 mg/kg x 1 sc).

3.2.4 Antibiotics

In the preliminary causal prophylactic test, spiramycin has a minimum fully effective dose of 30 - 100 mg/kg. Lincomycin hydrochloride was less active (MFED = > 100 mg/kg). Both of these compounds are to be re-examined, when causal prophylactic testing recommences, to establish the presence or absence of residual

activity.

3.3 Gametocytocidal activity

Data from gametocytocidal activity tests are summarised in Tables 3 to 7 and detailed results are given in Tables 35 through 61. An innovation in this test system is the inclusion of a GD (gametocytocidal dose)$_{50}$ and GD_{90} obtained from a dose response curve plotted on log : probit graph paper. The GD_{90} is compared with that of primaquine and expressed as a Primaquine Index (PI_{90}).

3.3.1 8-aminoquinolines

Twelve 8-aminoquinolines, including primaquine diphosphate, have been examined in the gametocytocidal activity test. Primaquine was included as a reference standard for use with all tests and was found to have a GD_{90} of 33 mg/kg. This value has been used throughout for calculation of Primaquine Indices.

WR 182234 and WR 211814 were found to be almost as active as primaquine with PI_{90} values of 0.9 and 0.6 respectively. WR 228708 was the only other 8-aminoquinoline to show a reasonable degree of activity (PI_{90} = 0.24). The remaining eight compounds in this group were all appreciably less active.

TABLE 3 Gametocytocidal activity of 8-aminoquinolines.

WR	BN	LON	GD_{50}	GD_{90}	PI_{90}
2975AW[1]	BJ 08241	1711	1.3	33.0	1.0
182234	BE 17580	1720	12.3	38.5	0.86
211814	ZP 12775	1721	8.0	59.0	0.56
215295	ZN 43444	1722	230	1100*	0.03
238605	BH 69990	1727	135	2700*	0.01
243789	BJ 08189	1728	150	950*	0.03
246315	BJ 45691	1729	27.0	1100*	0.03
247705	BJ 51779	1730	300	3900*	<0.01
248412	BJ 59202	1731	>300	>>300	<<0.1
237375	BH 58120	1732	60.0	3500*	<0.01
228708	BG 66798	1733	36.0	138	0.24
194343	ZN 41968	1751	>300	>>300	<<0.1

[1] Primaquine diphosphate; * = interpolated graphically

3.3.2 Primaquine metabolites

TABLE 4 Gametocytocidal activity of some primaquine analogues.

WR	BN	LON	GD_{50}	GD_{90}	PI_{90}
ANC-IX-19[1]	(McChesney)	1783	180	440	0.08
249725	BK 69990	1931	NA100	-	-
15081	AY 15653	1801	>300	>>300	<<0.1
6890	BK 12713	1802	100	340	0.1
RCGJM-53[2]	(McChesney)	1810	105	460	0.07
199508 AD	BK 56500	1877	220	3250*	0.01

[1] = WR 249725; [2] = WR 199507 (5-hydroxyprimaquine)

NA = no activity; * = interpolated graphically

None of the six primaquine metabolites examined possess any marked degree of gametocytocidal activity. The best of these, WR 6890, had a PI_{90} of 0.1.

3.3.3 Quinine analogues

TABLE 5 Gametocytocidal activity of some quinine analogues.

WR	BN	LON	GD_{50}	GD_{90}	PI_{90}
Ph 4007	BK 64306	1884	31.0	365	0.09
Ph 4017	BK 64315	1885	20.0	90.0	0.37
Ph 4900	BK 64324	1886	13.5	92.0	0.36
Ph 4901	BK 64333	1887	>300	>>300	<<0.1

Our earlier observation of activity with the four quinine analogues has been confirmed in the current series of tests. The least active of the four was Ph 4901 and the flat nature of the dose response curve precluded us from obtaining a meaningful GD_{90}. A little more active was Ph 4007 with a GD_{90} of 365 (PI_{90} = 0.09) but Ph 4017 and Ph 4900 were very much more active. Ph 4017 had a GD_{90} of 90.0 mg/kg (PI_{90} = 0.37) and Ph 4900 had the same degree of activity with a GD_{90} of 92.0 mg/kg (PI_{90} = 0.36).

3.3.4 Floxacrine analogues

TABLE 6 Gametocytocidal activity of two floxacrine analogues.

WR	BN	LON	GD_{50}	GD_{90}	PI_{90}
245082	BK 02771	1752	70.0	2100*	0.02
246976	BK 02780	1753	11.0	255	0.13

* = interpolated graphically

Two floxacrine analogues, WR 245082 and WR 246976, have been examined for gametocytocidal activity. WR 246976 has approximately six times the activity of WR 245082 (PI_{90} values are 0.13 and 0.02 respectively).

3.3.5 Quinolines/quinoline-methanols

One quinoline-methanol, mefloquine, and two quinolines were tested in the gametocytocidal test system. Neither of the quinolines, WR 44450 AD and WR 102796 AD, show high levels of activity, and although mefloquine was active in this system, the GD_{90} level was not reached in this test. Further investigations of mefloquine and other amino-alcohols are planned.

TABLE 7 Gametocytocidal activity of mefloquine and two quinolines.

WR	BN	LON	GD_{50}	GD_{90}	PI_{90}
44450 AD	AY 29540	1740	215	2000*	0.02
102796 AD	BC 78878	1741	34.0	>300	<0.1
142490[1]	BH 10371	1100	11.0	>60	<0.55

[1] Mefloquine ; * graphically interpolated

3.4 Sporontocidal activity

Summarised results are included in Tables 8 through 14 and detailed test results are presented in Tables 62 through 101. As with the gametocytocidal test, it should be possible to quantify the sporontocidal effect and express it as a sporontocidal dose (SD_{50} and SD_{90}) when an extended test is done. In the current report, however, we are presenting preliminary test data and activity in this single dose test can only be expressed qualitatively. Since no positive drug control has been included in this preliminary test series, and no extended dose range tests have yet been performed, the classification of activity is necessarily arbitrary. Further studies may indicate that other contributory factors, such as generalised cytotoxicity, are playing a significant part in oocyst suppression and the criteria currently employed in determining activity levels may require revision. Full tests, using an extended dose range and including pyrimethamine and/or cycloguanil as positive drug controls, will be performed on those compounds which have shown activity in the preliminary test.

3.4.1 8-aminoquinolines

TABLE 8 Sporontocidal activity of 8-aminoquinolines.

WR	BN	LON	ACTIVITY	% SUPPRESSION
225448 AG	BH 58522	1709	INACTIVE	15.1
5990	AG 99266	1715	ACTIVE	43.4
181023	BE 50003	1719	SLIGHTLY ACTIVE	39.1
182234	BE 17580	1720	INACTIVE	9.8
211814	ZP 12775	1721	SLIGHTLY ACTIVE	27.7
215295	ZN 43444	1722	ACTIVE	41.5
228000	ZN 81499	1723	INACTIVE	14.5
228583	ZN 78910	1724	ACTIVE	51.7
233627	BH 13989	1725	ACTIVE	58.5
235485	BH 35770	1726	ACTIVE	48.3
238605	BH 69990	1727	INACTIVE	21.3
243789	BJ 08189	1728	ACTIVE	44.9
246315	BJ 45691	1729	ACTIVE	55.1
247705	BJ 51779	1730	ACTIVE	67.1
248412	BJ 59202	1731	INACTIVE	1.7
237375	BH 58120	1732	INACTIVE	9.7
228708	BG 66798	1733	INACTIVE	23.1
242511 AA	BH 89438	1734	INACTIVE	0
242511 AB	BJ 78592	1736	ACTIVE	47.8
194343	ZN 41968	1751	SLIGHTLY ACTIVE	27.9
249725	BK 69990	1931	ACTIVE	57.4
251855 AA	BK 71178	1932	ACTIVE	39.8

A total of twenty-two 8-aminoquinolines have been examined in the preliminary screening test. Eight of these show no significant activity at the standard concentration (0.05%) used in this test. Three compounds (WR 181023, WR 211814 and WR 194343) show slight activity and the remaining ten compounds are active. None of the 8-aminoquinolines tested have been fully active at the dose used. The highest levels of activity were found with WR 249725 and WR 247705 which produced approximately 60 and 70 per cent suppression of oocysts respectively.

3.4.2 Putative primaquine metabolites

TABLE 9 Sporontocidal activity of some putative primaquine metabolites.

WR	BN	LON	ACTIVITY	% SUPPRESSION
199508 AD	BK 56500	1877	SLIGHTLY ACTIVE	29.0
199508	ZP 43350	1940	SLIGHTLY ACTIVE	30.7

Two samples of putative metabolites of primaquine have been submitted for sporontocidal activity testing. Both of these samples (WR 199508 AD and 199508) proved to be 6-hydroxy primaquine and gave almost identical results in the test, demonstrating slight activity.

3.4.3 Quinine analogues

All four of the quinine analogues submitted demonstrated a marked toxicity to mosquitoes, with Ph 4007 killing all of the mosquitoes exposed to the 0.05 per cent concentration used in our

preliminary test. The remaining three compounds also exhibited toxicity in varying degrees at this dose and, consequently, even the low level of activity shown by Ph 4900 must be regarded as probably resulting from a generalised cytotoxicity.

TABLE 10 Sporontocidal activity of some quinine analogues.

WR	BN	LON	ACTIVITY	% SUPPRESSION
Ph 4007	BK 64306	1884	LETHAL TO MOSQUITOES	
Ph 4017	BK 64315	1885	INACTIVE	0
Ph 4900	BK 64324	1886	ACTIVE	39.3
Ph 4901	BK 64333	1887	INACTIVE	0

3.4.4 Floxacrine analogues

TABLE 11 Sporontocidal activity of some floxacrine analogues.

WR	BN	LON	ACTIVITY	% SUPPRESSION
245082	BK 02771	1752	INACTIVE	0
246976	BK 02780	1753	SLIGHTLY ACTIVE	37.7
249684 AB	BK 51550	1870	ACTIVE	69.0
250548 AA	BK 51621	1871	SLIGHTLY ACTIVE	39.3
250547	BK 51630	1872	ACTIVE	58.6

Four of the five floxacrine analogues tested showed some degree of sporontocidal activity. The most active, WR 249684 AB,

showed almost 70 per cent suppression of oocysts, WR 250547 was nearly as active, producing approximately 60 per cent suppression, whilst WR 246976 and WR 250548 AA suppressed oocyst development by almost 40 per cent. The fifth analogue, WR 245082 was totally inactive at the test concentration, probably as a consequence of the extreme insolubility of this compound.

3.4.5 Mannich bases

TABLE 12 Sporontocidal activity of two Mannich bases.

WR	BN	LON	ACTIVITY	% SUPPRESSION
194965 AG	BG 56327	1707	ACTIVE	39.8
228258 AH	BJ 30663	1708	INACTIVE	9.2

No significant activity was demonstrable with WR 228258 AH but WR 194965 produced almost 40 per cent suppression.

3.4.6 Quinolines

TABLE 13 Sporontocidal activity of two quinolines.

WR	BN	LON	ACTIVITY	% SUPPRESSION
44450 AD	AY 29540	1740	SLIGHTLY ACTIVE	24.3
102796 AD	BC 78878	1741	SLIGHTLY ACTIVE	34.9

Both of the quinolines tested, WR 44450 AD and WR 102796 AD, were slightly active in the preliminary test.

3.4.7 Miscellaneous compounds

a) WR 9792 (guanylhydrazone) demonstrated no significant

activity against oocysts of P.y.nigeriensis.

b) WR 158124 had a reasonable level of activity and caused approximately 40 per cent suppression of oocyst development.

c) WR 203659 (clindamycin) is totally inactive in this test system at the dose tested.

TABLE 14 Sporontocidal activity of three miscellaneous compounds.

WR	BN	LON	ACTIVITY	% SUPPRESSION
9792	AJ 63248	1716	INACTIVE	14.2
158124	BD 22997	1718	ACTIVE	40.6
203659	ZN 39913	1909	INACTIVE	0

3.5 Combination studies

The bulk of the studies on drug interactions in this department are carried out under the terms of a WHO contract. Since, however, some of the compounds employed were supplied originally to us by WRAIR, the relevant results are summarised here for information.

Detailed data sheets are appended as Tables102 through 194 and isobolograms are shown in Figures 1 to 14.

3.5.1 Mefloquine/spiramycin

This combination appears to produce a low degree of synergism.

3.5.2 Mefloquine/tetracycline

This combination was at best additive when tested using fixed ratios.

3.5.3 Mefloquine/minocycline

An additive effect resulted from this combination.

3.5.4 Mefloquine/clindamycin

When tested using fixed ratios, this combination was found to be more than additive.

3.5.5 Halofantrine/spiramycin

There is some suggestion of enhancement of the activity of halofantrine when using a combination of these compounds.

3.5.6 Halofantrine/chloroquine

The results obtained with this combination are indicative of a substantial degree of antagonism. This situation, when taken together with the rapidity with which halofantrine resistance may be induced experimentally in a chloroquine-resistant strain of *P.yoelii* and the blood schizontocidal test data on the halofantrine resistant line (reported in 3.6), is strongly suggestive of a shared receptor site for the two compounds.

3.5.7 Halofantrine/primaquine

Marked antagonism also occurs between halofantrine and primaquine. This is reflected in a reduced sensitivity to

primaquine in halofantrine resistant lines (see 3.6).

3.5.8 Halofantrine/pyrimethamine

The use of this combination results in a reasonable degree of synergism.

3.5.9 Halofantrine/sulfadiazine

This combination produces no more than an additive effect.

3.5.10 Halofantrine/clindamycin

There is no evidence of anything more than an additive effect with this combination.

3.5.11 Halofantrine/spiramycin

The combination of these two compounds apparently produces a degree of potentiation.

3.5.12 Halofantrine/tetracycline

At best an additive effect results from this combination and a further experiment is required to eliminate the possibility of antagonism.

3.5.13 Halofantrine/minocycline

This combination produces a clear synergistic response.

3.5.14 Floxacrine/cycloguanil

Although this combination has been claimed to be possibly synergistic in a patent claim (HOECHST AG 1979), the evidence

obtained in our test indicates that it is additive . Further studies are to be undertaken to resolve this contradiction.

3.5.15 Floxacrine/quinine

This combination also appears to have at best an additive effect and is possibly even slightly anagonistic, in spite of a patent claim (vide supra) for synergism.

3.5.16 Floxacrine/tetracycline

Results of our interaction study indicate an additive effect.

3.5.17 Floxacrine/erythromycin

There is at least an additive effect obtained with this combination and, possibly, slight synergism occurs.

3.5.18 Floxacrine/chloroquine

The combination of these two compounds produces a slightly antagonistic effect.

3.5.19 Floxacrine/primaquine

This combination produced an additive effect in our test system.

3.6 Development of drug resistance

During the period covered by this report, studies have been made on the acquisition of resistance by strains of malaria

malaria to two compounds, halofantrine and quinine, using our relapse technique.

In the case of halofantrine, resistant lines were developed from a drug sensitive strain of P.berghei (N strain) and also from the moderately chloroquine-resistant NS strain of P.yoelii. This latter strain is, however, insufficiently sensitive to quinine to allow the serial passage of the strain under drug pressure for the purpose of developing resistance since there is not a long enough delay produced by even the maximum tolerated dose to permit evaluation of change. Therefore, we developed quinine resistance only in the drug sensitive N strain.

3.6.1 Halofantrine resistance

Two lines of halofantrine resistant rodent malaria have been developed. The line derived from P.berghei N strain (N/HAL) showed a rapid acquisition of resistance to the maximum dose permitting recrudescence (5 mg/kg) with complete resistance being apparently reached by the eighth passage. This resistance was unstable as it was promptly lost as a result of freezing at this stage and it required a further six passages after retrieval from liquid nitrogen to restore this level of resistance. The strain was then passaged under drug pressure for eighteen more passages, during which time the resistance remained consistent, prior to the removal of drug pressure. When passaged without drug the delay to 2 % parasitaemia rapidly reverted to that of the original sensitive parent line (Figure 15).

The resistance level of the N/HAL strain was checked in the four day test at passage 31 and, at that stage , possessed a resistance factor of 2.8 (ED_{90} =3.6 mg/kg X 4 sc) compared with

the parent strain which had an ED_{90} of 1.3 mg/kg.

The NS derived strain, NS/HAL, showed an even greater propensity for developing resistance to halofantrine with almost complete resistance to a dose of 30 mg/kg being apparent after a single passage under drug pressure. This resistance was not lost in cryopreservation but withdrawal of drug pressure after 37 passages caused rapid reversion to the original level of sensitivity as measured by the 2 % delay time (Figure 16). Resistance was checked by the four day test technique at passage 35 and at that point the NS/HAL had a resistance factor of 13.3 (ED_{90} = 560 mg/kg, interpolated graphically). The parent NS strain had an ED_{90} of 42 mg/kg.

Both the N/HAL and the NS/HAL were also tested for sensitivity to chloroquine, primaquine, mefloquine and quinine in the four day test. There was a reduced sensitivity to each of these compounds in both strains.

These data are summarised in Table 195, together with those of the quinine-resistant line, and detailed reports are included in Tables 196 through 210.

3.6.2 Quinine resistance

Owing to the innate insensitivity of the NS strain to quinine, it was only possible to utilise the drug sensitive N strain for the development of a quinine-resistant line (N/1923). A preliminary experiment showed that the N strain would recrudesce following a single dose of 600 mg/kg of quinine given orally. Resistance to quinine developed relatively slowly, requiring more than thirty passages under drug pressure before a reasonably consistent, high level of resistance was attained. The

development of quinine resistance is depicted graphically in Figure 17.

The level of resistance in the N/1923 strain was assessed by the four day test for blood schizontocidal activity at passage 56. The parent strain was included as a direct comparison and it was found that the ED_{90} of quinine in the parent strain was 95 mg/kg X 4 po, whilst in the N/1923 strain a dose of 600 mg/kg X 4 orally produced virtually no effect.

After withdrawal of drug pressure (Figure 18), the resistance level remained constant for eighteen passages before the strain began to revert to sensitivity. Even after fifty two passages without drug pressure, this strain has still not stabilised as a completely sensitive line comparable with the parent strain.

3.7 Mode of action studies

A corollary to the idea that haemin, released during the digestion of haemoglobin, is a site for binding of antimalarial schizontocides is the proposition that resistance to these drugs may involve changes in quantity or structure of the protein(s) involved in the complexation of haemin as malaria pigment (Warhurst,1981). We have investigated the composition of malaria pigment in two strains of P.falciparum, NF54 (chloroquine sensitive) and K1 (chloroquine-resistant), with the following results.

The major polypeptide detected on SDSPAGE was present in all preparations of both strains and had a molecular weight (M_r) of 14.3 ± 0.8 K in NF54 and 14.6 ±0.55 K in K1. It comprised 73 and 78 per cent of the total Coomassie blue staining protein and 40 and 55 per cent of the total labelled (^{3}H-phenylalanine) protein.

The metabolic labelling of this component *in vitro* indicates that it is parasite derived.

Another polypeptide was found in eighty per cent of NF54 and all K1 pigment preparations. The M_r values were 30 K and 29.7 ± 0.56 K respectively. This polypeptide comprised 13.4 per cent (NF54) and 3.9 per cent (K1) of total protein and 12.9 per cent and 11.6 per cent of total labelled protein. In addition, a third polypeptide was found in eighty per cent of preparations of both strains. This had a M_r of 66.6 ± 0.48 K in NF54 and 66.5 ± 0.05 K in K1 derived material. When labelled (K1 only) it had 2.5 per cent of the total radioactivity.

Depending on the preparation's purity and the stages labelled, other minor bands were seen with molecular weights of 73 - 76 K and 20 - 22 K. These were not consistently present and are considered to represent contamination of the pigment preparation with membranes, etc.

Purified pigment from NF54 and K1 strains was subjected to protein (Lowry) and haemin (pyridine haemochrome) estimations to determine the relative proportions of haemin and protein. Combined data from eight estimations indicated that the relative proportions in NF54 were 52.32 per cent protein plus 10.03 per cent haemin. Similar estimations on a series of six K1 pigment preparations gave a result of 45.11 per cent protein plus 2.82 per cent haemin.

A 14 K polypeptide was reported as being precipitated from *P.falciparum* schizont preparations by a (? monoclonal) antibody (TDR/IMMAL/SWG(6)84.3). This may be the same polypeptide that we are finding, which would seem to be the major haemin-binding protein of *P.falciparum*.

Yamada and Sherman (1979) reported a 15 K pigment associated polypeptide in P.lophurae, which they suggested was a degraded monomer of globin. This was probably also a parasite derived haemin-binding protein.

Our observations would indicate that haemin is released in the digestive vacuoles and is available in trace amounts to bind to blood schizontocides such as chloroquine and quinine.

Studies on the aminoacid composition of the 14 K polypeptide indicate marked differences between the chloroquine-sensitive NF54 and the chloroquine-resistant K1 strains of P.falciparum.

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5. APPENDICES

5.1 BLOOD SCHIZONTOCIDAL TEST DATA

TABLE 15

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

LON	WR & BN		[illegible]		[illegible]		RC		N/1100		N/1923							
			ED 90	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
1932	251855 AA BK 71178	Sc	0.25	0.67														
1956	BK 74491	Sc	0.6	3.4														
1957	BK 73127	Sc	0.5	2.1														
2022	Amodiaquine	Sc	0.8	2.7	25.5	9.4	>60	>22.2	75.0	27.8	>60	>22.2						

[illegible]

SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 16

BLOOD SCHIZONTICIDE

COMPOUND NAME WR 251855 AA BK 71178

OR NUMBER LON 1932 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) 30 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPR / Control PPR %
	0.1	5		-	57.9 ± 2.4
	0.3	5		-	28.1 ± 4.2
N	1.0	5	1	-	4.2 ± 0.3
	3.0	5		-	0.1 ± 0.1
	10.0	5		-	0
	Ø	10		22.6	
ED_{50}(range) 0.25 (0.15 - 0.5)					
ED_{90}(range) 0.67 (0.4 - 1.4)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

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[illegible] 17

COMPOUND NAME WR BK 74491

CP NUMBER [illegible] 956 PARASITE [illegible] PLASMA

FORMULATION [illegible] ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD [illegible] MG/KG [illegible]

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPR / Control PPR
	0.1	5		-	90.4 ± 5.4
	0.3	5		-	42 ± [illegible]
N	1.0	5		-	[illegible]
	3.0	5		-	[illegible]
	10.0	5		-	[illegible]
	30.0	5		-	[illegible]
	Ø	10		22.6	

ED_{50}(range)	0.6 (0.2 - 2.4)
ED_{90}(range)	3.4 ([illegible] - 13.5)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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COMPOUND NAME WR BK73.27

CR NUMBER LON 1957 PARASITE [illegible] Pibergne

FORMULATION Tween 80 H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD 2.00 MG/KG x 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRE/Control TAP
	0	5		-	91.6 ± 3.3
	0.3	5		-	50.9 ± 5.[illegible]
N_2	0	5		-	47.0 ± 4.[illegible]
	3.0	5		-	39.6 ± [illegible]
	10.0	5		-	4.5 ± [illegible]
	30.0	5		-	0.0 ± 0.0
	Ø	0		92.6	

ED_{50} range 0.5 (0.2 - 2.5)

ED_{90} (range) 2 (0.8 - 0.0)

Resistance factor I_{90}

ED_{50} range

ED_{90} range

Resistance factor I_{90}

Principal Investigator: Professor W. Peters

Department of Medical Protozoology

[illegible] Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 19

(BLOOD SCHIZONTOCIDE)

COMPOUND NAME

OR NUMBER ...Amodiaquine..... PARASITE (SUB)SPECIES ..P. berghei...

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..>60.. MG/KG x 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0.1	5		–	94.4 ± 2.7
	0.3	5		–	72.1 ± 7.6
N	1.0	5	1	–	61.4 ± 5.5
	3.0	5		–	37.0 ± 3.8
	10.0	5		–	0.[illegible] ± 0.[illegible]
	30.0	5		–	0
	Ø	10		20.9	
ED_{50}(range) 0.8 (0.4 - 1.5)					
ED_{90}(range) 2.7 (1.3 - 5.4)					
	0.1	5		–	71.3 ± 7.2
	0.3	5		–	55.5 ± 4.6
	1.0	5		–	50.9 ± 3.9
NS	3.0	5	1	–	43.3 ± 2.8
	10.0	5		–	14.0 ± 4.2
	30.0	5		–	9.8 ± 2.7
	60.0	5		–	7.8 ± 2.6
	Ø	10		20.9	
ED_{50}(range) 0.6 (0.3 - 1.4)					
ED_{90}(range) 25.5 (11.5 - 54)					
Resistance factor I_{90} 9.4					

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SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 20

(BLOOD SCHIZONTICIDE)

COMPOUND NAME

OR NUMBER Amodiaquine PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >60 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x 100
	1.0	5		-	100
	3.0	5		-	84.7 ± 12.2
RC	10.0	5	1	-	95.6 ± 1.5
	30.0	5		-	65.7 ± 17.7
	60.0	5		-	62.3 ± 15.0
	Ø	10		7.7	
ED_{50}(range) >60					
ED_{90}(range) >60					
Resistance factor I_{90}>22.2					
	3.0	5		-	100 ± 2.5
	10.0	5		-	44.4 ± 4.4
N 1100	30.0	5	1	-	30.4 ± 3.9
	60.0	5		-	20.0 ± 5.3
	Ø	10		10.8	
ED_{50}(range) 9.5(6.0 – 18.5)					
ED_{90}(range) 75.0(49.0 - 150)					
Resistance factor I_{90} 27.8					

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SUMMARY OF ANTIMALARIAL DRUG TESTS — Table 21

BLOOD SCHIZONTICIDE

COMPOUND NAME

OR NUMBER ...Amodiaquine..... PARASITE (SUB)SPECIES . P. berghei

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >60... MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated/Control %
	0.3	5		-	85.[illegible] ± 5.4
	1.0	5		-	64.[illegible] ± 3.[illegible]
N 1923	3.0	5	1	-	58.9 ± 3.9
	10.0	5		-	47.6 ± 3
	30.0	5		-	40.3 ± 2.7
	60.0	5		-	34.3 ± 6.0
	Ø	10		7.4	
ED_{50}(range) 7.0 (2.1 - 26.5)					
ED_{90}(range) > 60					
Resistance factor I_{90} >22.2					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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5.2 CAUSAL PROPHYLACTIC TEST DATA

TABLE 22

SUMMARY OF CAUSAL PROPHYLACTIC TESTS

LON	BN	KR	MPED mg/kgx1	RESIDUAL ACTIVITY at D+2	COMMENT
1801	BK 12713	15081	10 - 30	NIL AT 30	AQD
1802	AY 15653	6890	30 - 100	NIL AT 100	MAQ
1877	BK 56500	199508 AD	>100	NIL AT 100	6-OH PRIMAQUINE
1783	ANC-IX-19		NA 100	NIL AT 100	6-OCH_3 PRIMAQUINE (McChesney)
1908	RCGJM 97		30 - 100	PRESENT AT 30	3-bromo-primaquine (McChesney)
1884	BK 64306	Ph 4007	>300	NIL AT 300	QUININE ANALOGUES
1885	BK 64315	Ph 4017	NA 300	NIL AT 300	
1886	BK 64324	Ph 4900	NA 300	NIL AT 300	
1887	BK 64333	Ph 4901	>300	NIL AT 300	
1872	BK 51630	250547AA	>1.0	PRESENT AT 0.3	FLOXACRINE ANALOGUE
1941			30-100		SPIRAMYCIN PRELIMINARY SCREEN
1944			>100		LINCOMYCIN HCL PRELIMINARY SCREEN

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CAUSAL PROPHYLAXIS TEST NO: 2624 DATE: 26.3.84

COMP. NO: 1801 WR 15081 BOTTLE NO: BK 12713

FORMULATION: Tween 80 H_2O ROUTE: s.c. ~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

[illegible] ↗ [illegible] mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		CMP 2" P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 4.87	(c) 2.92				
3.0	3/3	3/3	(b) 4.61	(d) 2.90	0	0	NIL	INACTIVE
10.0	2/3	3/3	(b) >8.20	(d) 2.87	>3.33	0	>3.33	ACTIVE
30.0	0/3	3/3	(b) >14.00	(d) 2.96	>9.13	0.04	>9.09	FULLY ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

TABLE 23

[illegible] ACTIVE DOSE ....10.0 - 30.0.... mg/kg

[illegible] ~~PRESENT~~ AT ....30.0.... mg/kg

MAPPED AT ..... mg/kg

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TABLE 21

CAUSAL PROPHYLAXIS TEST NO: 2624 DATE: 26.3.84

COMPOUND: LON/ 1802 WR 6890 BOTTLE NO: AY 15653

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 4.87	(c) 2.92				
10.0	3/3	3/3	(b) 4.89	(d) 2.90	0.02	0	NIL	INACTIVE
30.0	2/3	3/3	(b) >7.90	(d) 3.25	>3.03	0.33	>2.70	ACTIVE
100.0	0/3	3/3	(b) >14.00	(d) 2.93	>9.13	0.01	>9.12	FULLY ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE ....30.0 - 100.... mg/kg

RESIDUAL ACTIVITY: NIL

~~PRESENT~~ AT ....100.... mg/kg

MARKED AT ..... mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
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CAUSAL PROPHYLAXIS TEST NO: 2624 DATE: 26.3.84

COMPOUND: LON/ 1877 WR 199508 AD BOTTLE NO: BK56500

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		CMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 4.87	(c) 2.92				
30.0	3/3	3/3	(b) 4.91	(d) 2.96	0.04	0.04	NIL	INACTIVE
100.0	3/3	3/3	(b) 6.61	(d) 2.96	1.74	0.04	1.70	SLIGHTLY ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM EFFECTIVE ACTIVE DOSE ....>100.... mg/kg

RESIDUAL ACTIVITY: NIL

~~PRESENT~~ AT ....100.... mg/kg

MAX. DOSE AT ..... mg/kg

PRINCIPAL INVESTIGATOR: [illegible]
Department of Medicine [illegible]
[illegible]

TABLE 2

CAUSAL PROPHYLAXIS TEST NO: 2465 DATE: 25 1 85

COMPOUND: LON/ 1783 ANC - IX - 19 BOTTLE NO:

FORMULATION: Tween 80/H_2O ROUTE: s.c./~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
			(a)	(c)				
Ø	5/5		5.16					
			(b)	(d)				
60.0	3/3		4.99		0	NIL	NIL	INACTIVE
			(b)	(d)				
100.0	3/3		4.49		0	NIL	NIL	INACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE .....mg/kg

RESIDUAL ACTIVITY: NIL

~~PRESENT~~ AT ....100.0.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
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TABLE 26

CAUSAL PROPHYLAXIS TEST NO: 2542 DATE: 13.2.84

COMPOUND: LON/ 1908 3-bromo-primaquine diphosphate BOTTLE NO: RCGJM 97

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mgm/kg	PATENCY RATE		CMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 5.89	(c) 3.35				
10.0	3/3	3/3	(b) 4.88	(d) 3.17	0	0	0	INACTIVE
30.0	3/3	3/3	(b) 5.79	(d) 4.14	0	0.79	0	SLIGHT RESIDUAL ACTIVITY ONLY
100.0	0/3	3/3	(b) >14.00	(d) 5.18	>8.11	1.83	>6.28	FULLY ACTIVE - SOME RESIDUAL ACTIVITY
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MAXIMUM FULLY ACTIVE DOSE ....30.0 - 100.0....mg/kg

RESIDUAL ACTIVITY: ~~NIL~~

PRESENT AT ....30.0.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W TRAGER
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

CAUSAL PROPHYLAXIS TEST NO: 2608 DATE: 19 3 84

COMPOUND: LON/ 1884 Ph 4007 BOTTLE NO: BK 64306

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mgm/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 4.87	(c) 3.86				
100·0	3/3	3/3	(b) 4.93	(d) 3.57	0·06	0	NIL	INACTIVE
300·0	1/3	3/3	(b) >11.61	(d) 3.62	> 6·74	0	> 6·74	ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE .....> 300.....mg/kg

RESIDUAL ACTIVITY: NIL

~~PRESENT~~ AT .....300.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

TABLE 2

CAUSAL PROPHYLAXIS TEST NO: 2608

DATE: 19.3.84

COMPOUND: LON/ 1885 Ph 4017

BOTTLE NO: BK 64315

FORMULATION: Tween 80/H_2O

ROUTE: sc/~~ip/po~~

TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice

PARASITE: P. yoelii nigeriensis

STRAIN: NIG

DOSE mgm./kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 4.87	(c) 3.86				
100.0	3/3	3/3	(b) 5.42	(d) 3.54	0.55	0	0.55	INACTIVE
300.0	3/3	3/3	(b) 5.40	(d) 3.54	0.53	0	0.53	INACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE .....mg/kg

RESIDUAL ACTIVITY: NIL

~~PRESENT~~ AT .....300.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

TABLE 29

CAUSAL PROPHYLAXIS TEST NO: 2608 DATE: 19.3.84

COMPOUND: LON/ 1886 Ph 4900 BOTTLE NO: BK 64324

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mgm/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 4.87	(c) 3.86				
100.0	3/3	3/3	(b) 5.12	(d) 3.53	0.25	0	NIL	INACTIVE
300.0	3/3	3/3	(b) 4.92	(d) 3.58	0.05	0	NIL	INACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

TABLE 3(i)

MINIMUM FULLY ACTIVE DOSE .....mg/kg

RESIDUAL ACTIVITY: NIL

~~PRESENT~~ AT ...300.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

CAUSAL PROPHYLAXIS TEST No: 2608 DATE: 19 3 84

COMPOUND: LON/ 1887 Pr 4901 BOTTLE No: BK 64333

FORMULATION: Tween 80/H_2O ROUTE: s.c. TIME AFTER INFECTION: 2 HOURS

HOST: ♂ IFW mice PARASITE: P. yoelii nigeriensis STRAIN: 31G

DOSE mg/kg	PATENCY RATE		GMP 27 P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a-(d-c))	
Ø	5/5	5/5	(a) 4.81	(c) 3.80				
100.0	3/3	3/3	(b) 6.85	(d) 3.80	1.98	0	1.98	SLIGHTLY ACTIVE
300.0	2/3	3/3	(b) > 8.88	(d) 3.00	> 3.99	0	> 3.99	ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE ...> 300.....mg/kg

RESIDUAL ACTIVITY: NIL

~~[illegible]~~ AT ....300.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

TABLE 31

CAUSAL PROPHYLAXIS TEST NO: 2542 DATE: 13.2.84

COMPOUND: LON 1872 WR 250547 AA BOTTLE NO: BK 51630

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ IFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	5/5	5/5	(a) 5.89	(c) 3.35				
0.1	3/3	3/3	(b) 5.13	(d) 3.48	0	0.13	NIL	INACTIVE
0.3	3/3	3/3	(b) 5.69	(d) 4.06	0	0.71	NIL	RESIDUAL ACTIVITY ONLY
1.0	3/3	3/3	(b) 7.36	(d) 5.69	1.47	2.34	NIL	RESIDUAL ACTIVITY ONLY
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE .....mg/kg

RESIDUAL ACTIVITY: ~~NIL~~

PRESENT AT ....0.3.....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

CAUSAL PROPHYLAXIS TEST NO: 2821 DATE: 19.6.84

COMPOUND: LON/ 1941 Spiramycin BOTTLE NO:

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	3/3		(a) 5.46	(c)				
30.0	2/3		(b) > 9.75	(d)	> 4.29			ACTIVE
100.0	0/3 *		(b) > 14.00	(d)	> 8.54			FULLY ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE 30.0 - 100.0 mg/kg

RESIDUAL ACTIVITY: NIL

PRESENT AT ..... mg/kg

MARKED AT ..... mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

* 1/3 DIED

TABLE 3.3

CAUSAL PROPHYLAXIS TEST NO: 2821 DATE: 19.6.84

COMPOUND: LON/ 1944 Lincomycin hydrochloride BOTTLE NO:

FORMULATION: Tween 80/H_2O ROUTE: sc/~~ip/po~~ TIME AFTER INFECTION: 2 HOURS

HOST: ♂ TFW mice PARASITE: P. yoelii nigeriensis STRAIN: NIG

DOSE mg/kg	PATENCY RATE		GMP 2% P		ACTIVITY VALUES			COMMENT
	Sporozoite infected	Sporozoite and blood infected	Sporozoite infected	Sporozoite and blood infected	Total activity (b-a)	Residual activity (d-c)	Prophylactic activity (b-a)-(d-c)	
Ø	3/3		(a) 5.46	(c)				
30.0	2/3 *		(b) 6.87	(d)	1.41			SLIGHTLY ACTIVE
100.0	1/3		(b) > 11.65	(d)	> 6.19			ACTIVE
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				
			(b)	(d)				

MINIMUM FULLY ACTIVE DOSE ....> 100.....mg/kg

RESIDUAL ACTIVITY: NIL

PRESENT AT .....mg/kg

MARKED AT .....mg/kg

PRINCIPAL INVESTIGATOR: PROFESSOR W PETERS
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

* 1/5 DED

TABLE 31

5.3 GAMETOCYTOCIDAL TEST DATA

SUMMARY OF ANTIMALARIAL TESTS — TABLE 3.5

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LDN 1711 WR 2975 AW BJ 05241 Primaquine diphosphate

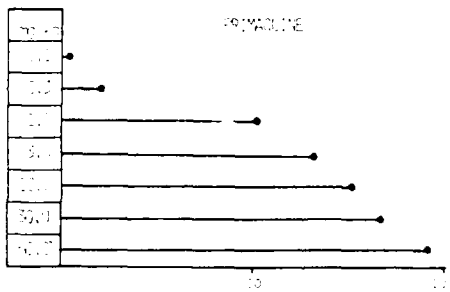
FORMULATION : TWEEN 80 : H_2O ROUTE : [illegible]

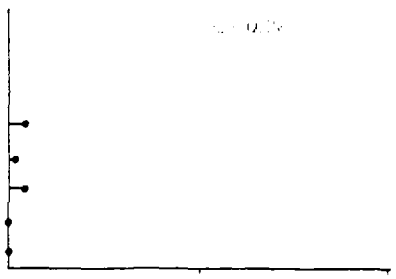
MAXIMUM FULLY TOLERATED DOSE : > 60 mg/kg [illegible] EXPERIMENT No. 2373 DATE 23 33

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : 3° TRW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	[illegible]
2	45	16	13	14	13	3	21	10	48	16	17.8	[illegible]
	15	11										
1.0	13	3	10	8	3	6	4	7	13	20	8.7	48.9 ± 8.5
3.0	8	5	6	7	5	2	2	3	18	5	6.[illegible]	34.2 ± 8.9
10.0	2	1	4	6	5	5	2	8	9	1	4.3	24.2 ± 4.5
30.0	1	1	1	6	3	4	7	3	1	2	2.9	6.3 ± 3.4
60.0	0	0	2	1	1		2	0	0	0	0.7	[illegible]





Gametocytocidal dose

[illegible]

[illegible] 33.0

PRIMAQUINE INDEX [illegible]

[illegible] Investigator [illegible]

[illegible] Medical Protozoology

[illegible] Medicine

SUMMARY OF ANTIMALARIAL TESTS TABLE 3.6

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : CN 1720 WR 182234 BE 17580

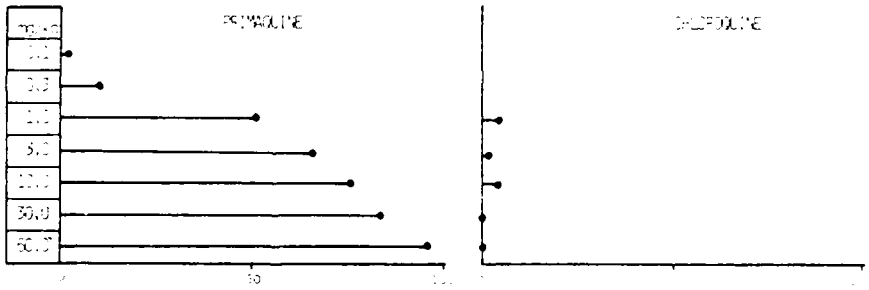
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / PO / IV~~

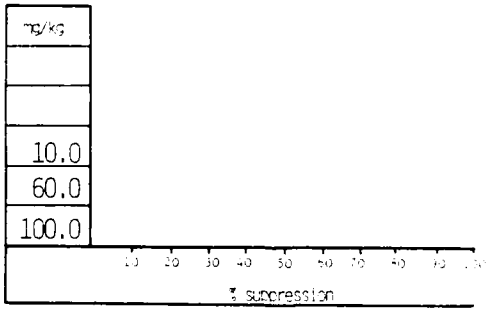
MAXIMUM FULLY TOLERATED DOSE : > 100 mg / kg X 1 EXPERIMENT No.: 2422 DATE : 7.12.83

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
ø	15	16	12	7	16	11	14	16	18	10	14.0	100
	16	14	19	16	10							
10.0	7	4	8	4	8	5	8	6	4	10	6.4	45.7 ± 4.3
60.0	4	3	0	1	0	1	3	2	2	1	1.7	12.0 ± 2.3
100.0	0	0	1	2	0	2	1	0	0	1	0.7	0.5 ± 0.5





Gametocytocidal dose

ED_{50} 12.3 (3.5 - 22.5)

ED_{90} 38.5 (11.0 - 70.0)

PRIMAQUINE INDEX : ED_{90} 1.2

Principal Investigator : Prof. Dr W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS TABLE 3

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1721 WR 211814 ZP 12775

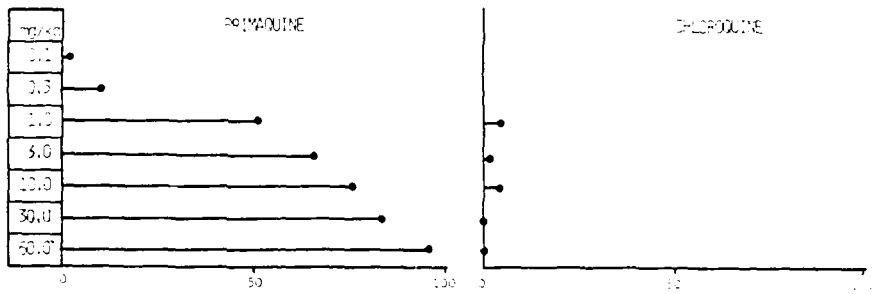
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / SC / IV~~

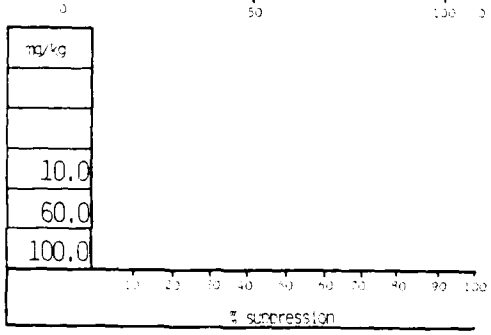
MAXIMUM FULLY TOLERATED DOSE : >100 mg / kg X 1 EXPERIMENT No.: 2422 DATE 7.12.83

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL	
♂	15	16	12	7	16	11	14	16	18	10	14.0	100	
	16	14	19	16	10								
10.0	8	0	0	6	5	4	3	9	5	6	4.8	34.3	6.4
60.0	7	2	1	2	0	3	1	3	1	0	2.0	14.3	5.0
100.0	2	1	2	1	2	0	0	0	1	0	0.75	5.4	1.4
	0	0											





Gametocytocidal dose

ED_{50} : 8.0 (4.0 - 15.5)

ED_{90} : 59.0 (28.0 - 110)

PRIMAQUINE INDEX : PI_{50} 1.8

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 3 S

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : CN 1722 WR 215295 ZN 43444

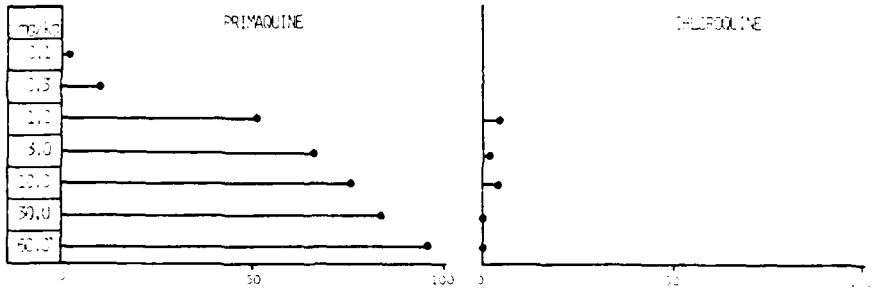
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / PO / ++~~

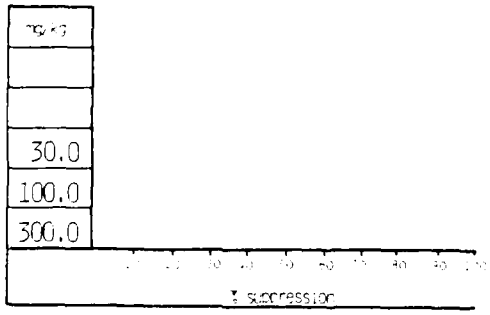
MAXIMUM FULLY TOLERATED DOSE : > 300 mg / kg X 1 EXPERIMENT No.: 2422 DATE : 7.12.83

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
0	15	16	12	7	16	11	14	16	18	10	14.0	100
	16	14	19	16	10							
30.0						From Experiment 2151						96.8
100.0	14	13	14	8	9	8	7	13	15	6	9.9	70.7 ± 6.4
300.0	8	9	6	7	3	9	5	5	7	6	6.5	46.4 ± 4.3





Gametocytocidal dose

ID_{50} : 230 (160 - 330)

ID_{90} : 1100 (740 - 1500)

PRIMAQUINE INDEX : PI_{50} 33.3

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS TABLE 3.9

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LOT 1727 WR 238605 BH 69990

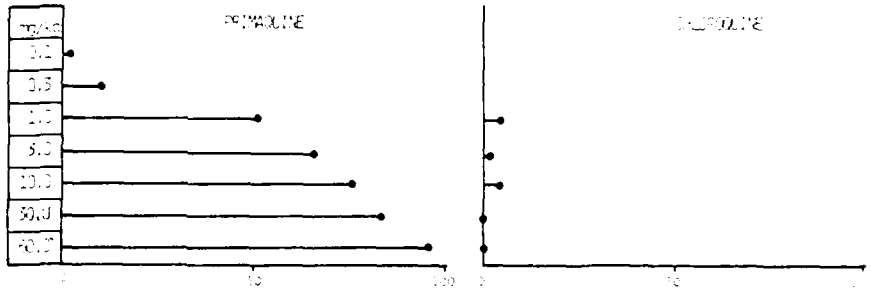
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / PO / IV~~

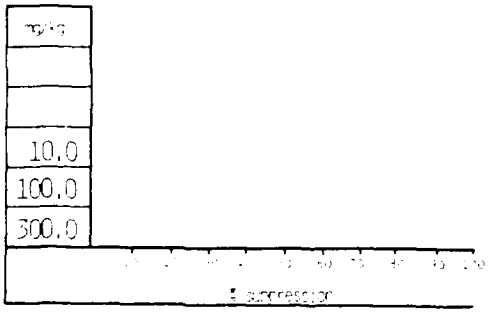
MAXIMUM FULLY TOLERATED DOSE : >300 mg / kg x 1 EXPERIMENT No.: 2453 DATE 11.1.84

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TEW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
♂	47	73	38	35	20	38	30	28	29	16	33.5	100
	15											
10.0	20	36	28	30	22	31	28	50	37	22	30.4	90.7 ± 4.0
100.0	19	14	7	27	23	2	20	17	14	23	16.0	47.8 ± 7.5
	12	14										
300.0	10	16	16	20	20	11	12	16	21	15	14.7	43.9 ± 3.3





Gametocytocidal dose

GD_{50} : 135 (48 - 270)

GD_{90} : 2700 (950 - 5400)

PRIMAQUINE INDEX : PI_{90} : 81.8

Parasitological Investigations : Professor W. Peters

Department of Medical Parasitology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS TABLE 10

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1728 WR 243789 BJ08189

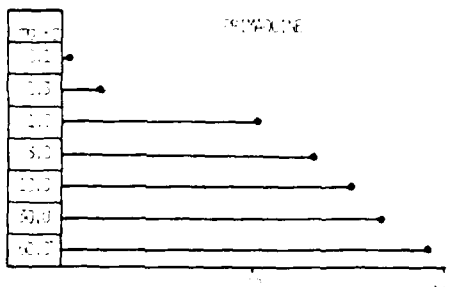
FORMULATION : TWEEN 80 / H_2O ROUTE : SC ~~IP / PO / IV~~

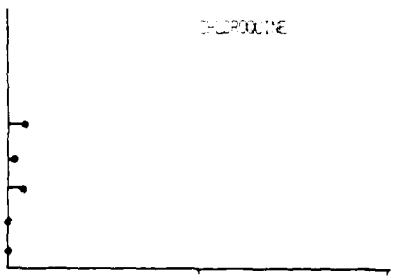
MAXIMUM FULLY TOLERATED DOSE : >300 mg / kg X 1 EXPERIMENT No.: 2453 DATE : 11.1.84

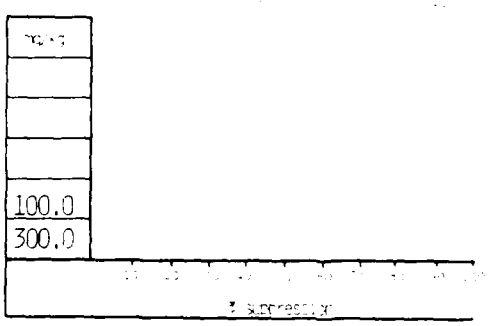
PARASITE : Plasmodium voelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	DOCYST COUNTS D+7										MEAN	% CONTROL
0	47	73	38	35	20	38	30	28	29	16	33.5	100
	15											
100.0	19	11	18	13	20	38	16	12	11	32	18.6	55.6 ± 7.0
	15											
300.0	7	20	14	8	11	6	11	15	13	12	12.4	37.0 ± 4.2







Gametocytocidal dose

Σ_{50} 150 (90 - 215)

Σ_{90} 950 (570 - 1350)

PRIMAQUINE INDEX PI_{50} 28.8

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS TABLE 11

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1729 WR 246315 BJ 45691

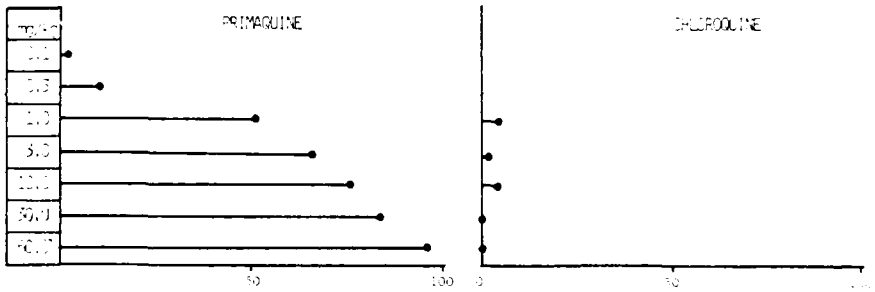
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / PO / IV~~

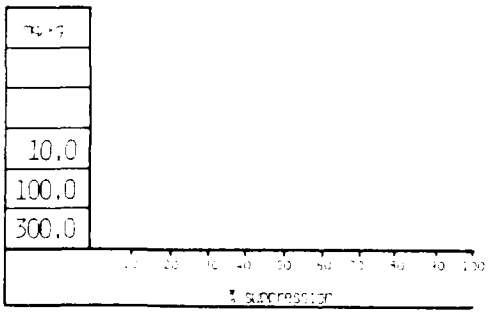
MAXIMUM FULLY TOLERATED DOSE : > 300 mg / kg X 1 EXPERIMENT No.: 2453 DATE : 11.1.84

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
0	47	73	38	35	20	38	30	28	29	16	33.5	[illegible]
	15											
10.0	18	26	24	12	20	18	33	18	21	28	22.5	67.0 ± 6.3
	29											
100.0	16	12	18	14	17	10	17	12	19	8	13.6	40.7 ± 3.6
	7											
300.0	5	13	6	4	5	2	12	13	9	12	7.8	23.4 ± 3.3





Gametocytocidal dose

ID_{50} : 27.0 (10.0 - 60.0)

ID_{90} : 1100 (410 - 2500)

PRIMAQUINE MDEA : PI_{50} : 33.3

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SUMMARY OF ANTIMALARIAL TESTS — TABLE 12

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1730 WR 247705 BJ 51779

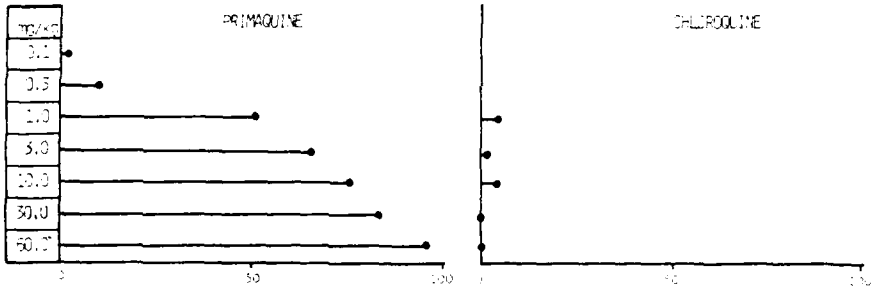
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / PO / IV~~

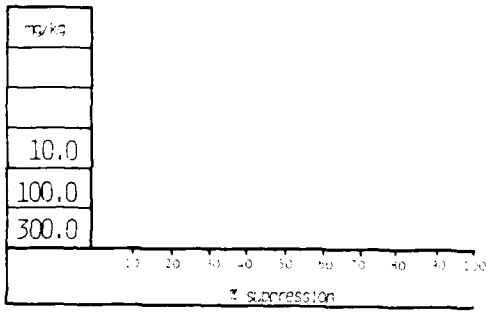
MAXIMUM FULLY TOLERATED DOSE : >300 mg / kg X 1 EXPERIMENT No.: 2501 DATE : 1.2.84

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
0	29	10	28	20	11	24	22	17	30	10	21.1	100
	10											
10.0	22	19	20	12	16	20	17	18	13	17	16.7	79.1 ± 4.3
	14	12										
100.0	17	23	13	18	9	27	17	21	6	0	15.1	71.6 ± 10.0
300.0	19	6	9	12	11	14	7	9	13	5	10.5	49.8 ± 6.6





Gametocytocidal dose

GD_{50} : 300 (180 - 480)

GD_{90} : 3900 (2350 - 6200)

PRIMAQUINE INDEX : PI_{50} : 118

Principal Investigator : Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS - TABLE 4.3

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1731 WR 248412 BJ 59202

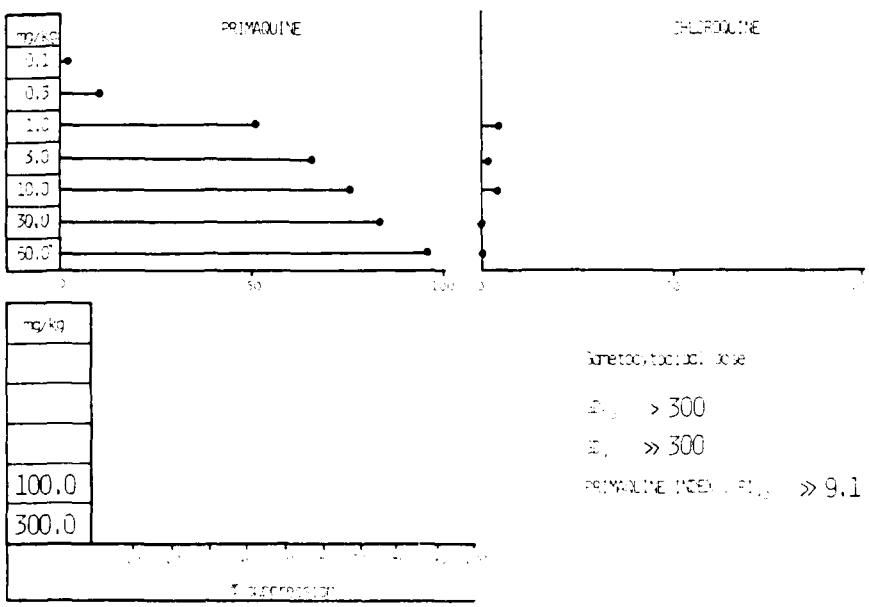
FORMULATION : TWEEN 80 / H_2O ROUTE : CC / ~~IP / PO / IV~~

MAXIMUM FULLY TOLERATED DOSE : > 300 mg / kg X 1 EXPERIMENT No.: 2501 DATE : 1.2.84

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
♂	29	10	28	20	11	24	22	17	30	10	21.1	100
	10											
100.0	21	13	13	17	20	18	12	16	10	18	16.0	75.8 ± 5.2
	18											
300.0	19	17	25	18	20	16	18	3	8	18	15.3	72.4 ± 8.6
	6											



Gametocytocidal dose

SD_{50} > 300

SD_{90} » 300

PRIMAQUINE INDEX : PI_{50} » 9.1

Principal Investigator : Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS - TABLE 1 1

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1732 WR 237375 BH 58120

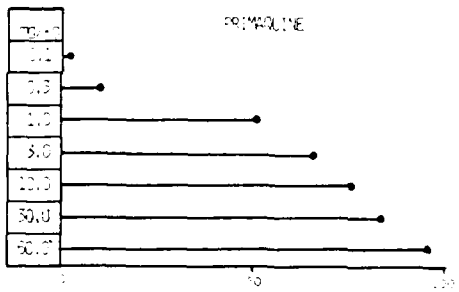
FORMULATION : TWEEN 80 / H_2O ROUTE : [illegible]

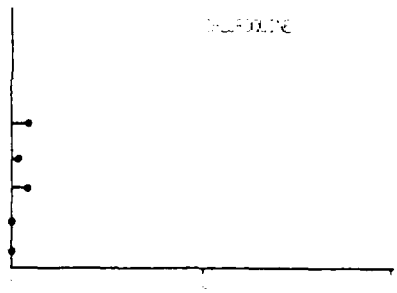
MAXIMUM FULLY TOLERATED DOSE : > 300 mg / kg < 1 EXPERIMENT No. : 2501 DATE 1.2.84

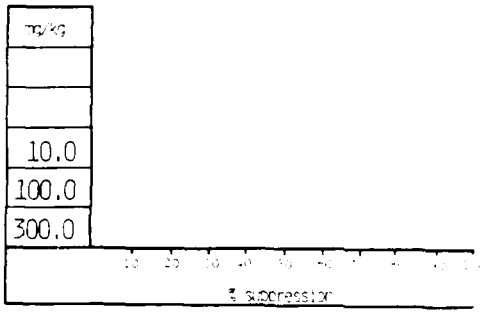
PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
∅	29	10	28	20	11	24	22	17	30	10	21.1	[illegible]
	10											
10.0	16	18	11	13	16	12	14	18	19	10	15.0	71.1 ± 4.3
	21	12										
100.0	13	11	26	5	8	23	22	7	5		13.3	63.0 ± 7.6
300.0	13	16	7	15	10	0	11	5	10	7	9.2	43.6 ± 7.6







Gametocytocidal dose

ID_{50} 60.0 (31 - 150

ID_{90} 3500 (1700 - 8000

PRIMAQUINE INDEX (ID_{50}) 106

Principal Investigator : Professor W. Peters

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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS - TABLE 1

GAMETOCYTOCIDAL ACTIVITY

COMPOUND: LON 1733 WR 228708 BG 66798

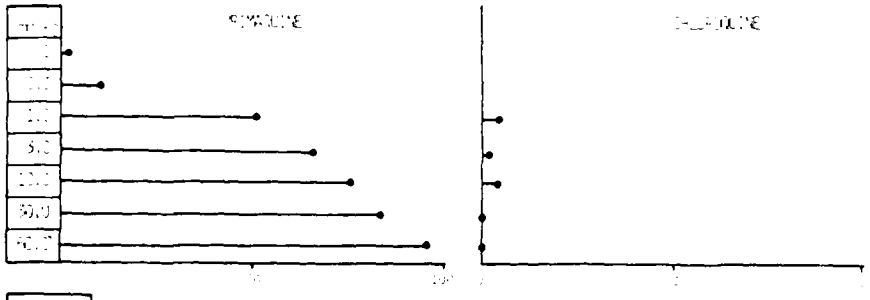
FORMULATION: TWEEN [illegible] ROUTE: [illegible]

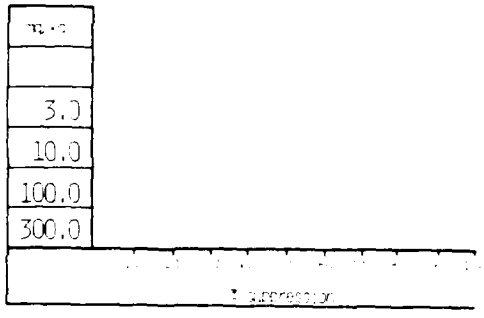
MAXIMUM FULLY TOLERATED DOSE: >300 mg/kg [illegible] EXPERIMENT No.: 2519 DATE: 8.2.84

PARASITE: Plasmodium vinckei nigeriensis

VERTEBRATE HOST: ♂ TFW MICE INVERTEBRATE HOST: Anopheles stephensi

DOSE mg/kg	DOCYST COUNTS D+7										MEAN	% CONTROL	
0	15	12	18	16	18	14	17	16	18	18	16.5	100	
	19												
3.0	27	22	12	14	14	20	19	19	16	18	18.1	100	1.5
10.0	12	9	8	7	10	11	3	6	10		8.4	50.9	5.5
100.0	7	7	6	0	5	0	0	7	5	0	3.7	22.4	4.2
300.0	9	0	0	0	5	2	0	0	0	1	1.7	10.3	5.5





Gametocytocidal dose

D_{50} 36.0 (8.0 - 76.0)

D_{90} 138.0 (44.0 - 220)

PRIMAQUINE INDEX (P_{50}) 4.2

Principal Investigator: Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS [illegible] TABLE [illegible]

GAMETOCYTOCIDAL ACTIVITY

COMPOUND [illegible] 1751 WR 194343 ZN 41368

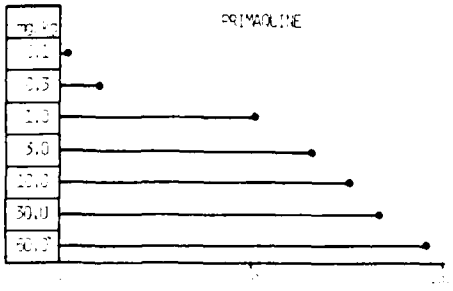
FORMULATION [illegible] TWEEN 80 [illegible] ROUTE [illegible]

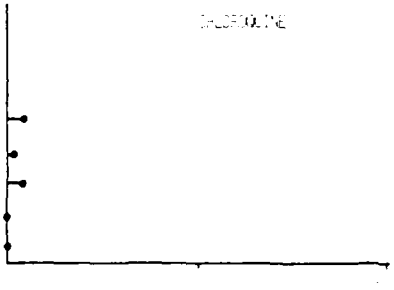
MAXIMUM FULLY TOLERATED DOSE > 300 mg [illegible] EXPERIMENT No. 2532 DATE 15.2.84

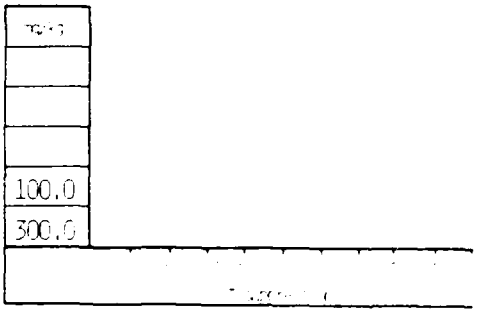
PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TEW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
∅	18	27	48	10	11	17	12	11	21	14	18.0	[illegible]
	9											
100.0	16	15	7	8	19	12	18	8	13	25	13.5	75.0 ± 6.1
300.0	7	10	8	16	17	14	22	7	10	9	12.0	66.6 ± 6.1







Gametocytocidal dose

[illegible] > 300

[illegible] » 300

PRIMAQUINE INDEX [illegible] » 9.1

[illegible]

[illegible]

[illegible]

SUMMARY OF ANTIMALARIAL TESTS — TABLE 1 7

GAMETOCYTOCIDAL ACTIVITY

COMPOUND LON 1783 ANC-IX-19 (McChesney) - WR 249725

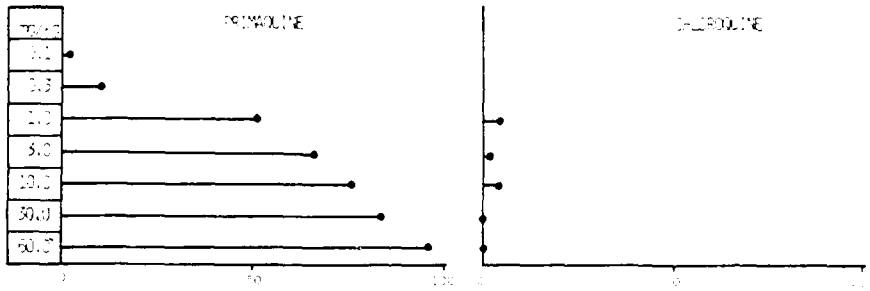
FORMULATION : TWEEN 80 H_2O ROUTE : [illegible]

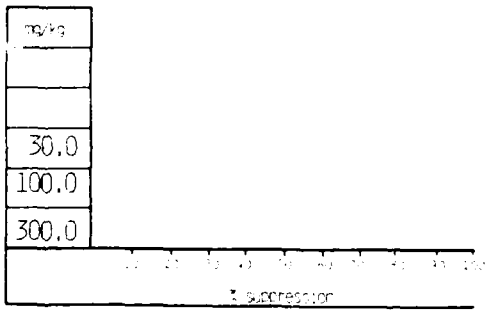
MAXIMUM FULLY TOLERATED DOSE : >300 mg/kg x 1 EXPERIMENT No. 2481 DATE 25.1.84

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
0	15	18	17	19	20	24	18	23	17	25	19.0	[illegible]
	14	12	23	21								
30.0	21	25	20	27	26	14	25	18	8	15	19.9	100 ± 10.0
100.0	5	14	13	3	1	10	13	14	9	14	9.6	50.5 ± 6.8
300.0	7	14	2	5	8	12	8	7	10	8	8.1	42.6 ± 6.3





Gametocytocidal dose

GD_{50} : 180 (85 - 295)

GD_{100} : 440 (210 - 740)

PRIMAQUINE INDEX PI_{50} 13.3

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 1[illegible]

GAMETOCYTOCIDAL ACTIVITY

COMPOUND: LON 1801 WR 15081 AY 15653

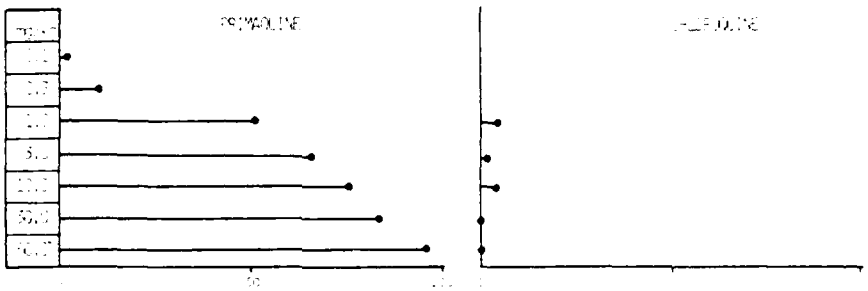
FORMULATION: TWEEN 80 - H_2O ROUTE: SC ~~IP / PO / IV~~

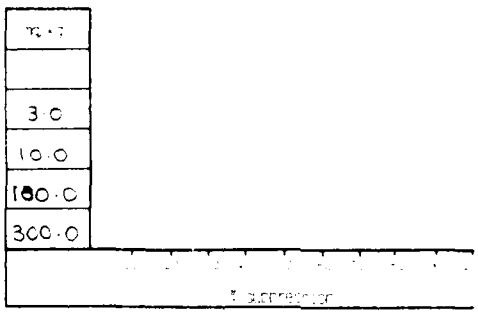
MAXIMUM FULLY TOLERATED DOSE: >300 mg/kg [illegible] EXPERIMENT No.: 2632 DATE: 4.4.84

PARASITE: Plasmodium vaelii nigeriensis

VERTEBRATE HOST: ♂ TFW MICE INVERTEBRATE HOST: Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
Ø	11	39	14	22	16	24	15	14	13	33	20.1	100
3.0	15	5	20	12	13	11	22	21	12	21	15.2	75.6 ± 7.5
10.0	25	10	16	18	10	9	14	12			14.3	70.9 ± 6.8
100.0	11	7	12	19	22	13	28	12	8	18	15.0	74.6 ± 6.5
300.0	7	11	17	12	17	16	21	14			14.4	71.5 ± 8.1





Gametocytocidal dose

Ø > 300

Ø, ≫ 300

PRIMAQUINE INDEX [illegible] ≫ 9.1

Principal Investigator: Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS — TABLE 1.9

GAMETOCYTOCIDAL ACTIVITY

COMPOUND: [illegible]1802 WR 6890 BK 12713

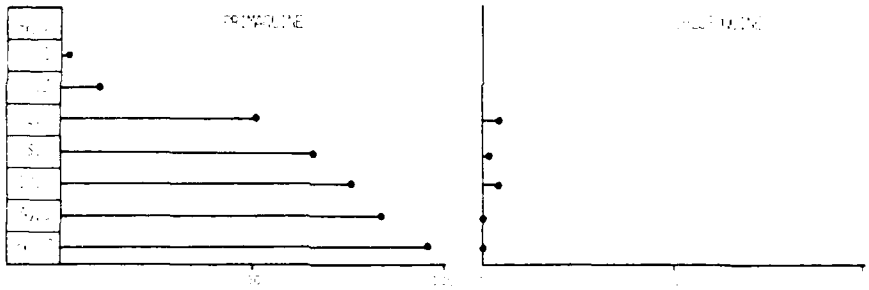
FORMULATION: TWEEN 80 [illegible] ROUTE: [illegible]

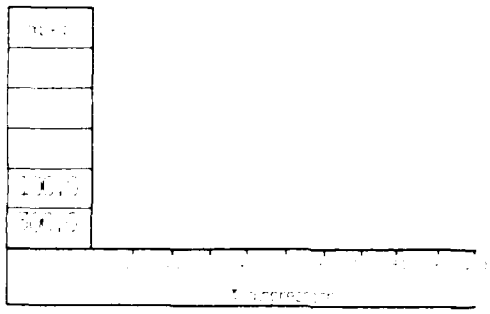
MAXIMUM FULLY TOLERATED DOSE: > 300 mg/kg × 1 EXPERIMENT No.: 2560 DATE: 29.2.84

PARASITE: Plasmodium Vellii nigeriensis

VERTEBRATE HOST: [illegible] TEW MICE INVERTEBRATE HOST: Anopheles stephensi

DOSE mg/kg	DOCYST COUNTS D+7										MEAN	[illegible]
0	30	33	29	39	17	18	30	24	20	17	25.7	[illegible]
100.0	8	9	16	10	13	20	13	10	15	17	13.1	51.0 ± 2.3
300.0	6	2	2	1	7	2	3	1	2	5	3.1	12.1 ± 1.4





Gametocytocidal dose

[illegible] 100(90 - 110)

[illegible] 340(290 - 370)

PRIMAQUINE INDEX [illegible] 10.3

Principal Investigator: Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS — TABLE 5.0

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1810 RCGJM53 (McChesney) - WR 199507 - 5-hydroxyprimaquine

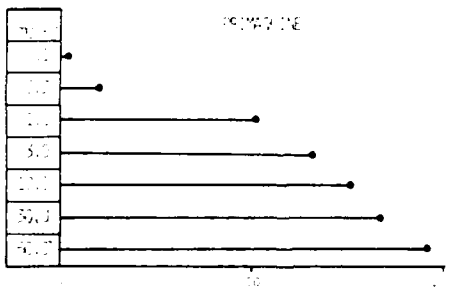
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~[illegible]~~

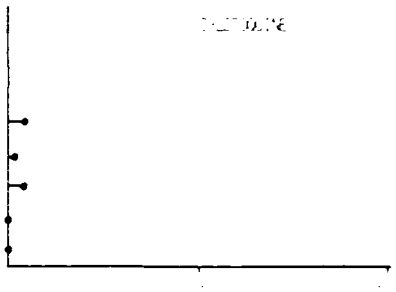
MAXIMUM FULLY TOLERATED DOSE : >300 mg / kg X 1 EXPERIMENT No. 2481 DATE 25.1.84

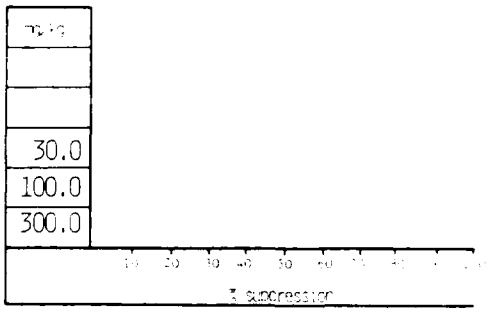
PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
Ø	15	18	17	19	20	24	18	23	17	25	19.0	100
Ø	14	12	23	21								
30.0	9	16	8	12	18	24	15	25	17	19	16.3	85.8 ± 5.2
100.0	6	13	26	10	13	10	5	11	12	6	10.5	55.3 ± 7.4
	5	9										
300.0	8	4	2	3	0	5	4	5	0	2	3.3	17.4 ± 4.2







Gametocytocidal dose

[illegible] 105 (80 - 140)

[illegible] 460 (350 - 610)

PRIMAQUINE INDEX : [illegible] 13.9

Principal Investigator : Professor W. Peters

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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 5.1

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1877 WR 199508 AD BK 56500

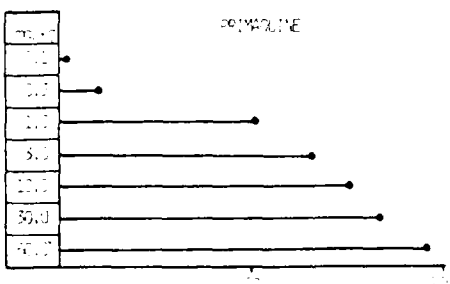
FORMULATION : TWEEN 80 / H_2O ROUTE : [illegible]

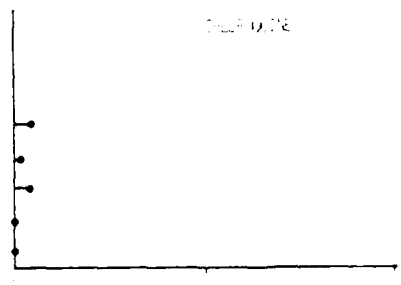
MAXIMUM FULLY TOLERATED DOSE : >300 mg [illegible] EXPERIMENT No. 2560 DATE 29.2.84

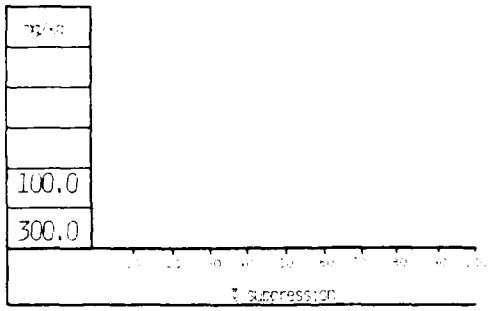
PARASITE : Plasmodium voelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
ø	30	33	29	39	17	18	30	24	20	17	25.7	[illegible]
100.0	19	17	14	20	17	27	8	14	21	11	16.8	65.4 ± 6.9
300.0	17	6	16	10	13	10	15	12	11	9	11.9	46.3 ± 4.3







Gametocytocidal dose

ø 220 (150 - 310)

ED_{50} 3250 (2200 - 4500)

PRIMAQUINE INDEX [illegible] 98.5

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TEST - TABLE 5.2

GAMETOCYTOCIDAL ACTIVITY

COMPOUND: LON 1931 WR 249725 BK 69990

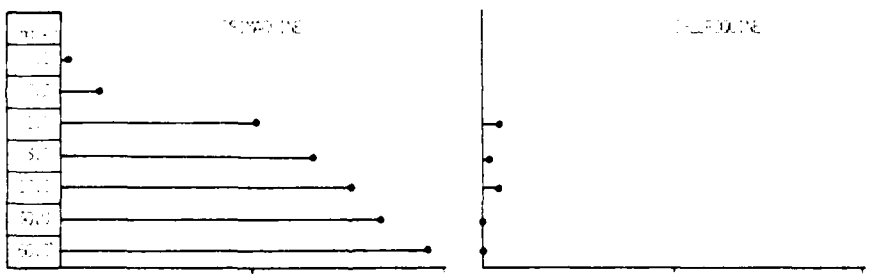
FORMULATION: TWEEN 80 / H_2O ROUTE: [illegible]

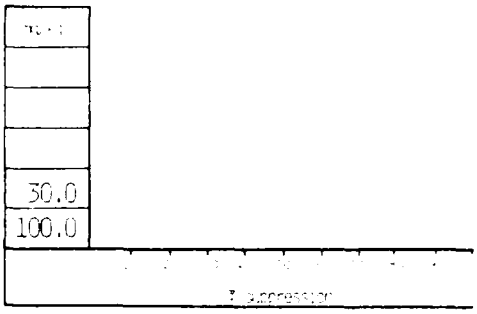
MAXIMUM FULLY TOLERATED DOSE: >100 mg/kg X 1 EXPERIMENT No.: 2645 DATE: 11.4.85

PARASITE: Plasmodium yoelii nigeriensis

VERTEBRATE HOST: ♂ TEW MICE INVERTEBRATE HOST: Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
0	21	13	18	8	20	24	6	11	14	12	15.5	100
	23											
30.0	19	12	21	11	18	13	23	18	20	19	16.9	100 ± 2.9
	12											
100.0	22	14	18	11	16	20	14	13	19	8	15.5	100 ± 4.8





Gametocytocidal dose

1. >> 100

2. >> 100

PRIMAQUINE INDEX >> 3.0

Principal Investigator: Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS — TABLE 5.3

GAMETOCYTOCIDAL ACTIVITY

COMPOUND: [illegible] 1884 Ph 4007 BK 64306

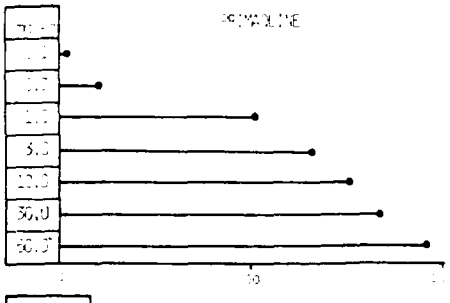
FORMULATION: TWEEN 80 [illegible] ROUTE: [illegible]

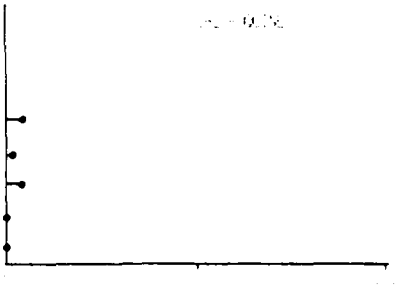
MAXIMUM FULLY TOLERATED DOSE: > 100mg [illegible] EXPERIMENT No.: 2589 DATE: 14.3.84

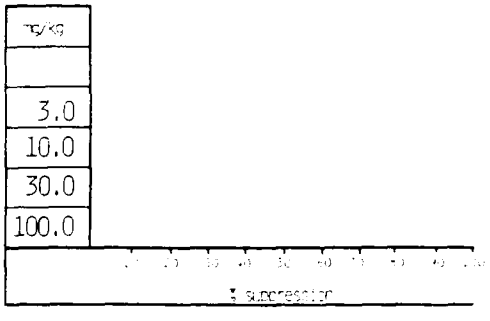
PARASITE: Plasmodium yoelii nigeriensis

VERTEBRATE HOST: [illegible] MICE INVERTEBRATE HOST: Anopheles stephensi

DOSE mg/kg	DOCKET COUNTS D+7										MEAN	% [illegible]
[illegible]	12	16	23	16	20	16	17	18	17	24	17.9	[illegible]
3.0	18	13	16	18	15	10	21	17	20	16	16.4	91.6 ± 4.4
10.0	13	22	15	15	8	11	14	7	12	15	13.2	73.7 ± 6.1
30.0	8	6	7	11	9	8	14	4	9	8	8.4	46.9 ± 5.6
100.0	7	6	3	9	7	5	9	8	4	0	5.8	32.4 ± 5.0







Gametocytocidal dose

[illegible] 31.0 (18.5 - 87.0)

[illegible] 365 (220 - 1000)

PRIMAQUINE INDEX [illegible] 11.1

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible]

GAMETOCYTOCIDAL ACTIVITY

COMPOUND [illegible] 1885 Ph 4017 BK 64315

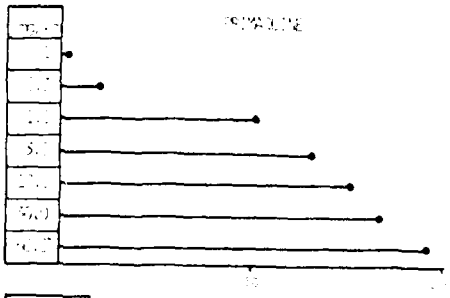
FORMULATION TWEEN 80 [illegible] ROUTE [illegible]

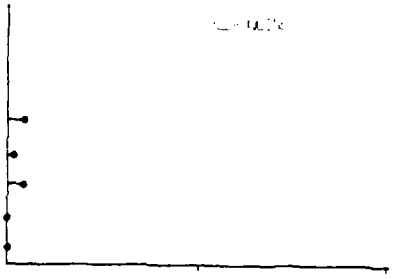
MAXIMUM FULLY TOLERATED DOSE >100mg [illegible] EXPERIMENT No. 2589 [illegible] 14.3.84

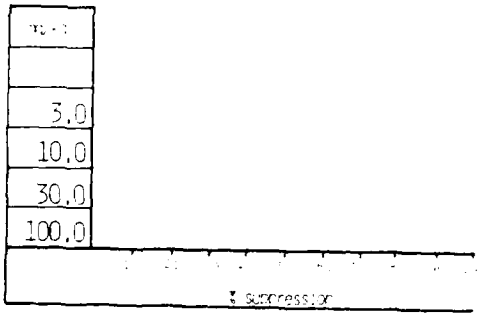
PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST [illegible] TEW MICE INVERTEBRATE HOST Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	[illegible]
0	12	16	23	16	20	16	17	18	17	24	17.9	[illegible]
3.0	19	16	14	10	20	25	18	14	11	16	16.3	91.1 ± 4.4
10.0	13	16	14	18	21	15	16	11	14	10	14.8	82.7 ± 4.4
30.0	2	3	6	4	3	8	4	9	5	1	4.5	25.1 ± 4.5
100.0	4	2	5	0	4	3	0	3	6	6	3.3	18.4 ± 3.4







Gametocytocidal dose

[illegible] 20.0 (10.5 - 39.0)

[illegible] 90.0 (47.0 - 175)

PRIMAQUINE INDEX [illegible] 2.7

Principal Investigator Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 5.7

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1886 Ph 4900 BK 64324

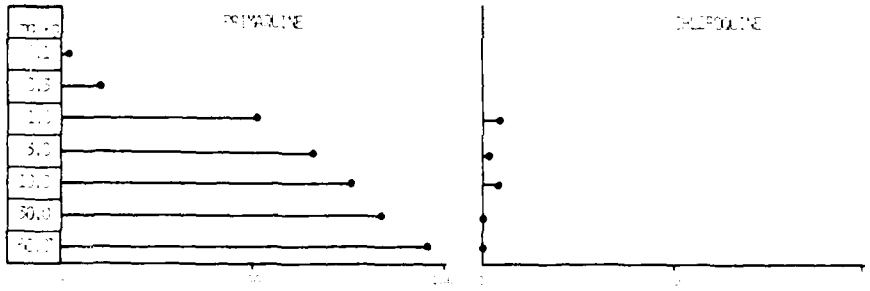
FORMULATION : TWEEN SC / H_2O ROUTE : SC / ~~IP / PO / IV~~

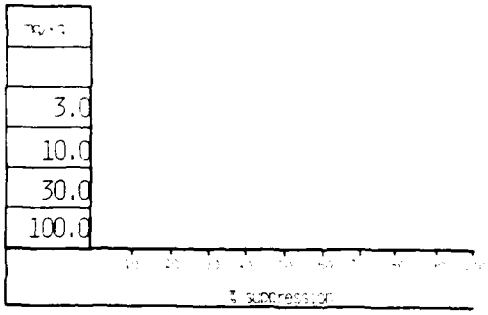
MAXIMUM FULLY TOLERATED DOSE : >100 mg / kg X 1 EXPERIMENT No.: 2589 DATE : 14.3.84

PARASITE : Plasmodium vaelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
Ø	12	16	23	16	20	16	17	18	17	24	17.9	100
3.0	14	13	16	20	10	28	11	22	9	18	16.1	89.0 ± 5.0
10.0	10	10	14	12	8	14	9	11	10	7	10.5	58.7 ± 3.9
30.0	4	1	2	3	6	4	3	6	5	8	4.2	23.5 ± 3.9
100.0	0	6	5	1	2	3	4	1	0	0	2.2	12.3 ± 3.4





Gametocytocidal dose

SD_{50} : 13.5 (8.0 - 30.0)

SD_{90} : 92.0 (54.0 - 200)

PRIMAQUINE INDEX : FI_{50} 2.8

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS - TABLE 5 [illegible]

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1887 Ph 4901 BK 64333

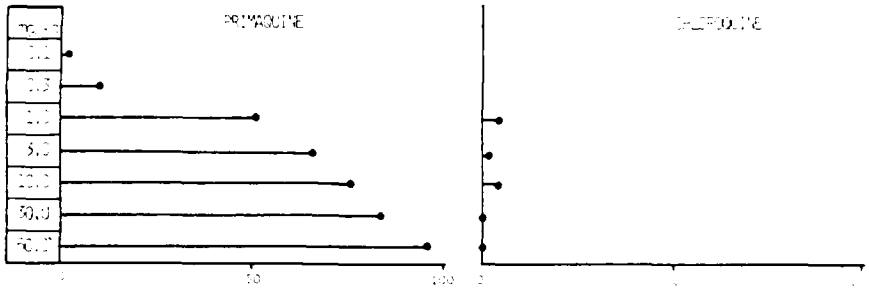
FORMULATION : TWEEN 80 / H_2O ROUTE : SC / ~~IP / PO / IV~~

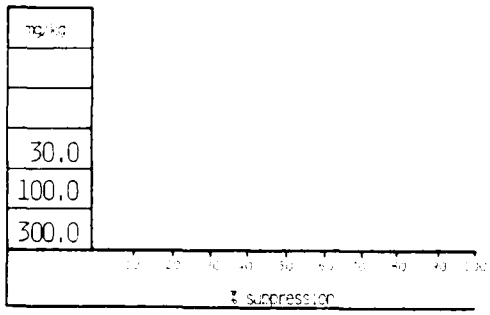
MAXIMUM FULLY TOLERATED DOSE : > 300 mg / kg X 1 EXPERIMENT No : 2576 DATE 7.3.84

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephens.

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% [illegible]
ø	21	16	20	22	19	25	13	6	21		18.1	[illegible]
30.0	15	14	19	15	18	18	20	12	24	12	16.7	92.3 ± 3.4
100.0	18	15	23	19	11	13	16	11	10	14	15.0	82.9 ± 4.5
300.0	12	11	14	8	12	14	10	17	13	7	11.2	61.9 ± 6.6
	5											





Gametocytocidal dose

SD_{50} : > 300

SD_{90} : > 300

PRIMAQUINE INDEX : PI_{50} > 9.1

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible] TABLE 5.7

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1752 WR 245082 BK 02771

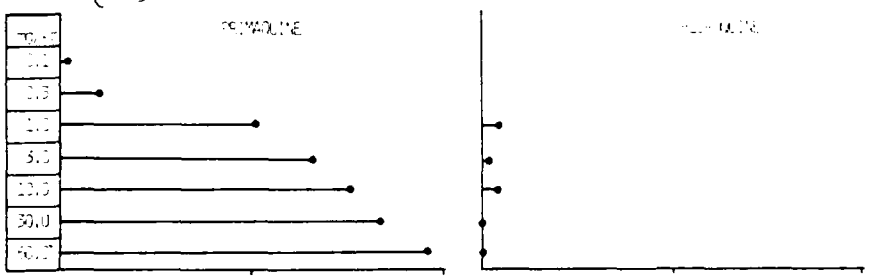
FORMULATION : TWEEN 80 H_2O ROUTE : [illegible]

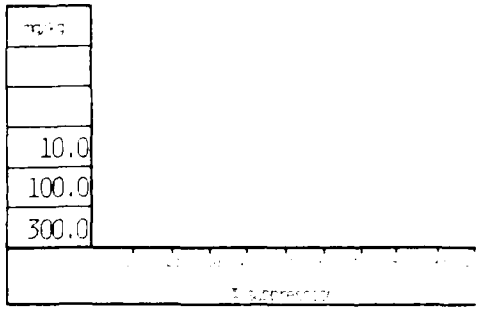
MAXIMUM FULLY TOLERATED DOSE : >300 mg [illegible] EXPERIMENT No. 2532 DATE 15.2.84

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	OOCYST COUNTS D+7										MEAN	% CONTROL
∅	18	27	48	10	11	17	12	11	21	14	18.0	[illegible]
	9											
10.0	16	18	11	19	14	15	12	13	10	15	14.7	81.7 ± 4.4
	19											
100.0	24	14	4	5	5	12	2	4	3	2	7.3	40.6 ± 8.9
	6											
300.0	6	7	3	12	5	6	5	4	9	8	6.2	34.4 ± 5.0
	3											





Gametocytocidal dose

$\varnothing$ 70.0 (28.0 - 185

$\varnothing_1$ 2100 (850 - 5500

PRIMAQUINE INDEX [illegible] 63.6

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TEST — TABLE 5.8

GAMETOCYTOCIDAL ACTIVITY

COMPOUND : LON 1753 WR 246976 BK 02780

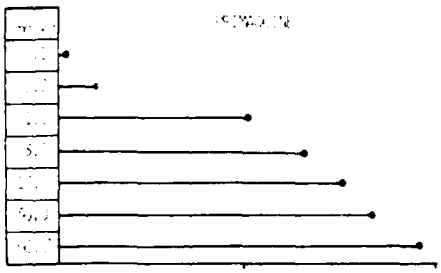
FORMULATION : TWEEN 80 [illegible] ROUTE [illegible]

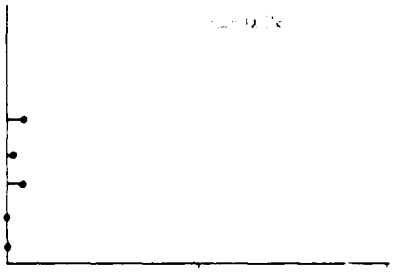
MAXIMUM FULLY TOLERATED DOSE : >300 mg/kg [illegible] EXPERIMENT No. 2532 [illegible] 15.2.84

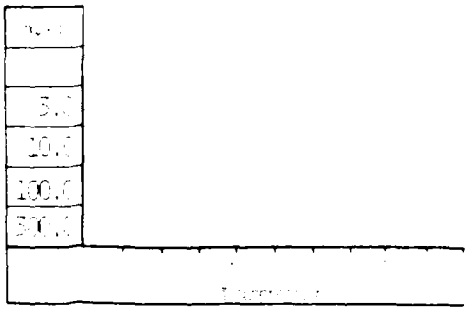
PARASITE : Plasmodium vinckei nigeriensis

VERTEBRATE HOST : [illegible] TFW MICE INVERTEBRATE HOST : Anopheles stephensi

DOSE mg/kg	[illegible]										MEAN	[illegible]
0	18	27	48	10	11	17	12	11	21	14	18.0	[illegible]
	9											
3.0	10	12	13	17	9	16	8	15	12	10	12.2	67.8 ± 5.[illegible]
10.0	11	18	11	6	12	4	8	15	10	14	10.9	60.[illegible] ± [illegible]
100.0	4	4	4	3	5	6	6	4	7		4.6	25.[illegible] ± 1.7
300.0	2	1	3	1	2	0	1	1	2		1.3	7.2 ± 1.7







[illegible]

[illegible] 11.[illegible] 6.2 - 23.[illegible]

[illegible] 255 140 - 51[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

SUMMARY OF ANTIMALARIAL [illegible]

GAMETOCYTOCIDAL ACTIVITY

COMPOUND LON 1740 WR 44450 AD AY 29540

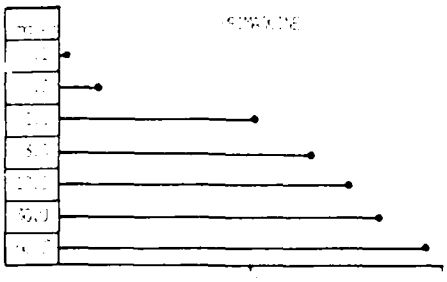
FORMULATION [illegible] TWEEN 80 [illegible] ROUTE [illegible]

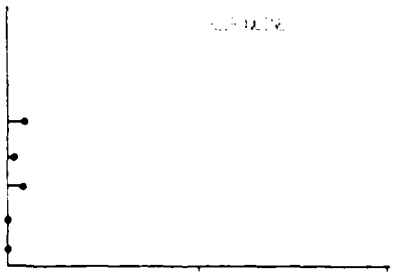
MAXIMUM FULLY TOLERATED DOSE >300 mg [illegible] EXPERIMENT No. 2513 [illegible]

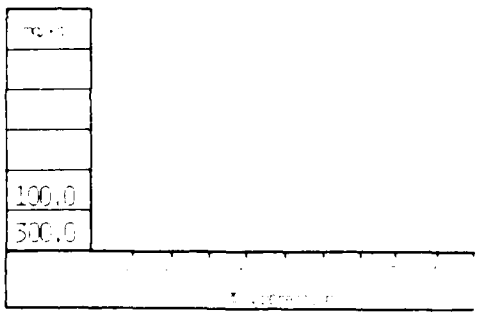
PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST [illegible] TFW MICE INVERTEBRATE HOST Anopheles stephensi

DOSE mg/kg	DOCKET COUNTS [illegible]										MEAN	[illegible]
[illegible]	15	12	18	16	18	14	17	16	18	18	16.5	[illegible]
	19											
100.0	15	14	10	8	13	6	11	7	4	10	10.2	68.[illegible] ± 6.7
	14											
300.0	15	8	2	7	3	12	7	9	4		7.1	43.[illegible] ± 7.[illegible]







Gametocytocidal dose

[illegible] 215 155 - 320

[illegible] 2000 1450 - 3000

PRIMAQUINE INDEX [illegible] 60.0

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible] 1741 WR 102796 AD BC 78878

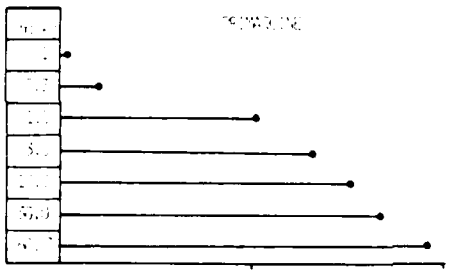
[illegible]

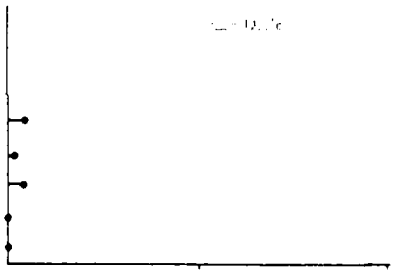
[illegible] >500 [illegible] 2513 [illegible]

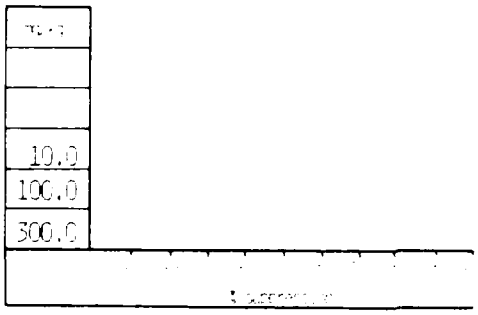
[illegible]

[illegible]

[illegible]	[illegible]										[illegible]	[illegible]
[illegible]	15	12	18	16	18	14	17	16	13	18	16.5	[illegible]
	19											
10.0	22	13	18	7	9	11	14	10	18	9	12.8	60.1 ± [illegible]
	8											
100.0	16	3	5	9	10	6	9	6			[illegible]	41.6 ± [illegible]
300.0	2	7	7	9	4	5	6	4	5	[illegible]	[illegible]	29.7 ± [illegible]







[illegible]

[illegible] 54 [illegible]

[illegible] >500

[illegible] >[illegible]

[illegible]

[illegible]

[illegible]

[illegible] - [illegible] 61

[illegible]

[illegible] 1100 WR 142490 BH 10371 Mefloquine

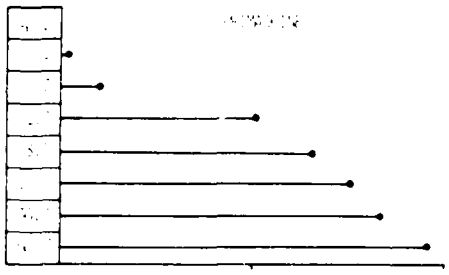
[illegible]

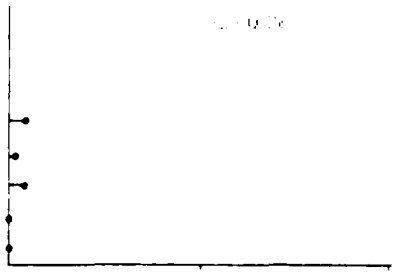
[illegible] >60 [illegible] 2481 [illegible] 25.1.84

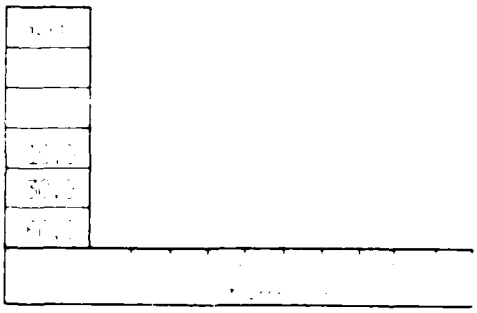
[illegible]

[illegible]

[illegible]	[illegible]										[illegible]	[illegible]
[illegible]	15	18	17	19	20	24	18	23	17	25	19.[illegible]	[illegible]
	14	12	23	21								
10.0	12	16	5	3	9	18	6	13	6	12	[illegible]	[illegible] ± [illegible]
30.0	9	10	6	13	7	2	4	1	17	6	7.5	[illegible] ± 8.4
60.0	4	3	11	3	4	12	8	11	4	7	6.7	[illegible] ± [illegible]







[illegible]

[illegible] 11.[illegible] - 4.0 - 24.0

[illegible] >60.0

[illegible] >1.8

[illegible]

5.4 SPIRENTOIDAL TEST DATA

SUMMARY OF ANTIMALARIAL TESTS — B 2

SPOROGONTOCIDAL ACTIVITY

COMPOUND : CDN 1709 WR 225448 AG BH 58522

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 1 DAY.

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : XXXXXXXXXXXXXXXX XXXX; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2760 DATE : 30.5.84

PRELIMINARY TEST

CONCENTRATION %	OOCYST COUNTS										MEAN	[illegible]
0	15	26	14	73	82	77	17	22	34	36	35.[illegible]	[illegible]
0.05	36	44	25	23	29	27	40	23	37	[illegible]	[illegible]	34.[illegible] ± 4.[illegible]

XXXXXXXXXXXXXXXXXXXXXXXXXXXX INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION %	OOCYST COUNTS										MEAN	[illegible]
0												

-
0.05

SUMMARY OF ANTIMALARIAL TESTS [illegible] 63

SPORONTOCIDAL ACTIVITY

COMPOUND: [illegible] 1715 WR 5990 AG 99266

FORMULATION: DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE: ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE: Plasmodium yoelii nigeriensis

VERTEBRATE HOST: ♂ TFW MICE INVERTEBRATE HOST: Anopheles stephensi

TOXICITY: ~~[illegible]~~; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER: 2760 DATE: 30.5.84

PRELIMINARY TEST

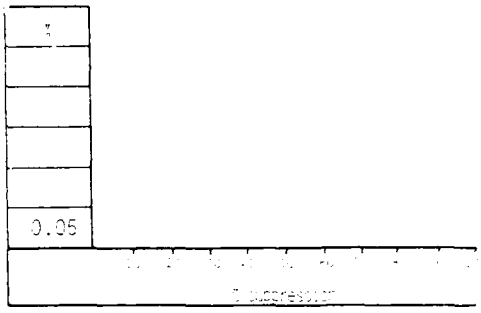
CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	[illegible]
0	15	26	14	73	82	37	17	22	34	38	35.8	[illegible]
0.05	27	25	14	10	20	28	31	19	12	24	20.3	56.6 ± 5.9
	13											

~~[illegible]~~ / ACTIVE ~~[illegible]~~ ~~[illegible]~~ AT [illegible]

EXTENDED TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												[illegible]

%
0.05
[illegible]



% suppression

SPORONTOCIDAL [illegible]

[illegible]

[illegible]

Principal Investigator: Professor W. Peters

Department of Medical Protozoology,

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS

SPORONTOCIDAL ACTIVITY

COMPOUND : LSN 1719   WR 181023   BE 50003

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE   INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : XXXXXXXXXXXXXXXXXXXX / NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2760   DATE : 30.5.84

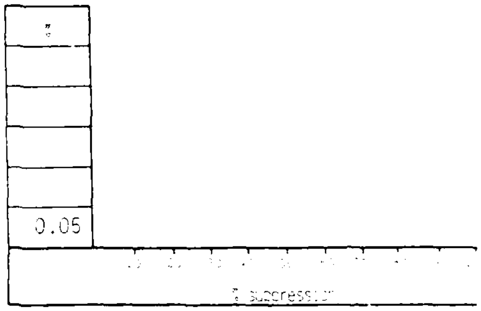
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	15	26	14	73	32	37	17	22	34	38	35.8	[illegible]
0.05	25	20	30	16	29	15	23	18	25	21	21.8	60.9 ± 4.

XXXXXXXXXXXXXXXXX / SLIGHTLY ACTIVE / XXXXXXX AT [illegible] %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												[illegible]



SPORONTOCIDAL DOSE (%)

ID₅₀ [illegible]

ID₉₀ [illegible]

Principal Investigator : Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS [illegible]

SPORONTOCIDAL ACTIVITY

COMPOUND : UM 1720 WR 182234 BE 17580

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX~~ ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2760 DATE : 30.5.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% INHIBITION
2	15	26	14	73	82	37	17	22	34	38	35.8	[illegible]
0.05	45	16	41	21	50	16	32	14	66	22	32.3	90.2 ± [illegible]

~~XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX~~ INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% INHIBITION
2												[illegible]

%
0.05

% CONCENTRATION

SPORONTOCIDAL DOSE [illegible]

[illegible]

[illegible]

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — [illegible] 6 [illegible]

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1721 WR 211814 ZP 12775

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~[illegible]~~ ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2760 DATE : 30.5.84

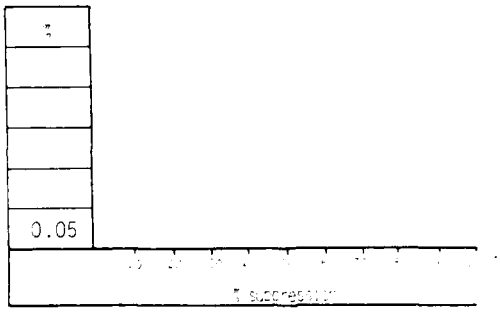
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
♂	15	26	14	73	82	37	17	22	34	38	35.8	[illegible]
0.05	10	42	20	18	13	30	23	39	45	19	25.9	72.3 ± [illegible]

~~[illegible]~~ - SLIGHTLY ACTIVE ~~[illegible]~~ AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
♂												[illegible]



[illegible]

[illegible]

[illegible]

Principal Investigator : Professor [illegible] Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS [illegible]

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1722 WR 215295 ZN 43444

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~[illegible]~~ / NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2776 DATE : 6.6.84

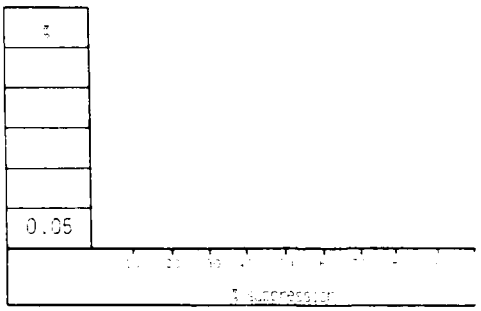
PRELIMINARY TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										[illegible]	[illegible]
2	6	16	25	20	15	24	13	12	22	[illegible]	[illegible]	[illegible]
	58											
[illegible]	15	9	28	13	14	7	5	13	[illegible]	[illegible]	[illegible]	[illegible]

~~[illegible]~~ ACTIVE / ~~[illegible]~~ AT [illegible]

EXTENDED TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										[illegible]	[illegible]
2												[illegible]



[illegible]

[illegible]

[illegible]

Principal Investigator : Professor A. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS - [illegible] 6 -

SPORONTOCIDAL ACTIVITY

COMPOUND : CDN 1723 WR 228000 ZN 81499

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TRW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~[illegible]~~ ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2776 DATE : 6.6.84

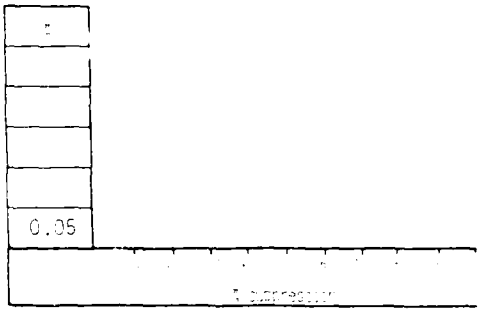
PRELIMINARY TEST

CONCENTRATION %	OOCYST COUNTS D + 7										MEAN	% INHIBITION
2	6	16	25	20	15	24	13	12	22	17	20.7	[illegible]
	58											
[illegible]	16	16	16	17	24	19	19	15	18	17	17.7	85.5 ± [illegible]

~~[illegible]~~ INACTIVE AT DOSE 2

EXTENDED TEST

CONCENTRATION %	OOCYST COUNTS D + 7										MEAN	% INHIBITION
2												[illegible]



SPORONTOCIDAL [illegible]

ED_{50}

ED_{90}

Principal Investigator : Professor W. Peters

Department of Medical Protozoology,

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — 69

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1724 WR 228583 ZN 78910

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : XXXXX XX XXXXXXXXX XXXXXXX; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2776 DATE 6.6.84

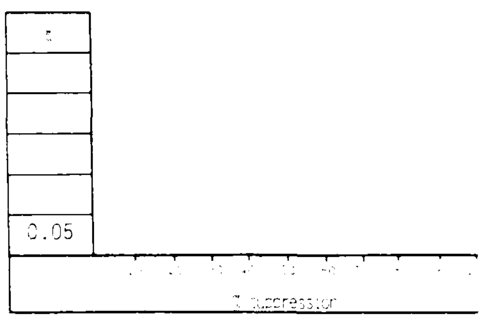
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	6	16	25	20	15	24	13	12	22	17	20.7	[illegible]
	58											
0.05	7	18	17	15	11	8	19	9	7	14	12.5	48.3 ± 5.[illegible]

XXXXXXXXXX ACTIVE XXXXXXXXXXXXXXXXXX AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												[illegible]



SPORONTOCIDAL VALUES (%)

ED50

ED90

Principal Investigator : Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS - PAGE 70

SPORONTOCIDAL ACTIVITY

COMPOUND : CN 1725 WR 233627 BH 13989

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TPW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~XXXXXXXXXXXXXXXXXXXXXXXX~~ : NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2776 DATE : 6.6.84

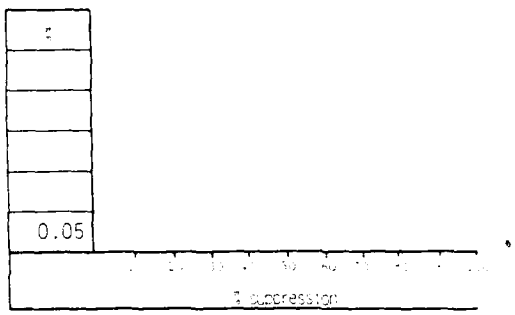
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
2	6	16	25	20	15	24	13	12	22	17	20.7	[illegible]
	58											
0.05	4	9	6	12	16	2	15	12	1		8.6	41.5 ± [illegible]

~~XXXXX ACTIVE~~ / ACTIVE / ~~XXXXXXXXXXXXXXXXXXXXXXXX~~ AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
2												[illegible]



Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS - [illegible]

SPORONTOCIDAL ACTIVITY

COMPOUND : LN 1726 WR 235485 BH 35770

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : 3 TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~[illegible]~~ NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2776 DATE : 6.6.84

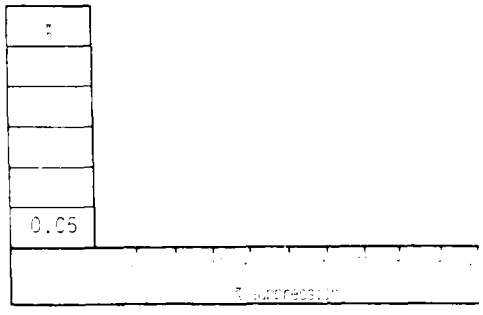
PRELIMINARY TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	% INHIBITION
2	6	16	25	20	15	24	13	12	22	17	20.7	[illegible]
	58											
0.05	5	13	8	3	9	17	15	19	11	7	10.7	51.7 ± [illegible]

~~[illegible]~~ / ACTIVE / ~~[illegible]~~ AT 0.05 %

EXTENDED TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	% INHIBITION
2												[illegible]



SPORONTOCIDAL DOSE [illegible]

[illegible]

[illegible]

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS [illegible]

SPORONTOCIDAL ACTIVITY

COMPOUND : LUN 1727 WR 238605 BH 69990

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : 3 TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~[illegible]~~ NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2776 DATE : 6.6.84

PRELIMINARY TEST

CONCENTRATION %	OOCYST COUNTS D + 7										MEAN	[illegible]
2	6	16	25	20	15	24	13	12	22	17	26.7	[illegible]
	58											
0.05	33	7	21	10	11	16	6	15	5	4	16.3	78.7 ± [illegible]
	19	16										

~~FULLY ACTIVE / ACTIVE / [illegible] ACTIVE~~ INACTIVE AT [illegible]

EXTENDED TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	[illegible]
2												[illegible]

%
0.05
[illegible]

SPORONTOCIDAL [illegible]

[illegible]

[illegible]

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

[illegible]

[illegible]

COMPOUND [illegible] WR [illegible]

FORMULATION [illegible]

ROUTE [illegible]

[illegible]

[illegible]

[illegible]

EXPERIMENT NUMBER [illegible]

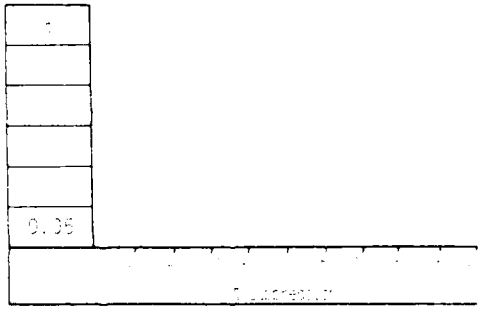
PRELIMINARY TEST

CONCENTRATION %	[illegible]										MEAN	[illegible]
[illegible]	6	[illegible]	25	[illegible]	15	24	13	12	22	17	20.7	[illegible]
	58											
[illegible]	24	[illegible]	11	[illegible]	[illegible]	3	15	23	4	18	11.4	55.1 ± [illegible]

[illegible]

EXTENDED TEST

CONCENTRATION %	[illegible]										MEAN	[illegible]
[illegible]												[illegible]



[illegible]

Principal Investigator : Professor W. Peter

Department of Medical Protozoology

Liverpool School of Hygiene & Tropical Medicine

[illegible]

[illegible]

[illegible] [illegible] WR 246316 [illegible] 46641

FORMULATION [illegible]

ROUTE [illegible]

PARASITE [illegible]

VERTEBRATE HOST [illegible] INVERTEBRATE HOST [illegible]

TOXICITY [illegible]

EXPERIMENT NUMBER 2776 DATE [illegible].6.84

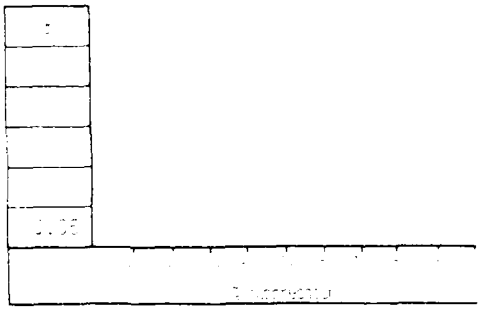
PRELIMINARY TEST

CONCENTRATION %	OOCYST COUNTS [illegible]									MEAN	[illegible]
2	6	16	25	[illegible]	15	24	[illegible]	12	22	[illegible]	21.7	[illegible]
	58										
[illegible]	5	12	25	7	[illegible]	[illegible]	[illegible]	[illegible]	7	12	[illegible]	44.? ± [illegible]

[illegible] ACTIVE [illegible]

EXTENDED TEST

CONCENTRATION %	OOCYST COUNTS [illegible]									MEAN	[illegible]
2											[illegible]



[illegible]

[illegible]

[illegible]

Principal Investigator [illegible]

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 7 [illegible]

SPOROZOICIDAL ACTIVITY

COMPOUND: [illegible] WR 247705 BJ 51779

FORMULATION: [illegible] SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE: ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE: Plasmodium yoelii nigeriensis

VERTEBRATE HOST: [illegible] TFW MICE INVERTEBRATE HOST: Anopheles stephensi

TOXICITY: [illegible], NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2776 DATE: 6.6.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	[illegible]
2	6	16	25	20	15	24	13	12	22	17	20.7	[illegible]
	58											
0.05	7	2	8	10	7	11	7	2	11	3	6.8	[illegible]

[illegible] / ACTIVE / [illegible] AT 0.05 %

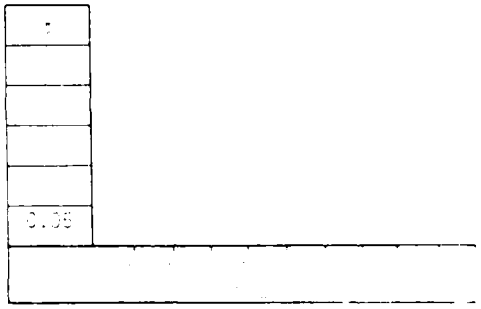
EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	[illegible]
2												[illegible]

%
0.05

[illegible]

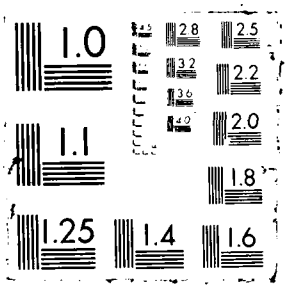
[illegible]



[illegible]

AD-A185 118 CHEMOTHERAPY OF RODENT MALARIA(U) LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE (ENGLAND) DEPT OF MEDICAL PROTOZOOLOGY W PETERS JUL 85 DAMD17-84-C-4018 2/3

UNCLASSIFIED F/G 6/15 NL


1.0
2.8
2.5
3.2
2.2
3.6
4.0
2.0
1.1
1.8
1.25
1.4
1.6

SUMMARY OF ANTIMALARIAL TESTS — TABLE 76

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1731 WR 248412 BJ 59202

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : <u>Plasmodium yoelii nigeriensis</u>

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : <u>Anopheles stephensi</u>

TOXICITY : [illegible] ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2796 DATE : 13.6.84

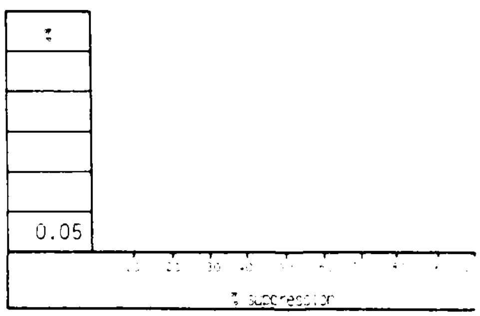
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	41	16	12	40	14	12	19	42	20	24	23.8	[illegible]
	31	15										
0.05	25	39	12	18	46	13	36	8	20	17	23.4	98.3 ± 6.6

[illegible] INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												[illegible]



[illegible]

[illegible]

[illegible]

Principal Investigator : Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 7 7

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1732 WR 237375 BH 58120

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY : ~~TOXIC TOXIC stephensi~~ NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2796 DATE 13.6.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	[illegible]
♂	41	16	12	40	14	12	19	42	20	24	23.3	[illegible]
	31	15										
[illegible]	42	29	35	20	24	17	14	10	8	16	21.5	90.3 ± [illegible]

~~FULLY ACTIVE / ACTIVE / SLIGHTLY ACTIVE~~ / INACTIVE [illegible]

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										[illegible]	[illegible]
♂												[illegible]

[illegible]
[illegible]

[illegible]

[illegible]

[illegible]

SUMMARY OF ANTIMALARIAL TEST [illegible]

SPOROGONOCIDAL ACTIVITY

COMPOUND NO. 1733 WR 228708 BG 66798

FORMULATION DISSOLVED SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE PLASMODIUM [illegible]

VERTEBRATE HOST 2 TPN MICE INVERTEBRATE HOST Aedes aegypti

[illegible] EFFECTIVENESS

EXPERIMENT NUMBER 2796 DATE 13.6.84

PRELIMINARY TEST

CONCENTRATION %	[illegible]										MEAN	[illegible]
2	41	16	12	40	14	13	19	42	20	24	23.3	[illegible]
	31	15										
[illegible]	4	10	20	14	16	21	28	15	13	22	[illegible]	[illegible]

FULLY ACCIDEX X ACCIDEX X EXCESSIVE ACCIDEX X [illegible]

LATER TEST

CONCENTRATION %	[illegible]										MEAN	[illegible]
2												[illegible]

SUMMARY OF ANTIMALARIAL TESTS [illegible]

CHORONTOCIDAL ACTIVITY

COMPOUND [illegible] 1734 WR 242511 AA BH 89438

FORMULATION DISSOLVED SUSPENDED IN [illegible] AQUEOUS SUCROSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR [illegible]

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST [illegible] TEW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY [illegible]

EXPERIMENT NUMBER 2796 DATE [illegible]

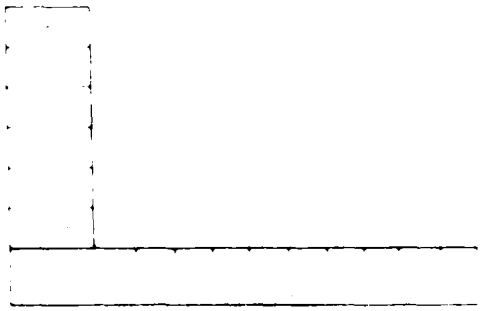
PRELIMINARY TEST

CONCENTRATION %	[illegible]										[illegible]	[illegible]
[illegible]	41	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	31	[illegible]										
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]										

[illegible]

EXTENDED TEST

CONCENTRATION %	[illegible]										[illegible]	[illegible]
[illegible]												



SUMMARY OF ANTIMALARIAL TESTS [illegible] 80

PERIODICAL ACTIVITY

COMPOUND [illegible] 7736 WR 242511 AB BU 78592

FORMULATION [illegible] SUSPENDED IN [illegible] AQUEOUS [illegible]

ROUTE [illegible] ADMINISTRATION [illegible]

PARASITE [illegible]

VERTEBRATE [illegible] INVERTEBRATE [illegible]

[illegible]

EXPERIMENT NUMBER [illegible] DATE [illegible]

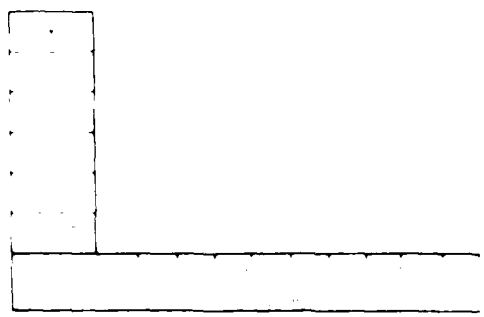
PRELIMINARY TEST

CONCENTRATION %	[illegible]										[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]										
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

OTHER TEST

CONCENTRATION %	[illegible]										[illegible]	[illegible]
[illegible]												[illegible]



[illegible]

SUMMARY OF ANTIMALARIAL TESTS — TABLE 81

SPORONTOCIDAL ACTIVITY

COMPOUND LON 1751 WR 194343 ZN 41968

FORMULATION DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST 3 TFW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY TOXIC TO A. stephensi 40.0% ~~[illegible]~~ 50 mortality

EXPERIMENT NUMBER 2796 DATE 13.6.84

PRELIMINARY TEST

CONCENTRATION (%)	OOCYST COUNTS 2 + 7										MEAN	[illegible]
2	41	16	12	40	14	12	19	42	20	24	[illegible]	[illegible]
	31	15										
[illegible]	27	13	18	12	15	18					17.2	[illegible]

~~FULLY ACTIVE / ACTIVE / [illegible]~~ SLIGHTLY ACTIVE ~~[illegible]~~ [illegible]

EXTENDED TEST

CONCENTRATION (%)	OOCYST COUNTS 2 + 7										MEAN	[illegible]
2												[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

SUMMARY OF ANTIMALARIAL TESTS — TABLE 82

SPORONTOCIDAL ACTIVITY

COMPOUND LON 1877 WR 199508 AD BK 56500

FORMULATION DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST 3 TFW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY ~~TOXIC TO A stephensi AT ---%~~ ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2816 DATE 20.6.84

PRELIMINARY TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
[illegible]	15	56	19	16	16	15	14	18	19	26	21.4	[illegible]
[illegible]	10	45	17	9	6	9	17	12	18	9	15.2	71.0 ± 7.2

~~FULLY ACTIVE / ACTIVE~~ / SLIGHTLY ACTIVE / ~~INACTIVE AT 0.05 %~~

EXTENDED TEST

CONCENTRATION (%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
[illegible]												[illegible]

SUMMARY OF ANTIMALARIAL TESTS — TABLE 83

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1940 WR 199508 ZP 43350

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : [illegible] NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2830 DATE : 27.6.84

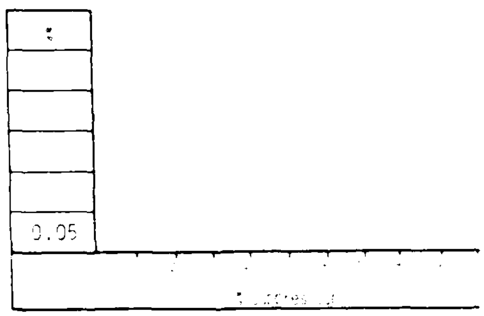
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	30	19	32	25	41	21	10	13	9	28	24.9	100
	46											
0.05	4	14	12	6	4	3	60	33	19	33	17.3	69.3 ± 8.5
	16	3										

[illegible] SLIGHTLY ACTIVE [illegible] AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												100



Principal Investigator : Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1931 WR 249725 BK 69990

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : XXXXXXXXXXXXXXXXXXXXX ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2830 DATE : 27.6.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	30	19	32	25	41	21	10	13	9	28	24.9	100
	46											
0.05	12	14	8	13	1	14	10	16	7	11	10.6	42.6 ± 6.0

XXXXXXXXX ACTIVE / XXXXXXXXXXXXXXXX AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												100

%
0.05

% suppression

SPORONTOCIDAL DOSE (%)

SD_{50} :

SD_{90} :

Principal Investigator : Professor ...
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS

SPORONTOCIDAL ACTIVITY

TABLE 85

COMPOUND : LON 1932 WR 251855 AA BK 71178

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : TOXIC TO A.stephensi AT .05% ; ~~NO TOXIC EFFECTS SEEN~~ 92 % mortality

EXPERIMENT NUMBER : 2830 DATE : 27.6.84

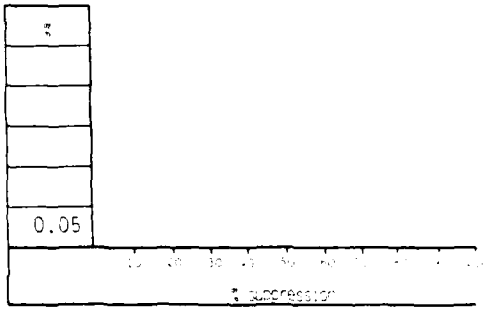
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
∂	30	19	32	25	41	21	10	13	9	28	24.9	100
	46											
0.05	18	12									15.0	60.2

~~FULLY ACTIVE~~ / ACTIVE / ~~SLIGHTLY ACTIVE~~ ~~INACTIVE~~ AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
∂												100



%
0.05

10 20 30 40 50 60 70 80 90 100

% suppression

SPORONTOCIDAL DOSE (%)

LpD_{50}

LpD_{100}

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 8 6

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1884 Ph 4007 BK 64306

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelli nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : TOXIC TO A.stephensi AT .05% ; ~~[illegible]~~ 100 % mortality

EXPERIMENT NUMBER : 2816 DATE : 20.6.84

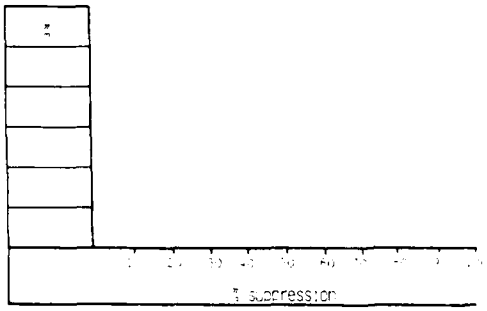
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
Ø	15	56	19	16	16	15	14	18	19	26	21.4	100
0.05												TOXIC

FULLY ACTIVE / ACTIVE / SLIGHTLY ACTIVE / INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
Ø												



SPORONTOCIDAL DOSE (S)

SD_{50} :

SD_{90} :

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 87

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1885 Ph 4017 BK 64315

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : TOXIC TO A.stephensi AT .05 % ; ~~NO TOXIC EFFECTS SEEN~~ 80 % mortality

EXPERIMENT NUMBER : 2816 DATE : 20.6.84

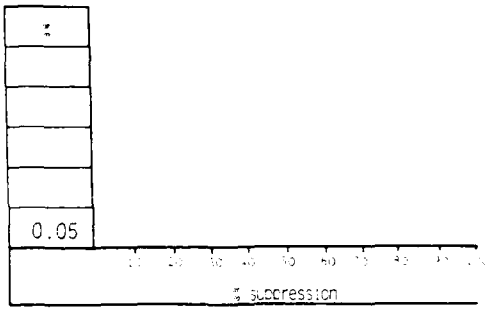
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	15	56	19	16	16	15	14	18	19	26	21.4	100
0.05	45	79	6	3	64	31					38.0	100 ± 13.[illegible]

~~FULLY ACTIVE / ACTIVE / SLIGHTLY ACTIVE~~ / INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												100



SPORONTOCIDAL DOSE (ID)

ID_{50} :

ID_{90} :

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS - TAB : S 5

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1886 Ph 4900 BK 64324

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : TOXIC TO A.stephensi AT .05% ; ~~NO TOXIC EFFECTS SEEN~~ 72 % mortality

EXPERIMENT NUMBER : 2816 DATE : 20.6.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	15	56	19	16	16	15	14	18	19	26	21.4	100
0.05	12	17	18	14	12	10	8				13.0	60.7 ± 4.7

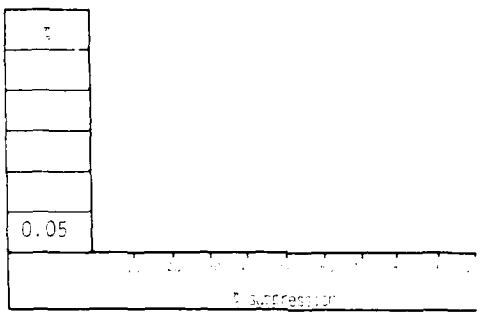
~~FULLY ACTIVE~~ ACTIVE ~~[illegible]~~ / ~~INACTIVE~~ AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												100

%
0.05

% suppression



SPORONTOCIDAL DOSE LEVEL

SpD_{50} :

SpD_{90}

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS [illegible]

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1887 Ph 4901 BK 64333

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY : TOXIC TO A.stephensi AT .05% ; [illegible] 92 % mortality

EXPERIMENT NUMBER : 2816 DATE : 20.6.84

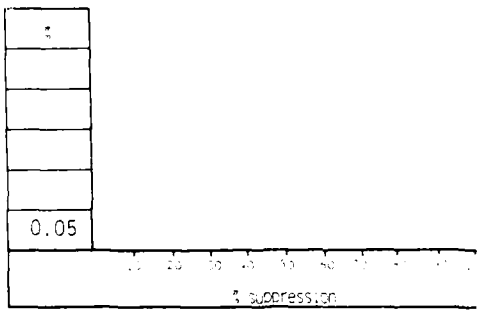
PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
Ø	15	56	19	16	16	15	14	18	19	26	21.4	[illegible]
0.05	100	58									79.0	100

[illegible] INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
Ø												[illegible]



[illegible]

[illegible]

[illegible]

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TEST [illegible] 90

SPORONTICIDAL ACTIVITY

COMPOUND [illegible] 1752 WR 245082 BK 02771

FORMULATION DISSOLVED SUSPENDED IN 5 % AQUEOUS GLUCOSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUGAR FEED FOR 7 DAYS

PARASITE Plasmodium berghei berghei

VERTEBRATE HOST [illegible] MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY [illegible] NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2796 DATE 13.6.84

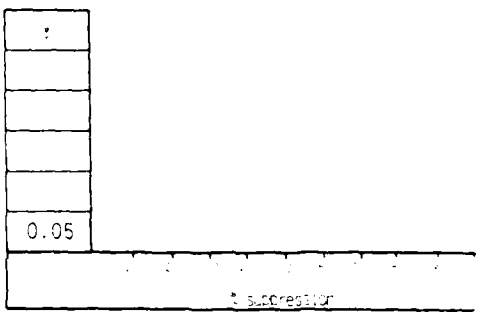
PRELIMINARY TEST

CONCENTRATION %	OOCYST COUNTS 0 + 7										MEAN	% ACT.
2	41	16	12	40	14	12	19	42	20	24	[illegible]	[illegible]
	31	15										
[illegible]	39	32	36	23	24	13	22	38	14	21	[illegible]	[illegible]

[illegible] INACTIVE AT [illegible]

EXTENDED TEST

CONCENTRATION %	OOCYST COUNTS 0 + 7										MEAN	% ACT.
2												[illegible]



Principal Investigator Professor W. Peters

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SUMMARY OF ANTIMALARIAL TESTS

PURONTOXIDAL ACTIVITY

[illegible] WR 44450 AD AY 29540

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]	[illegible]										[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]										
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

[illegible]	[illegible]										[illegible]	[illegible]
[illegible]												

SUMMARY OF ANTIMALARIAL TESTS [illegible]

PORONTOIDAL ACTIVITY

COMPOUND LSN 1741 WR 102796 AD BC 78879

FORMULATION DISSOLVED SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST [illegible] TFW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY TOXIC TO Aistephensi AT .05% [illegible] 40 mortality

EXPERIMENT NUMBER 2796 DATE 13.6.84

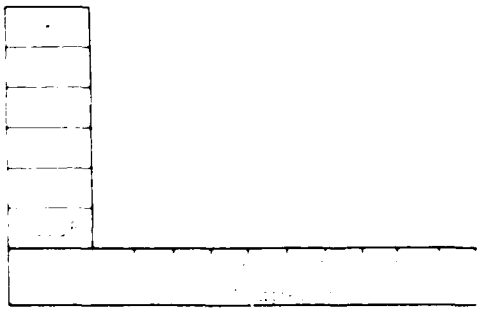
PRELIMINARY TEST

CONCENTRATION %	[illegible]										[illegible]	[illegible]
[illegible]	41	16	12	40	14	12	19	42	[illegible]	24	[illegible]	[illegible]
	31	16										
[illegible]	17	22	29	11	7	6					[illegible]	[illegible]

[illegible]

EXTENDED TEST

CONCENTRATION %	[illegible]										[illegible]	[illegible]
[illegible]												[illegible]



[illegible]

SUMMARY OF ANTIMALARIAL TESTS TABLE 99

SPOROGONTOCIDAL ACTIVITY

COMPOUND CDN 1716 WR 9792 AJ 63248

FORMULATION DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE Plasmodium yoelii nigeriensis

VERTEBRATE HOST ♂ TFW MICE INVERTEBRATE HOST Anopheles stephensi

TOXICITY ~~XXXXX XX X XXXXXXXXXX X XX XXXXX~~ / NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER 2760 DATE 30.5.84

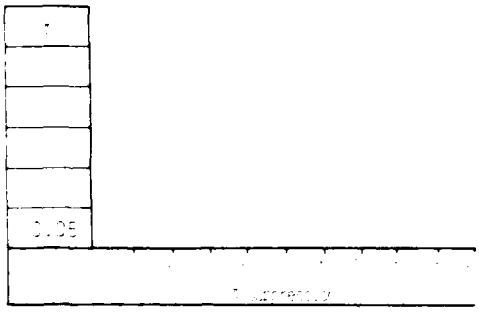
PRELIMINARY TEST

CONCENTRATION %	OOCYST COUNTS D + 7										MEAN	% CONTROL
2	15	26	14	73	82	37	17	22	34	38	35.8	[illegible]
[illegible]	30	27	40	13	36	18	35	22	64	16	30.7	85.8 ± 5.[illegible]

~~XPOLAXXXCXXX XXXCXXX XXXOLDXXLXXXCXXX~~ INACTIVE AT DOSE 2

DETAILED TEST

CONCENTRATION %	OOCYST COUNTS D + 7										MEAN	% CONTROL
2												[illegible]



[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

SUMMARY OF ANTIMALARIAL TESTS

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1718 WR 158124 BD 22997

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : XXXXX XX X Xstephensi X XX X X X% ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2760 DATE : 30.5.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0	15	26	14	73	82	37	17	22	34	38	35.8	100
0.05	18	16	17	26	20	33	24	16			21.3	59.4 ± 4.7

FULLY ACTIVE / PARTIALLY ACTIVE / SLIGHTLY ACTIVE / INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
0												100

%

0.05

% suppression

SPORONTOCIDAL DOSE (%)

SD_{50}

SD_{90}

Principal Investigator : Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL TESTS — TABLE 101

SPORONTOCIDAL ACTIVITY

COMPOUND : LON 1909 WR 203659 ZN 39913

FORMULATION : DISSOLVED / SUSPENDED IN 5 % AQUEOUS SUCROSE SOLUTION

ROUTE : ORAL ADMINISTRATION TO MOSQUITOES IN SUCROSE FEED FOR 7 DAYS

PARASITE : Plasmodium yoelii nigeriensis

VERTEBRATE HOST : ♂ TFW MICE INVERTEBRATE HOST : Anopheles stephensi

TOXICITY : ~~XXXX XX Anopheles XXXXXX~~ ; NO TOXIC EFFECTS SEEN

EXPERIMENT NUMBER : 2830 DATE : 27.6.84

PRELIMINARY TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
∂	30	19	32	25	41	21	10	13	9	28	24.9	100
	46											
0.05	47	10	60	101	72	37	23	22	6	13	37.4	100 ± 7.6

~~RULXXXACTIVE XXXACTIVE XXSLIGHTXXXACTIVE~~ / INACTIVE AT 0.05 %

EXTENDED TEST

CONCENTRATION(%)	OOCYST COUNTS D + 7										MEAN	% CONTROL
∂												

SPORONTOCIDAL [illegible]

[illegible]

[illegible]

Principal Investigator : Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

5.5 DRUG INTERACTION TEST DATA

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 102

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Mefloquine (M) +

OR NUMBER Spiramycin (SP)..... PARASITE (SUB)SPECIES ...P. berghei....

FORMULATION ..Tween 80 / H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	M 0.5 + SP 3.0	5		-	80.0 ± 11.7
	M 1.0 + SP 3.0	5		-	75.7 ± 9.7
N	M 2.0 + SP 3.0	5	1	-	46.2 ± 7.9
	M 3.0 + SP 3.0	5		-	2.7 ± 0.9
	Ø	10		14.9	
ED_{50}(range) 1.1 (0.6 - 2.1)					
ED_{90}(range) 2.7 (1.7 - 5.3)					
Resistance factor I_{90}					
	M 0.5 + SP 10.0	5		-	22.7 ± 4.3
	M 1.0 + SP 10.0	5		-	20.1 ± 7.0
N	M 3.0 + SP 10.0	5	1	-	16.4 ± 1.0
	M 10.0 + SP 10.0	5		-	2.7 ± 0.6
	Ø	10		14.9	
ED_{50}(range) 0.4 (0.2 - 0.7)					
ED_{90}(range) 1.4 (0.7 - 2.7)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 103

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Mefloquine (M) +

OR NUMBER Spiramycin (SP) ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O .. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	M 0.5 + SP 30.0	5		-	4.0 ± 0.7
	M 1.0 + SP 30.0	5		-	4.0 ± 1.9
N	M 2.0 + SP 30.0	5	1	-	2.7 ± 0.9
	M 3.0 + SP 30.0	5		-	2.0 ± 1.0
	Ø	10		14.9	
ED_{50}(range) < 0.5					
ED_{90}(range) < 0.5					
Resistance factor I_{90}					
	M 0.5 + SP 60	5		-	0.6 ± 0.3
	M 1.0 + SP 60	5		-	1.3 ± 0.7
N	M 2.0 + SP 60	5	1	-	1.0 ± 0.2
	M 3.0 + SP 60	5		-	1.3 ± 0.7
	Ø	10		14.9	
ED_{50}(range) < 0.5					
ED_{90}(range) < 0.5					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible] 10[illegible]

BLOOD [illegible]

COMPOUND NAME Spiramycin (SP) +

OR NUMBER Mefloquine ..... PARASITE [illegible] P berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD ..... MG/KG [illegible]

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated [illegible] / Control [illegible]
	SP 3.0 + M 0.5	5		–	80.0 ± 11.7
	SP 10.0 + M 0.5	5		–	22.7 ± 4.3
N	SP 30.0 + M 0.5	5	1	–	4.0 ± 0.7
	SP 60.0 + M 0.5	5		–	0.6 ± 0.3
	Ø	10		14.9	
ED_{50} (range)	5.3 (4.0 - 12.0)				
ED_{90} (range)	19.8 (12.5 - 36.5)				
Resistance factor I_{90}					
	SP 3.0 + M 1.0	5		–	75.7 ± 9.7
	SP 10.0 + M 1.0	5		–	20.1 ± 7.0
N	SP 30.0 + M 1.0	5	1	–	4.0 ± 1.9
	SP 60.0 + M 1.0	5		–	1.3 ± 0.7
	Ø	10		14.9	
ED_{50} (range)	5.0 (2.5 - 10.5)				
ED_{90} (range)	22.5 (11.5 - 47)				
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 105

BLOOD SCHIZONTOCIDES

COMPOUND NAME Spiramycin (SP) +
CODE NUMBER Mefloquine (M) PARASITE SUB SPECIES P. berghei

FORMULATION Tween 80 | H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD ..... MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRC/Control PRC
	SP 3.0 + M 2.0	5		-	46.2 ± 7.9
	SP 10.0 + M 2.0	5		-	16.4 ± 1.0
N	SP 30.0 + M 2.0	5	1	-	2.7 ± 0.9
	SP 60.0 + M 2.0	5		-	1.0 ± 0.2
	Ø	10		14.9	

ED_{50} range 2.4 (1.4 - 3.5)

ED_{90} range 15.0 (9.0 - 22.5)

Resistance factor I_{90}

	SP 3.0 + M 3.0	5		-	2.7 ± 0.9
	SP 10.0 + M 3.0	5		-	2.7 ± 0.6
N	SP 30.0 + M 3.0	5	1	-	2.0 ± 1.0
	SP 60.0 + M 3.0	5		-	1.3 ± 0.7
	Ø	10		14.9	

ED_{50} range < 3.0

ED_{90} range < 3.0

Resistance factor I_{90}

Principal Investigator: Professor [illegible]
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 106

BLOOD SCHIZONTOCIDES

COMPOUND NAME

OR NUMBER Halofantrine PARASITE (SUB SPECIES) P berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC ~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE MTD ..... MG/KG X ...

Strain	Daily dose mg/kg DD-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR%
	0.03	5		-	90.6 ± 3.1
	0.1	5		-	70.6 ± 2.9
N	0.3	5	1	-	61.0 ± 5.0
	1.0	5		-	9.2 ± 6.9
	3.0	5		-	0.6 ± 0.5
	Ø	10		23.1	

[illegible] 0.2(0.1 - 0.5)

[illegible] 0.8(0.3 - 1.6)

[illegible] factor [illegible]

ED_{50} range

ED_{90} range

Resistance factor [illegible]

Principal Investigator: Professor [illegible]

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible] PAGE 1 of [illegible]

BLOOD SCHIZONTICIDE

COMPOUND NAME

SR NUMBER Spiramycin PARASITE [illegible] P berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD ..... MG/KG [illegible]

Strain	Daily dose mg/kg DD-5+3	No. of mice	No. of experiments	Mean [illegible] parasite rate %	[illegible]
	1.0	5		-	87.0 ± 4.9
	3.0	5		-	84.8 ± 7.1
N	10.0	5	1	-	52.9 ± 5.9
	30.0	5		-	8.3 ± 3.9
	100.0	5		-	1.7 ± 0.6
	Ø	10		23.1	
ED_{50} (range) 6.2 (2.7 - 18.8)					
ED_{90} (range) 26.0 (11.3 - 78.0)					
Resistance factor I_{90}					
ED_{50} (range)					
ED_{90} (range)					
Resistance factor I_{90}					

Principal Investigator: Professor [illegible]
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

Spiramycin (SP) + Halofantrine (H) — F. berghei

Tween 80 / H_2O

	SP 1.0 + H 0.03	5		-	94.5 ± 3.4
	SP 3.0 + H 0.03	5		-	82.5 ± 4.9
N	SP 10.0 + H 0.03	5	1	-	45.8 ± 4.9
	SP 30.0 + H 0.03	5		-	4.9 ± 2.2
	SP 100 + H 0.03	5		-	3.4 ± 0.7
	Ø	10		23.1	

6.0 (2.5 - 12.8)

30.0 (13.0 - 64.0)

	SP 1.0 + H 0.1	5		-	90.0 ± 6.0
	SP 3.0 + H 0.1	5		-	70.1 ± 7.7
N	SP 10.0 + H 0.1	5	1	-	37.5 ± 7.9
	SP 30.0 + H 0.1	5		-	9.1 ± 3.7
	SP 100 + H 0.1	5		-	2.2 ± 0.9
	Ø	10		23.1	

ED_{50} range 5.8 (3.4 - 9.0)

ED_{90} range 29.0 (17.0 - 45.0)

Resistance factor I_{90}

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

Spiramycin (SP) + Halofantrine (H)

Tween 80 / H_2O

P berghe

	SP 1.0 + H 0.3	5	-	84.8 ± 3
	SP 3.0 + H 0.3	5	-	65.0 ± 8
N	SP 10.0 + H 0.3	5	-	46 ± 3.9
	SP 30.0 + H 0.3	5	-	8.7 ± 3.2
	SP 100 + H 0.3	5	-	0.9 ± 0.8
	Ø	10	23	

52 (21 - 100)

255 (100 - 470)

	SP 1.0 + H 1.0	5	-	5.2 ± 3.5
	SP 3.0 + H 1.0	5	-	2.2 ± 1.7
N	SP 10.0 + H 1.0	5	-	0
	SP 30.0 + H 1.0	5	-	0
	SP 100 + H 1.0	5	-	0
	Ø	10	23	

range 0.2 (0.1 - 0.5)

range 0.8 (0.4 - 1.8)

Resistance factor

Principal Investigator: Professor [illegible]
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

Halofantrine (HA) + Spiramycin (SP)

P berghei

Tween 80/ H_2O

	H 0 03 + SP 1 0	5		-	94 5 ± 3 4
	H 0 1 + SP 1 0	5		-	90 0 ± 6 0
N	H 0 3 + SP 1 0	5		-	84 8 ± 1 3
	H [illegible] + SP 1 0	5		-	5 2 ± 3 5
	H 3 0 + SP 1 0	5		-	0
	Ø	10		23 1	

0 2 (0.07 - 0 6)

0 6 (0 2 - 1 5)

	H 0 03 + SP 3 0	5		-	82 5 ± 4 9
	H 0 1 + SP 3 0	5		-	70 1 ± 7 7
N	H 0 3 + SP 3 0	5		-	65 0 ± 8 1
	H 1 0 + SP 3 0	5		-	2 2 ± 1 7
	H 3 0 + SP 3 0	5		-	0
	Ø	10			

0 1 (0.05 - 0 5)

0 4 (0 1 - 1 3)

Principal Investigator: Professor W Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 111

BLOOD SCHIZONTICIDES

COMPOUND NAME: Halofantrine (H) + Spiramycin (SP) ..... PARASITE SUB SPECIES: P. berghei .....

CODE NUMBER: .....

FORMULATION: Tween 80 / H_2O .. ROUTE OF ADMINISTRATION: SC ~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE MTD: ..... MG/KG X ...

Strain	Daily dose mg/kg DC-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPR % / Control PPR % x 100
	H 0.03 + SP 10.0	5		-	45.8 ± 4.9
	H 0.1 + SP 10.0	5		-	37.5 ± 7.9
N	H 0.3 + SP 10.0	5	1	-	46.1 ± 3.9
	H 1.0 + SP 10.0	5		-	0
	H 3.0 + SP 10.0	5		-	0
	Ø	10		23.1	
ED_{50} range	0.07 (0.03 - 0.3)				
ED_{90} range	0.2 (0.06 - 0.6)				
Resistance factor i_{90}					
	H 0.03 + SP 30.0	5		-	4.9 ± 2.2
	H 0.1 + SP 30.0	5		-	9.1 ± 3.7
N	H 0.3 + SP 30.0	5	1	-	8.7 ± 3.2
	H 1.0 + SP 30.0	5		-	0
	H 3.0 + SP 30.0	5		-	0
	Ø	10		23.1	
ED_{50} (range)	0.025 (0.004 - 0.03)				
ED_{90} (range)	0.09 (0.02 - 0.1)				
Resistance factor i_{90}					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 112

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..HALOFANTRINE..... PARASITE (SUB)SPECIES ..P. berghei...

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		–	91.7 ± 2.9
	0.3	5		–	75.3 ± 6.3
N	0.5	5	1	-	66.0 ± 9.4
	1.0	5		-	26.2 ± 7.6
	Ø	10		23.6	
ED_{50}(range) 0.3(0.3 - 1.2)					
ED_{90}(range) 1.7(1.0 - 3.3)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 113

COMPOUND NAME OR NUMBER .SPIRAMYCIN..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >20.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	5.0	5		–	83.3 ± 1.8
	10.0	5		–	61.2 ± 8.4
N	15.0	5	1	–	45.3 ± 11.4
	20.0	5		–	39.4 ± 3.9
	Ø	10		23.6	
ED_{50}(range) 13.5 ([illegible])					
ED_{90}(range) [illegible]					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 111

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER SPIRAMYCIN PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 5.0	5		-	68.6 ± 9.7
	0.3 + 5.0	5		-	41.5 ± 2.8
N	0.5 + 5.0	5	1	-	40.6 ± 3.0
	1.0 + 5.0	5		-	13.0 ± 7.9
	Ø	10		23.6	
ED_{50}(range) 0.27 (0.12 - 0.5)					
ED_{90}(range) 1.1 (0.5 - 2.1)				0.64 / 0.[illegible]	
Resistance factor I_{90}					
	0.1 + 10.0	5		-	47.2 ± 5.6
	0.3 + 10.0	5		-	47.9 ± 5.6
N,	0.5 + 10.0	5	1	-	42.2 ± 3.6
	1.0 + 10.0	5		-	1.9 ± 0.2
	Ø	10		23.6	
ED_{50}(range) 0.35 (0.26 0.48)					
ED_{90}(range) 0.65 (0.5 - 0.92)				0.38 / 0.1[illegible]	
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 115

COMPOUND NAME HALOFANTRINE +

OR NUMBER .SPIRAMYCIN..... PARASITE (SUB)SPECIES .P. berghei.....

FORMULATION .Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 15.0	5		–	84.1 ± 2.4
	0.3 + 15.0	5		–	67.4 ± 9.5
N	0.5 + 15.0	5	1	–	42.0 ± 11.0
	1.0 + 15.0	5		–	11.0 ± 3.7
	Ø	10		23.6	
ED_{50}(range) 0.3(0.19 - 0.52)					
ED_{90}(range) 0.8(0.5 - 1.4)					
Resistance factor I_{90}					
	0.1 + 20.0	5		–	73.7 ± 8.8
	0.3 + 20.0	5		–	38.1 ± 4.6
N	0.5 + 20.0	5	1	–	34.8 ± 4.5
	1.0 + 20.0	5		–	2.1 ± 1.0
	Ø	10		23.6	
ED_{50}(range) 0.22(0.13 - 0.4)					
ED_{90}(range) 0.54(0.32 - 1.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 116

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME SPIRAMYCIN +

OR NUMBER HALOFANTRINE..... PARASITE (SUB)SPECIES P.berghei.....

FORMULATION Tween 80 / H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	5.0 + 0.1	5		-	68.6 ± 9.7
	10.0 + 0.1	5		-	47.2 ± 5.6
N	15.0 + 0.1	5	1	-	84.1 ± 2.4
	20.0 + 0.1	5		-	73.7 ± 8.3
	Ø	10		23.6	
ED_{50}(range)					
ED_{90}(range) >20					
Resistance factor I_{90}					
	5.0 + 0.3	5		-	41.5 ± 2.8
	10.0 + 0.3	5		-	47.9 ± 5.6
N,	15.0 + 0.3	5	1	-	67.4 ± 9.5
	20.0 + 0.3	5		-	38.1 ± 4.6
	Ø	10		23.6	
ED_{50}(range)					
ED_{90}(range) >20					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 117

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME SPIRAMYCIN +

OR NUMBER .HALOFANTRINE..... PARASITE (SUB)SPECIES ..P.berghei....

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	5.0 + 0.5	5		-	40.6 ± 3.0
	10.0 + 0.5	5		-	42.2 ± 3.6
N	15.0 + 0.5	5	1	-	42.0 ± 11.0
	20.0 + 0.5	5		-	34.8 ± 4.5
	Ø	10		23.6	
ED_{50}(range)					
ED_{90}(range) > 20				> 0.23 0.2	
Resistance factor I_{90}					
	5.0 + 1.0	5		-	13.0 ± 7.9
	10.0 + 1.0	5		-	1.9 ± 0.2
N,	15.0 + 1.0	5	1	-	11.0 ± 3.7
	20.0 + 1.0	5		-	2.1 ± 1.0
	Ø	10		23.6	
ED_{50}(range) ~ 1.0					
ED_{90}(range) ~ 6.2				0.10 0.5	
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS [illegible] 11 -

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..Halofantrine..... PARASITE SUB SPECIES .P berghei

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated rate / control rate %
	0.1	5		-	94.8 ± 5.2
	0.3	5		-	91.4 ± 2.0
N	1.0	5	1	-	51.6 ± 14.1
	3.0	5		-	0.1 ± 0.1
	Ø	10		20.9	

ED_{50} (range)	0.5(0.1 - 1.3)
ED_{90} (range)	1.3(0.4 - 3.5)
Resistance factor I_{90}	

ED_{50} (range)	
ED_{90} (range)	
Resistance factor I_{90}	

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible] TABLE 119

[illegible]

COMPOUND NAME

CR NUMBER Chloroquine PARASITE SUB SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPT / Control PPT %
	0.1	5		-	82.8 ± 4.1
	0.3	5		-	80.1 ± 5.7
N	1.0	5	1	-	52.1 ± 7.6
	3.0	5		-	24.3 ± 8.5
	Ø	10		20.9	

ED_{50} range 0.8 (0.2 - 2.1)

ED_{90} range 3.1 (0.9 - 8.5)

Resistance factor I_{90}

ED_{50} (range)

ED_{90} (range)

Resistance factor I_{90}

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TEST [illegible] 1 [illegible]

BLOOD SCHIZONTOCIDE

COMPOUND NAME Halofantrine (H) +

OR NUMBER Chloroquine (CQ) PARASITE SUB SPECIES P berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG [illegible]

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated [illegible] / Control [illegible]
	H 0.1 + CQ 0.1	5		-	100 ± 2.5
	H 0.3 + CQ 0.1	5		-	88.8 ± 1.3
N	H 1.0 + CQ 0.1	5	1	-	50.2 ± 16.[illegible]
	H 3.0 + CQ 0.1	5		-	0.05 ± 0.05
	Ø	10		20.9	
ED_{50} (range) 0.7 (0.4 - 1.2)					
ED_{90} (range) 1.3 (0.8 - 2.3)					
Resistance factor I_{90}					
	H 0.1 + CQ 0.3	5		-	98.6 ± 2.8
	H 0.3 + CQ 0.3	5		-	86.6 ± 4.8
N	H 1.0 + CQ 0.3	5	1	-	44.8 ± 13.6
	H 3.0 + CQ 0.3	5		-	0.3 ± 0.2
	Ø	10		20.9	
ED_{50} (range) 0.6 (0.3 - 1.2)					
ED_{90} (range) 1.3 (0.5 - 2.6)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

MMARY OF ANTIMALARIAL DRUG TEST TABLE 121

BLOOD SCHIZONTOCIDES

COMPOUND NAME Halofantrine (H) +
TR NUMBER Chloroquine (CQ) PARASITE SUB SPECIES P berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC ~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	H0.1 + CQ1.0	5		-	89.0 ± 4.1
	H0.3 + CQ1.0	5		-	75.3 ± 3.1
N	H1.0 + CQ1.0	5	1	-	49.3 ± 11.3
	H3.0 + CQ1.0	5		-	0
	Ø	10		20.9	

ED_{50} (range)	0.6 (0.2 - 1.1)
ED_{90} (range)	1.1 (0.3 - 1.9)
Resistance factor I_{90}	

	H0.1 + CQ3.0	5		-	81.1 ± 2.7
	H0.3 + CQ3.0	5		-	74.0 ± 4.0
N	H1.0 + CQ3.0	5	1	-	26.5 ± 6.4
	H3.0 + CQ3.0	5		-	0
	Ø	10		20.9	

ED_{50} (range)	0.3 (0.1 - 0.8)
ED_{90} (range)	0.6 (0.3 - 1.9)
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1 2 2

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Chloroquine (CQ) +

OR NUMBER Halofantrine (H) ..... PARASITE (SUB)SPECIES P. berghei ....

FORMULATION ...Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	CQ 0·1 + H 0·1				100 ± 2·5
	CQ 0·3 + H 0·1				98·6 ± 2·8
N	CQ 1·0 + H 0·1				89·0 ± 4·1
	CQ 3·0 + H 0·1				81·1 ± 2·7
	Ø				
ED_{50}(range) 8·5 (6·6 - 11·0)					
ED_{90}(range) 37·0 (30·0 - 48·0)					
Resistance factor I_{90}					
	CQ 0·1 + H 0·3				88·8 ± 1·3
	CQ 0·3 + H 0·3				86·6 ± 4·8
N	CQ 1·0 + H 0·3				75·3 ± 3·1
	CQ 3·0 + H 0·3				74·0 ± 4·0
	Ø				
ED_{50}(range) 7·8 (1·5 - 27·0)					
ED_{90}(range) > 100					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1 2 3

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Chloroquine (CQ) +

OR NUMBER Halofantrine (H) ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O .. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRS / Control PRS
	CQ 0·1 + H 1·0				50·2 ± 16·1
	CQ 0·3 + H 1·0				44·8 ± 13·6
N	CQ 1·0 + H 1·0				49·3 ± 11·3
	CQ 3·0 + H 1·0				26·5 ± 6·4
	Ø				
ED_{50}(range) 0·2(<0·1 - 0·6)					
ED_{90}(range) 23·3(3·3 - 80)					
Resistance factor I_{90}					
	CQ 0·1 + H 3·0				0·05 ± 0·05
	CQ 0·3 + H 3·0				0·3 ± 0·2
N	CQ 1·0 + H 3·0				0
	CQ 3·0 + H 3·0				0
	Ø				
ED_{50}(range) < 0·1					
ED_{90}(range) < 0·1					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

WRAIR ANTIMALARIAL DRUG TEST [illegible] PAGE 121

[illegible]

CHEMICAL NAME

WR NUMBER: Primaquine PARASITE SUB-SPECIES: P. berghei

FORMULATION: Tween 80/H_2O ROUTE OF ADMINISTRATION: SC ~~[illegible]~~

MAXIMUM TOLERATED DOSE (MTD) .... MG/KG [illegible]

Strain	Daily dose mg/kg (D0-D+3)	No. of mice	No. of experiments	Mean control parasite rate %	Treated as % control
	0.1	5		-	92.5 ± 3.6
	0.3	5		-	93.1 ± 2.4
N	1.0	5		-	63.0 ± 5.[illegible]
	3.0	5		-	34.4 ± 4.0
	Ø	10		20.8	

ED_{50} range: 1.5 (1.1 - 2.2)

ED_{90} range: 5.8 (4.1 - 8.4)

Resistance factor I_{90}:

ED_{50} range

ED_{90} range

Resistance factor I_{90}

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1.2.5
BLOOD SCHIZONTOCIDES)

COMPOUND NAME Halofantrine (H) +
OR NUMBER Primaquine (PQ) ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRR / Control PRR x100
	H 0.1 + PQ 0.1	5		-	98.1 ± 2.6
	H 0.3 + PQ 0.1	5		-	92.2 ± 0.9
N	H 1.0 + PQ 0.1	5	1	-	70.2 ± 5.6
	H 3.0 + PQ 0.1	5		-	0
	Ø	10		20.8	
ED_{50} (range) 0.7 (0.2 - 1.3)					
ED_{90} (range) 1.1 (0.3 - 2.0)					
Resistance factor I_{90}					
	H 0.1 + PQ 0.3	5		-	96.6 ± 2.3
	H 0.3 + PQ 0.3	5		-	82.1 ± 3.5
N	H 1.0 + PQ 0.3	5	1	-	66.3 ± 8.0
	H 3.0 + PQ 0.3	5		-	0.01 ± 0.01
	Ø	10		20.8	
ED_{50} (range) 0.7 (0.2 - 1.3)					
ED_{90} (range) 1.2 (0.3 - 2.1)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1.2.6

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Halofantrine (H) +

OR NUMBER Primaquine (PQ)..... PARASITE (SUB)SPECIES P. berghei....

FORMULATION ...Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	H 0.1 + PQ 1.0	5		-	100 ± 1.7
	H 0.3 + PQ 1.0	5		-	98.5 ± 2.6
N	H 1.0 + PQ 1.0	5	1	-	66.3 ± 5.4
	H 3.0 + PQ 1.0	5		-	0.1 ± 0.1
	Ø	10		20.8	
ED_{50}(range) 0.9(0.6 - 1.3)					
ED_{90}(range) 1.5(1.0 - 2.2)					
Resistance factor I_{90}					
	H 0.1 + PQ 3.0	5		-	94.9 ± 2.1
	H 0.3 + PQ 3.0	5		-	96.3 ± 1.8
N	H 1.0 + PQ 3.0	5	1	-	70.5 ± 9.0
	H 3.0 + PQ 3.0	5		-	0.4 ± 0.4
	Ø	10		20.8	
ED_{50}(range) 1.0(0.6 - 1.5)					
ED_{90}(range) 1.9(1.2 - 2.9)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1.2.7

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Primaquine (PQ) +

OR NUMBER Halofantrine (H)..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION ...Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x 100
	PQ 0·1 + H 0·1	5		-	98·1 ± 2·6
	PQ 0·3 + H 0·1	5		-	96·6 ± 2·3
N	PQ 1·0 + H 0·1	5	1	-	100 ± 1·7
	PQ 3·0 + H 0·1	5		-	94·9 ± 2·1
	Ø	10		20·8	
ED_{50}(range) > 3·0					
ED_{90}(range) > 3·0					
Resistance factor I_{90}					
	PQ 0·1 + H 0·3	5		-	92·2 ± 0·9
	PQ 0·3 + H 0·3	5		-	82·1 ± 3·5
N	PQ 1·0 + H 0·3	5	1	-	98·5 ± 2·6
	PQ 3·0 + H 0·3	5		-	96·3 ± 1·8
	Ø	10		20·8	
ED_{50}(range) > 3·0					
ED_{90}(range) > 3·0					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 128

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Primaquine (PQ) +

CR NUMBER Halofantrine (H) ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR / Control PR x 100
	PQ 0·1 + H 1·0	5		-	70·2 ± 5·6
	PQ 0·3 + H 1·0	5		-	66·3 ± 8·0
N	PQ 1·0 + H 1·0	5	1	-	66·3 ± 5·4
	PQ 3·0 + H 1·0	5		-	70·5 ± 9·0
	Ø	10		20·8	
ED_{50}(range) > 3.0					
ED_{90}(range) > 3.0					
Resistance factor I_{90}					
	PQ 0·1 + H 3·0	5		-	0
	PQ 0·3 + H 3·0	5		-	0·01 ± 0·01
N	PQ 1·0 + H 3·0	5	1	-	0·1 ± 0·1
	PQ 3·0 + H 3·0	5		-	0·4 ± 0·4
	Ø	10		20·8	
ED_{50}(range) < 0.1					
ED_{90}(range) < 0.1					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 129

(BLOOD SCHIZONTICIDES)

COMPOUND NAME

OR NUMBER .HALOFANTRINE..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION .Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO~~/IV

MAXIMUM TOLERATED DOSE (MTD) .>3.0. MG/KG X 4..

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRE / Control PRE
	0.1	5		–	80.1 ± 2.3
	0.3	5		–	85.4 ± 2.9
N	1.0	5	1	–	44.4 ± 7.2
	3.0	5		–	0
	C	10		22.5	
ED_{50}(range) 0.7(0.4 - 1.4)					
ED_{90}(range) 1.2(0.7 - 2.2)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 130

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER SULFADIAZINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >30 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		–	88.8 ± 2.3
	0.3	5		–	63.0 ± 11.5
P.	1.0	5	1	–	25.1 ± 12.8
	3.0	5		–	0.4 ± 0.2
	Ø	10		22.5	
ED_{50}(range) 0.47 (0.3 - 0.8)					
ED_{90}(range) 1.1 (0.7 - 1.9)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 131

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER SULFADIAZINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0.1 + 0.1	5		–	91.6 ± 3.4
	0.3 + 0.1	5		–	85.0 ± 5.5
N	1.0 + 0.1	5	1	–	41.8 ± 10.5
	3.0 + 0.1	5		–	0
	Ø	10		22.5	
ED_{50}(range) 0.5(0.1 - 1.1)					
ED_{90}(range) 0.9(0.3 - 2.0)					
Resistance factor I_{90}					
	0.1 + 0.3	5		–	82.8 ± 4.8
	0.3 + 0.3	5		–	56.0 ± 17.1
N	1.0 + 0.3	5	1	–	12.4 ± 7.0
	3.0 + 0.3	5		–	0
	Ø	10		22.5	
ED_{50}(range) 0.3(0.2 - 0.6)					
ED_{90}(range) 0.7(0.3 - 1.2)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 132

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER SULFADIAZINE..... PARASITE (SUB)SPECIES ..P.berghei...

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR / Control PR x100
	0.1 + 1.0	5		-	30.6 ± 8.5
	0.3 + 1.0	5		-	11.7 ± 4.2
N	1.0 + 1.0	5	1	-	1.3 ± 1.3
	3.0 + 1.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.05 (0.02 - 0.1)					
ED_{90}(range) 0.2 (0.15 - 0.3)					
Resistance factor I_{90}					
	0.1 + 3.0	5		-	1.2 ± 1.0
	0.3 + 3.0	5		-	0
N	1.0 + 3.0	5	1	-	0
	3.0 + 3.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.02 (0.1 - 0.02)					
ED_{90}(range) 0.04 (0.05 - 0.04)					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 133

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME SULFADIAZINE +

OR NUMBER HALOFANTRINE..... PARASITE (SUB)SPECIES ..Pbrg...

FORMULATION ..Tw 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0	5		–	91.6 ± 3.4
	0.3 + 0.1	5		–	8[illegible] ± 4.9
N	1.0 + 0.1	5	1	–	30.6 ± 8.9
	3.0 + 0.1	5		–	1.2 ± 1.0
	Ø	10		22.5	
ED_{50}(range) 0.45(0.25 - 0.8)					
ED_{90}(range) 1.3(0.7 - 2.2)					
Resistance factor I_{90}					
	0.1 + 0.3	5		–	85.1 ± [illegible]
	0.3 + 0.3	5		–	56.6 ± 17.1
N	1.0 + 0.3	5	1	–	1.7 ± [illegible]
	3.0 + 0.3	5			[illegible]
	Ø	10		22.5	
ED_{50}(range) 0.3(0.16 - 0.5)					
ED_{90}(range) 0.7(0.3 - 1.1)					
Resistance factor I_{90}					

Principal Investigator: Professor [illegible]

Department of Medical Protozoology

[illegible] Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 131

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME SULFADIAZINE +

OR NUMBER HALOFANTRINE..... PARASITE (SUB)SPECIES ..Pibergei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 1.0	5		–	41.8 ± 16.0
	0.3 + 1.0	5		–	12.4 ± 7.0
N	1.0 + 1.0	5	1	–	1.3 ± 1.3
	1.0 + 1.0	5		–	0
	Ø	10		22.5	
ED_{50}(range) 0.1(0.05 - 0.17)					
ED_{90}(range) 0.3(0.17 - 0.5)					
Resistance factor I_{90}					
	0.1 + 3.0	5		–	0
	0.3 + 3.0	5		–	0
N	1.0 + 3.0	5	[illegible]	–	0
	3.0 + 3.0	[illegible]		–	0
	Ø	[illegible]		[illegible]	
ED_{50}(range) < [illegible]					
ED_{90}(range) < [illegible]					
Resistance factor I_{90}					

[illegible]

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 135

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER HALOFANTRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥1.0 MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	97.4 ± 4.0
	0.3	5		-	96.8 ± 3.7
N	0.5	5	1	-	92.2 ± 4.4
	1.0	5		-	24.5 ± 6.2
	Ø	10		23.3	
ED_{50}(range) 0.5(5.8 - 1.2)					
ED_{90}(range) 1.5(1.1 - 2.2)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 136

COMPOUND NAME OR NUMBER .Pyrimethamine..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >0.3.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.01	5		-	86.9 ± 3.6
	0.03	5		-	79.8 ± 4.1
N	0.1	5	1	-	45.1 ± 4.4
	0.3	5		-	36.3 ± 10.1
	Ø	10		23.3	
ED_{50}(range) 0.1 (0.02 - 0.25)					
ED_{90}(range) 1.2 (0.6 - 2.8)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 137

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER PYRIMETHAMINE..... PARASITE (SUB)SPECIES P. falciparum

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0.01	5		-	89.4 ± 1.5
	0.3 + 0.01	5		-	86.7 ± 4.9
N	0.5 + 0.01	5	1	-	35.5 ± 9.5
	1.0 + 0.01	5		-	17.9 ± 6.6
	Ø	10		23.3	
ED_{50}(range) 0.46 (0.35 - 0.65)					
ED_{90}(range) 0.95 (0.7 - 1.4)					
Resistance factor I_{90}					
	0.1 + 0.03	5		-	90.0 ± 7.6
	0.3 + 0.03	5		-	81.0 ± 5.2
N,	0.5 + 0.03	5	1	-	73.4 ± 9.1
	1.0 + 0.03	5		-	29.8 ± 5.2
	Ø	10		23.3	
ED_{50}(range) 0.58 (0.23 - 1.7)					
ED_{90}(range) 1.8 (0.73 - 3.5)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 13 b

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER PYRIMETHAMINE..... PARASITE (SUB)SPECIES P. [illegible]

FORMULATION Tween 80/ H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0.1	5		-	69.8 ± 6.3
	0.3 + 0.1	5		-	63.0 ± 3.3
N	0.5 + 0.1	5	1	-	41.5 ± 1.6
	1.0 + 0.1	5		-	29.5 ± 12.3
	Ø	10		23.3	
ED_{50}(range) 0.4 (0.25 - 0.72)					
ED_{90}(range) 2.6 (1.5 - 3.0)					
Resistance factor I_{90}					
	0.1 + 0.3	5		-	[illegible]
	0.3 + 0.3	5		-	18.9 ± [illegible]
N_1	0.5 + 0.3	5	1	-	[illegible]
	1.0 + 0.3	5		-	[illegible]
	Ø	10		23.3	
ED_{50}(range) [illegible]					
ED_{90}(range) [illegible]					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 139

COMPOUND NAME PYRIMETHAMINE +

OR NUMBER HALOFANTRINE ..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION .Tween80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.01 + 0.1	5		–	89.4 ± 1.5
	0.03 + 0.1	5		–	90.0 ± 7.6
N	0.1 + 0.1	5	1	–	69.8 ± 6.3
	0.3 + 0.1	5		–	47.7 ± 1.5
	Ø	10		23.3	
ED_{50}(range) 0.25(0.16 - 0.43)					
ED_{90}(range) 2.3(1.5 - 4.[illegible])					
Resistance factor I_{90}					
	0.01 + 0.3	5		–	86.7 ± 4.9
	0.03 + 0.3	5		–	81.0 ± 5.[illegible]
N	0.1 + 0.3	5	1	–	63.0 ± 3.[illegible]
	0.3 + 0.3	5		–	18.9 ± 7.7
	Ø	10		23.3	
ED_{50}(range) 0.11(0.05 - 0.16)					
ED_{90}(range) 0.46(0.3[illegible] - 0.6[illegible])					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) — TABLE 140

COMPOUND NAME PYRIMETHAMINE + HALOFANTRINE
OR NUMBER ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 in H_2O .. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0.01 + 0.5	5		–	35.5 ± 9.5
	0.03 + 0.5	5		–	73.4 ± 9.1
N	0.1 + 0.5	5	1	–	41.3 ± 10.6
	0.3 + 0.5	5		–	4.3 ± 2.5
	Ø	10		23.3	
ED_{50}(range) 0.06 (0.04 - 0.1)					
ED_{90}(range) 0.23 (0.14 - 0.36)					
Resistance factor I_{90}					
	0.01 + 1.0	5		–	17.9 ± 6.6
	0.03 + 1.0	5		–	29.8 ± 8.2
N	0.1 + 1.0	5	1	–	29.5 ± 12.3
	0.3 + 1.0	5		–	1.9 ± 0.6
	Ø	10		23.3	
ED_{50}(range) 0.02 (0.01 - 0.08)					
ED_{90}(range) 0.11 (0.05 - 0.35)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 141

COMPOUND NAME OR NUMBER HALOFANTRINE..... PARASITE (SUB)SPECIES P. berghei....

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >1.0 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0.1	5		–	84.8 ± 4.0
	0.3	5		–	72.1 ± 4.7
N	0.5	5	1	–	63.1 ± 9.0
	1.0	5		–	48.3 ± 5.3
	Ø	10		23.7	
ED_{50}(range) 0.5 (0.3 – 1.1)					
ED_{90}(range) 3.4 (2.1 – 7.4)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1 1 2

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER .Minocycline..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >30.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		–	86.0 ± 3.3
	3.0	5		–	66.1 ± 5.0
N	10.0	5	1	–	40.5 ± 15.0
	30.0	5		–	22.4 ± 7.5
	Ø	10		23.7	
ED_{50}(range) 5.4(2.7-12.5)					
ED_{90}(range) 70.0(28.0-135)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 143

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER MINOCYCLINE..... PARASITE (SUB)SPECIES .[illegible].....

FORMULATION .Tw[illegible] SC | H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO~~/IV

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 1.0	5		-	[illegible]
	0.3 + 1.0	5		-	[illegible]
N	0.5 + 1.0	5	1	-	[illegible]
	1.0 + 1.0	5		-	[illegible]
	Ø	10		23.7	
ED_{50}(range) 0.45(0.27-1.0)					
ED_{90}(range) 2.3(1.4-5.1)					
Resistance factor I_{90}					
	0.1 + 3.0	5		-	[illegible]
	0.3 + 3.0	5		-	[illegible]
N,	0.5 + 3.0	5	1	-	[illegible]
	1.0 + 3.0	5		-	37.1 ± 5.1
	Ø	10		23.7	
ED_{50}(range) 0.48(0.24-1.0)					
ED_{90}(range) 1.7(0.8-3.5)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 1 4 1

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER MINOCYCLINE..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION .Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 10.0	5		-	[illegible]
	0.3 + 10.0	5		-	[illegible]
N	0.5 + 10.0	5	1	-	[illegible]
	1.0 + 10.0	5		-	[illegible]
	Ø	10		23.7	
ED_{50}(range) 0.45(0.26-0.95)					
ED_{90}(range) 2.1(1.2-4.2)					
Resistance factor I_{90}					
	0.1 + 30.0	5		-	27.6 ± [illegible]
	0.3 + 30.0	5		-	12.3 ± [illegible]
N,	0.5 + 30.0	5	1	-	[illegible] ± [illegible]
	1.0 + 30.0	5		-	0.7 ± 0.1
	Ø	10		23.7	
ED_{50}(range) 0.05(0.03-0.1)					
ED_{90}(range) 0.25(0.15-0.45)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 1 4 5

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME MINOCYCLINE +

OR NUMBER HALOFANTRINE..... PARASITE (SUB)SPECIES P.berghei.....

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 0.1	5		-	[illegible]
	3.0 + 0.1	5		-	[illegible]
N	10.0 + 0.1	5	1	-	[illegible]
	30.0 + 0.1	5			[illegible]
	Ø	10		[illegible]	
ED_{50}(range) 13.0(2.7 - 44)					
ED_{90}(range) 64.0(13.0 - 215)					
Resistance factor I_{90}					
	1.0 + 0.3	5		-	[illegible]
	3.0 + 0.3	5		-	[illegible]
N	10.0 + 0.3	5	1		[illegible]
	30.0 + 0.3	5		-	[illegible]
	Ø	10		[illegible]	
ED_{50}(range) 8.3(1.4 - 27.0)					
ED_{90}(range) 33.0(5.7 - 105)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE [illegible]

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME [illegible]

OR NUMBER [illegible] PARASITE (SUB-SPECIES [illegible]

FORMULATION [illegible] ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	10 + 0.5	5		-	[illegible]
	30 + 0.5	5		-	[illegible]
N	100 + 0.5	5	1		[illegible]
	300 + 0.5	5			[illegible]
	0	10		[illegible]	
ED_{50}(range) 3.8(1.[illegible] - 9.4)					
ED_{90}(range) 17.0(5.0 - 41.5)					
Resistance factor I_{90}					
	1.0 + 1.0	5			[illegible]
	3.0 + 1.0	5			[illegible]
N_1	10.0 + 1.0	5	1	-	[illegible]
	30.0 + 1.0	5		-	[illegible]
	0	10		[illegible]	
ED_{50}(range) 2.0(0.8 - 7.1)					
ED_{90}(range) 8.0(3.0 - 28.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS [illegible] 1 1 7

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..HALOFANTRINE..... PARASITE (SUB)SPECIES ..[illegible]....

FORMULATION .Twan 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10.. MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR%
	0.1	5			[illegible]
	0.3	5			[illegible]
N	0.5	5	1		[illegible]
	1.0	5			[illegible]
	Ø	10		27.0	
ED_{50}(range) [illegible]					
ED_{90}(range) [illegible]					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible]

COMPOUND NAME

OR NUMBER [illegible] PARASITE [illegible]

FORMULATION [illegible] ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD) [illegible] MG/KG

Strain	Daily dose mg/kg DD-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPR %
ED_{50} (range)					
ED_{90} (range)					
Resistance factor I_{90}					
ED_{50} (range)					
ED_{90} (range)					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TEST [illegible] 11[illegible]

[illegible] SCHIZONTOCIDES

COMPOUND NAME [illegible] +

OR NUMBER [illegible] PARASITE (SUB-SPECIES) [illegible]

FORMULATION [illegible] ROUTE OF ADMINISTRATION : SC ~~[illegible]~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRI / Control PRI
	0.1 + 1.0	[illegible]			[illegible]
	0.3 + 1.0	5			[illegible]
N	0.5 + 1.0	5	1		[illegible]
	1.0 + 1.0	5			[illegible]
	[illegible]	[illegible]		[illegible]	
ED_{50} (range)	[illegible]				
ED_{90} (range)	[illegible]				
Resistance factor I_{90}					
	0.1 + [illegible]	[illegible]			[illegible]
	[illegible] + [illegible]	[illegible]			[illegible]
[illegible]	0.5 + [illegible]	[illegible]	1		[illegible]
	[illegible] + [illegible]	[illegible]			[illegible]
	[illegible]	[illegible]		[illegible]	
ED_{50} (range)	[illegible]				
ED_{90} (range)	[illegible]				
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 1[illegible]

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME [illegible]

OR NUMBER [illegible] PARASITE (SUB SPECIES) [illegible]

FORMULATION [illegible] ROUTE OF ADMINISTRATION : SC/IP/~~PO~~/IV

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPE / Control PPE
[illegible]	[illegible]	[illegible]			[illegible]
[illegible]	[illegible]	[illegible]			[illegible]
[illegible]	[illegible]	[illegible]			[illegible]
	[illegible]				[illegible]
	[illegible]			[illegible]	
ED_{50} (range) [illegible]					
ED_{90} (range) [illegible]					
Resistance factor I_{90}					
	[illegible]	[illegible]			[illegible]
	[illegible]	[illegible]			[illegible]
[illegible]	[illegible]	[illegible]	[illegible]		[illegible]
	[illegible]	[illegible]			[illegible]
	[illegible]	10		[illegible]	
ED_{50} (range) [illegible]					
ED_{90} (range) [illegible]					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 151

COMPOUND NAME CLINDAMYCIN +

OR NUMBER HALOFANTRINE ..... PARASITE SUB SPECIES [illegible]

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG x ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRR / Control PRR %
	10 + 0.1	5		-	[illegible]
	30 + 0.1	5			[illegible]
N	100 + 0.1	5	1	-	[illegible]
	300 + 0.1	5			[illegible]
	Ø	10		24[illegible]	
ED_{50} (range) [illegible]					
ED_{90} (range) [illegible]					
Resistance factor I_{90}					
	10 + 0.3	5		-	[illegible]
	30 + 0.3	5		-	[illegible]
N	100 + 0.3	5	1	-	[illegible]
	300 + 0.3	5			[illegible]
	Ø	10		27.0	
ED_{50} (range) 4 [illegible]					
ED_{90} (range) [illegible]					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TEST [illegible]

[illegible]

COMPOUND NAME [illegible]

OR NUMBER [illegible] PARASITE [illegible]

FORMULATION [illegible] ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD) [illegible] MG/KG [illegible]

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated RBC / Control RBC
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ED_{50} range					
ED_{90} range					
Resistance factor I_{90}					
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ED_{50} (range) [illegible]					
ED_{90} (range) [illegible]					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 153

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER [illegible] PARASITE (SUB)SPECIES [illegible]

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC ~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) [illegible] MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPT / Control PPT
	[illegible]	[illegible]			[illegible]
	[illegible]	[illegible]			[illegible]
	[illegible]	[illegible]			[illegible]
	[illegible]	[illegible]			[illegible]
	[illegible]	[illegible]		[illegible]	
ED_{50} (range)					
ED_{90} (range)					
Resistance factor I_{90}					
ED_{50} (range)					
ED_{90} (range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS - TABLE 1 [illegible]

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER [illegible] PARASITE (SUBSPECIES [illegible]

FORMULATION [illegible] ROUTE OF ADMINISTRATION : SC/~~IP/PO/~~IV

MAXIMUM TOLERATED DOSE (MTD) >[illegible] MG/KG X [illegible]

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	[illegible]	5		–	[illegible]
	[illegible]	5		–	[illegible]
N	[illegible]	5	[illegible]	–	[illegible]
	[illegible]	5		–	[illegible]
	[illegible]	5		[illegible]	
ED_{50}(range [illegible]					
ED_{90}(range [illegible]					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 1 5 5

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER TETRAHYDRINE ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 1.0	5		-	50.4 ± 4.4
	0.3 + 1.0	5		-	51.1 ± 4.5
N	0.5 + 1.0	5	1	-	33.2 ± 4.9
	1.0 + 1.0	5		-	34.3 ± 3.0
	0	10		26.6	
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					
	0 + 3.0	5		-	75.3 ± 2.1
	0.3 + 3.0	5		-	69.5 ± 4.1
N_1	0.5 + 3.0	5	1	-	52.9 ± 5.9
	1.0 + 3.0	5		-	48.0 ± 2.5
	0	10		26.6	
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 1 5 6

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME HALOFANTRINE +

OR NUMBER TETRACYCLINE..... PARASITE (SUB)SPECIES ..P.berghei....

FORMULATION ..Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 10.0	5		-	73.6 ± 2.0
	0.3 + 10.0	5		-	44.7 ± [illegible]
N	0.5 + 10.0	5	1	-	40.5 ± 2.4
	1.0 + 10.0	5		-	31.7 ± 3.4
	Ø	10		26.6	
ED_{50}(range) 0.5 (0.[illegible] - 1.2)					
ED_{90}(range) 3.5 (4.0 - 32.0)					
Resistance factor I_{90}					
	0.1 + 30.0	5		-	75.1 ± 2.3
	0.3 + 30.0	5		-	56.0 ± 5.3
N	0.5 + 30.0	5	1	-	40.2 ± 4.4
	1.0 + 30.0	5		-	35.2 ± 3.4
	Ø	10		26.6	
ED_{50}(range) 0.6 (0.3 - 1.5)					
ED_{90}(range) 13.5 (7.0 - 36.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 1 5 7

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME TETRACYCLINE +

OR NUMBER HALOFANTRINE PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	1.0 + 0.1	5		–	50.7 ± 4.3
	3.0 + 0.1	5		–	75.3 ± 2.1
N	10.0 + 0.1	5	1	–	73.6 ± 2.0
	30.0 + 0.1	5		–	75.1 ± 2.4
	Ø	10		26.6	
ED_{50}(range) > 30					
ED_{90}(range) > 30					
Resistance factor I_{90}					
	1.0 + 0.3	5		–	51.1 ± 4.5
	3.0 + 0.3	5		–	69.5 ± 4.[illegible]
N	10.0 + 0.3	5	1	–	44.9 ± 4.[illegible]
	30.0 + 0.3	5		–	56.0 ± 5.3
	Ø	10		26.6	
ED_{50}(range) 18.0 (5.2 - 47.0)					
ED_{90}(range) 1[illegible] (4.[illegible] - 4[illegible])					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 158

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME TETRACYCLINE +

OR NUMBER .HALOFANTRINE..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 0.5	5		-	39.2 ± 4.9
	3.0 + 0.5	5		-	52.9 ± 5.9
N	10.0 + 0.5	5	1	-	40.5 ± 3.4
	30.0 + 0.5	5		-	40.2 ± 4.4
	Ø	10		26.6	
ED_{50}(range)					
ED_{90}(range) >30					
Resistance factor I_{90}					
	1.0 + 1.0	5		-	34.3 ± 3.0
	3.0 + 1.0	5		-	48.0 ± 2.5
N,	10.0 + 1.0	5	1	-	31.7 ± 3.7
	30.0 + 1.0	5		-	35.2 ± 3.9
	Ø	10		26.6	
ED_{50}(range)					
ED_{90}(range) >30					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 159

COMPOUND NAME

OR NUMBER [illegible] PARASITE (SUB)SPECIES [illegible]

FORMULATION [illegible]/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) [illegible] MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRR / Control PRR X100
	[illegible]	5		-	[illegible]
	[illegible]	5		-	[illegible]
N	[illegible]	5		-	[illegible]
	[illegible]	5		-	[illegible]
	[illegible]	5		-	[illegible]
	[illegible]	10		25.3	
ED_{50}(range) [illegible]					
ED_{90}(range) [illegible]					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS - IAM 160

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..Quinine Hydrochloride PARASITE (SUB)SPECIES ..P. berghei....

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ~600 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR / Control PR x100
	10.0	5		-	95.2 ± 2.7
	30.0	5		-	61.3 ± 7.3
N	100.0	5	1	-	36.1 ± 7.9
	300.0	5		-	0
	600.0	5		-	0
	Ø	10		25.3	
ED_{50}(range) 45.0(23.0-90.0)					
ED_{90}(range) 85.0(43.0-175)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS · TABLE 161

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Floxacrine +

OR NUMBER .Quinine..... PARASITE (SUB)SPECIES .Pyrexia.....

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/~~IV~~ (F, Q)

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 3.0	5		–	88.0 ± 4.4
	0.3 + 3.0	5		–	82.7 ± 2.7
N	0.5 + 3.0	5	1	–	51.9 ± [illegible]
	1.0 + 3.0	5		–	0.7 ± 0.2
	3.0 + 3.0	5		–	0
	∅	10		25.3	
ED_{50}(range) 0.3(0.2 – 0.6)					
ED_{90}(range) 0.6(0.4 – 1.3)					
Resistance factor I_{90}					
	0.1 + 10.0	5		–	91.3 ± 2.9
	0.3 + 10.0	5		–	73.8 ± 7.7
N	0.5 + 10.0	5	1	–	56.2 ± 16.2
	1.0 + 10.0	5		–	0.08 ± 0.0[illegible]
	3.0 + 10.0	5		–	0
	∅	10		25.3	
ED_{50}(range) 0.4(0.2 – 0.7)					
ED_{90}(range) 0.6(0.3 – 1.1)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

COMPOUND NAME [illegible]

OR NUMBER ..Quinine..... PARASITE [illegible]

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : F G

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR%
	0.1 + 30.0	5		-	50.0 ± 2.2
	0.3 + 30.0	5		-	54.4 ± 13.9
N	0.5 + 30.0	5	1		25.1 ± 15.5
	1.0 + 30.0	5		-	0.4 ± 0.0
	3.0 + 30.0	5		-	0
	∅	10		25.3	
ED_{50}(range) 0.2(0.1 - 0.4)					
ED_{90}(range) 0.5(0.3 - 1.0)					
Resistance factor I_{90}					
	0.1 + 100.0	5		-	8.2 ± 3.0
	0.3 + 100.0	5		-	5.8 ± 1.4
N	0.5 + 100.0	5	1	-	4.1 ± 1.5
	1.0 + 100.0	5		-	0
	3.0 + 100.0	5		-	0
	0	10		25.3	
ED_{50}(range) 0.05(0.03 - 0.1)					
ED_{90}(range) 0.1(0.04 - 0.4)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS 163

(BLOOD SCHIZONTICIDE)

COMPOUND NAME Quinine +

OR NUMBER ..Floxacrine..... PARASITE (SUB)SPECIES ..P. berghei..

FORMULATION .Tw.Sc/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/~~IV~~ (F, Q)

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRT / Control PRT
	3.0 + 0.1	5		-	88.0 ± 4.4
	10.0 + 0.1	5		-	91.3 ± 2.9
N	30.0 + 0.1	5	1	-	80.0 ± 2.2
	100.0 + 0.1	5		-	8.2 ± 3.0
	∅	10		25.3	
ED_{50}(range) 35.0(25.0 - 62.0)					
ED_{90}(range) 90.0(67.0 - 170)					
Resistance factor I_{90}					
	3.0 + 0.3	5		-	82.7 ± 2.3
	10.0 + 0.3	5		-	73.8 ± 7.7
N	30.0 + 0.3	5	1	-	54.4 ± 13.7
	100.0 + 0.3	5		-	5.8 ± 1.4
	∅	10		25.3	
ED_{50}(range) 17.0(7.1 - 50.0)					
ED_{90}(range) 70.0(30.0 - 200)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL [illegible] - [illegible] 161

([illegible])

COMPOUND NAME Quinine +

OR NUMBER ..Flokacine..... PARASITE (SUB-SPECIES) .F [illegible]

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC ~~IP~~ F / PO ~~IV~~ Q

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated [illegible] / Control [illegible]
	3.0 + 0.5	5		-	51.9 ± 15.3
	10.0 + 0.5	5		-	56.2 ± 16.2
N	30.0 + 0.5	5	1	-	25.1 ± 15.5
	100.0 + 0.5	5		-	4.1 ± 1.9
	Ø	5		25.3	
ED_{50}(range) 11.5(7.8 - 20.[illegible])					
ED_{90}(range) 55.0([illegible])					
Resistance factor I_{90}					
	3.0 + [illegible]	5		-	0.7 ± 0.2
	[illegible]	5		-	0.0[illegible] ± 0.0[illegible]
N	[illegible]	5	1	-	0.4 ± 0.2
	[illegible]	5		-	0
	Ø	10		25.3	
ED_{50}(range) [illegible]					
ED_{90}(range) [illegible]					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters

Department of Medical Protozoology

London School of Hygiene & Tropical Medicine

COMPOUND NAME

CODE NUMBER FLOXACRINE

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION

MAXIMUM TOLERATED DOSE (MTD) ≥ 3.0 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated/Control %
	0.1	5		–	[illegible]
	0.3	5		–	[illegible]
N	0.5	5	1	–	[illegible]
	1.0	5		–	4.2 ± 3.0
	3.0	5		–	[illegible]
	Ø	10		25.3	
ED_{50}(range) 0.3 (0.2 – 0.5)					
ED_{90}(range) 0.5 (0.5 – 1.4)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

SUMMARY [illegible] ANTIMALARIA [illegible]

COMPOUND NAME

JR NUMBER CYCLOCOLOGIC [illegible]

FORMULATION Tweed 80/H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD) >10 MG/KG X 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	[illegible]
	0.3	5		-	[illegible]
	1.0	5		-	[illegible]
N	3.0	5	1	-	[illegible]
	5.0	5			[illegible]
	10.0	5		-	[illegible]
	[illegible]	[illegible]		[illegible]	

ED_{50} (range [illegible]

ED_{90} (range [illegible]

Resistance factor I_{90}

[illegible]

[illegible]

[illegible] NAME Flexacrine +

[illegible] NUMBER [illegible]

FORMULATION [illegible] H_2O [illegible] ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD) [illegible] MG/KG [illegible]

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	[illegible]
	[illegible]	5			[illegible]
	[illegible]	5			[illegible]
[illegible]	[illegible]	5	[illegible]		[illegible]
	[illegible]	5			[illegible]
	[illegible]	5			[illegible]
	[illegible]	[illegible]		[illegible]	
ED_{50} range	[illegible]				
ED_{90} range	[illegible]				
Resistance factor I_{90}					
	[illegible]	5		[illegible]	[illegible]
	[illegible]	5		[illegible]	[illegible]
[illegible]	[illegible]	5	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]		[illegible]	[illegible]
	[illegible]	5			[illegible]
	[illegible]				
[illegible]					
[illegible]					
[illegible]					

[illegible]

[illegible]

[illegible] NAME Flexacrine +

[illegible] NUMBER [illegible] PARASITE SUB-SPECIES [illegible]

FORMULATION Tween 80 H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR%
	0.1 + 3.0	5		-	25.5 ± 4.5
	0.3 + 3.0	5		-	24.[illegible] ± 2.4
N	0.5 + 3.0	5	1	-	3.4 ± 2.6
	1.0 + 3.0	5		-	0.[illegible] ± [illegible]
	3.0 + 3.0	5			0
	Ø	10		25.3	
ED_{50}(range) 0.03(0.[illegible] - 0.2)					
ED_{90}(range) 0.2(0.1 - 0.5)					
Resistance factor I_{90}					
	0.1 + 5.0	5		-	25.3 ± 4.5
	0.3 + 5.0	5		-	1[illegible] ± [illegible]
N	0.5 + 5.0	5	1	-	1.[illegible] ± [illegible]
	1.0 + 5.0	5			0.02 ± [illegible]
	3.0 + 5.0	5		-	0
	0	10		25.3	
ED_{50}(range) 0.1(0.[illegible] - 0.2)					
ED_{90}(range) 0.2(0.1 - 0.4)					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peter
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS - TABLE 169
TABLE 2 SCHIZONTOCIDES

COMPOUND NAME Cycloguanil +

OR NUMBER ..Floxacrine..... PARASITE (SUB)SPECIES ..Pibergei....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 0.1	5		-	52.6 ± 1.5
	1.0 + 0.1	5		-	35.8 ± 3.1
N	3.0 + 0.1	5	1	-	25.5 ± 4.5
	5.0 + 0.1	5		-	25.3 ± 4.8
	Ø	10		25.3	
ED_{50}(range) 0.3(0.2 - 0.5)					
ED_{90}(range) 21.0(11.0 - 48.0)					
Resistance factor I_{90}					
	0.3 + 0.3	5		-	45.8 ± 3.7
	1.0 + 0.3	5		-	30.8 ± 3.3
N	3.0 + 0.3	5	1	-	24.0 ± 2.4
	5.0 + 0.3	5		-	18.0 ± 6.4
	Ø	10		25.3	
ED_{50}(range) 0.3 [illegible]					
ED_{90}(range) [illegible]					
Resistance factor I_{90}					

Principal Investigator: Professor W. Peters
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London School of Hygiene & Tropical Medicine

COMPOUND NAME [illegible]

OR NUMBER [illegible]

FORMULATION [illegible] H_2O [illegible]

MAXIMUM TOLERATED DOSE (MTD) [illegible]

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of [illegible]	Mean [illegible] parasitemia [illegible]	[illegible]
	0.3 + 0.5	[illegible]			
	1.0 + 0.5	[illegible]			
N	3.0 + 0.5	[illegible]			
	5.0 + 0.5	[illegible]			
	0	[illegible]			
ED_{50} (range)					
ED_{90} (range)					
Resistance factor [illegible]					

[illegible]

[illegible] Tropical Medicine

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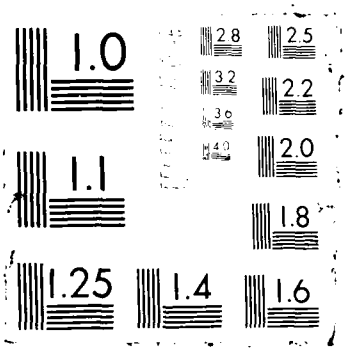
1.0
2.8
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2.0
1.1
1.8
1.25
1.4
1.6

SUMMARY OF ANTIMALARIAL DRUG TESTS

(BLOOD SCHIZONTOCIDES)

TABLE 171

COMPOUND NAME FLOXACRINE

OR NUMBER LIV 1528 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) > 1.0 MG/KG X 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	95.5 ± 5.7
	0.3	5		-	90.0 ± 2.9
N	0.5	5	1	-	43.6 ± 14.3
	1.0	5		-	0.3 ± 0.3
	Ø	10		22.5	
ED_{50}(range) 0.44 (0.31 - 0.52)					
ED_{90}(range) 0.64 (0.46 - 0.8)					
Resistance factor I_{90} 1.0		Isobolar Unit			
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 172

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER TETRACYCLINE..... PARASITE (SUB SPECIES) : P. berghei.....

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >100. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	95.4 ± 2.3
	10.0	5		-	78.4 ± 8.7
N	30.0	5	1	-	53.7 ± 10.9
	100.0	5		-	4.3 ± 2.0
	Ø	10		22.5	

ED_{50}(range)	20.0 (12.0 - 42.0)
ED_{90}(range)	67.0 (41.0 - 140)
Resistance factor I_{90}	1.0 Isobolar Unit

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 173

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME FLOXACRINE +

OR NUMBER TETRACYCLINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 3.0	5		-	95.6 ± 3.1
	0.3 + 3.0	5		-	57.6 ± 10.0
N	0.5 + 3.0	5	1	-	15.6 ± 6.7
	1.0 + 3.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.23(0.17 - 0.37)					
ED_{90}(range) 0.38(0.27 - 0.6)					
Resistance factor I_{90} 0.59		Isobolar Units			
	0.1 + 10.0	5		-	89.4 ± 3.2
	0.3 + 10.0	5		-	60.2 ± 4.4
N	0.5 + 10.0	5	1	-	1.9 ± 1.9
	1.0 + 10.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.22(0.14 - 0.35)					
ED_{90}(range) 0.36(0.24 - 0.58					
Resistance factor I_{90} 0.56		Isobolar Units			

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 171

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME FLOXACRINE +

OR NUMBER TETRACYCLINE..... PARASITE (SUB)SPECIES ...P. berghei....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 30.0	5		-	51.6 ± 10.4
	0.3 + 30.0	5		-	28.2 ± 7.0
N	0.5 + 30.0	5	1	-	2.6 ± 1.7
	1.0 + 30.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.17(<0.1 - 0.26)					
ED_{90}(range) 0.3(0.16 - 0.46)					
Resistance factor I_{90} 0.46	Isobolar Units				
	0.1 + 100.0	5		-	4.3 ± 1.6
	0.3 + 100.0	5		-	3.5 ± 0.6
N	0.5 + 100.0	5	1	-	0.3 ± 0.3
	1.0 + 100.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.03(0.02 - 0.05)					
ED_{90}(range) 0.1(0.05 - 0.19)					
Resistance factor I_{90} 0.16	Isobolar Units				

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 1 7 5

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME TETRACYCLINE +

OR NUMBER .FLOXALRINE..... PARASITE (SUB)SPECIES .P. berghei.....

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 0.1	5		–	95.6 ± 3.1
	10.0 + 0.1	5		–	88.4 ± 3.2
N	30.0 + 0.1	5	1	–	51.6 ± 10.4
	100.0 + 0.1	5		–	4.3 ± 1.6
	Ø	10		22.5	
ED_{50}(range) 22.0(12.0 - 40.0)					
ED_{90}(range) 80.0(44.0 - 140)					
Resistance factor I_{90} 1.2		Isobolar Units			
	3.0 + 0.3	5		–	57.6 ± 10.0
	10.0 + 0.3	5		–	60.2 ± 4.4
N	30.0 + 0.3	5	1	–	28.2 ± 7.0
	100.0 + 0.3	5		–	3.5 ± 0.6
	Ø	10		22.5	
ED_{50}(range) 7.5(2.7 - 18.0)					
ED_{90}(range) 39.0(14.0 - 95.0)					
Resistance factor I_{90} 0.58		Isobolar Units			

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 176

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME TETRACYCLINE +

OR NUMBER ..FLUXACRINE..... PARASITE (SUB)SPECIES ...P. berghei.....

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 0.5	5		-	15.6 ± 6.7
	10.0 + 0.5	5		-	11.9 ± 1.9
N	30.0 + 0.5	5	1	-	2.6 ± 1.7
	100.0 + 0.5	5		-	0.3 ± 0.3
	Ø	10		22.5	
ED_{50}(range) 0.95 (0.3 - 2.0)					
ED_{90}(range) 6.9 (2.2 - 14.0)					
Resistance factor I_{90} 0.1		Isobolar Units			
	3.0 + 1.0	5		-	0
	10.0 + 1.0	5		-	0
N	30.0 + 1.0	5	1	-	0
	100.0 + 1.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) < 3.0					
ED_{90}(range) < 3.0					
Resistance factor I_{90} < 0.04		Isobolar Units			

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 177

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..FLOXACRINE..... PARASITE (SUB)SPECIES .P. berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >1.0... MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	95.5 ± 5.7
	0.3	5		-	90.0 ± 2.9
N	0.5	5	1	-	43.6 ± 14.3
	1.0	5		-	0.3 ± 0.3
	0	10		22.5	
ED_{50}(range) 0.44(0.31 - 0.52)					
ED_{90}(range) 0.64(0.46 - 0.8)					
Resistance factor I_{90} 1.0		Isobolar Unit			
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 178

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER .ERYTHROMYCIN..... PARASITE (SUB)SPECIES ..P. berghei.....

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >600 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	30.0	5		–	91.6 ± 1.5
	100.0	5		–	70.4 ± 14.7
N	300.0	5	1	–	49.2 ± 9.6
	600 0	5		–	14.8 ± 8.2
	Ø	10		22.5	

ED_{50}(range)	190(113 - 370)
ED_{90}(range)	950(560 - 1850)
Resistance factor I_{90}	1.0 Isobolar Unit

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 179

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Floxacrine +

OR NUMBER Erythromycin PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 30.0	5		–	82.4 ± 6.7
	0.3 + 30.0	5		–	77.4 ± 7.9
N	0.5 + 30.0	5	1	–	22.1 ± 14.2
	1.0 + 30.0	5		–	0
	Ø	10		22.5	
ED_{50}(range) 0.23(0.13 - 0.43)					
ED_{90}(range) 0.38(0.21 - 0.7)					
Resistance factor I_{90} 0.59		Isobolar Units			
	0.1 + 100.0	5		–	79.1 ± 6.3
	0.3 + 100.0	5		–	69.2 ± 4.4
N	0.5 + 100.0	5	1	–	4.5 ± 1.6
	1.0 + 100.0	5		–	0
	Ø	10		22.5	
ED_{50}(range) 0.22(0.13 - 0.32)					
ED_{90}(range) 0.36(0.21 - 0.53)					
Resistance factor I_{90} 0.56		Isobolar Units			

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 180

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME FLOXACRINE +

OR NUMBER ERYTHROMYCIN..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 300.0	5		-	48.8 ± 14.2
	0.3 + 300.0	5		-	24.7 ± 9.1
N	0.5 + 300.0	5	1	-	2.0 ± 0.9
	1.0 + 300.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.12(0.08 - 0.23)					
ED_{90}(range) 0.24(0.16 - 0.46)					
Resistance factor I_{90} 0.38		Isobolar Units			
	0.1 + 600.0	5		-	18.4 ± 6.1
	0.3 + 600.0	5		-	3.3 ± 2.2
N	0.5 + 600.0	5	1	-	1.3 ± 1.2
	1.0 + 600.0	5		-	0
	Ø	10		22.5	
ED_{50}(range) 0.06(0.04 - 0.12)					
ED_{90}(range) 0.16(0.11 - 0.3)					
Resistance factor I_{90} 0.25		Isobolar Units			

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS - TABLE 181

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME ERYTHROMYCIN +

OR NUMBER FLOXACRINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0 + 0.1	5		-	82.4 ± 6.7
	100.0 + 0.1	5		-	79.1 ± 6.3
N	300.0 + 0.1	5	1	-	48.8 ± 14.2
	600.0 + 0.1	5		-	18.4 ± 6.1
	Ø	10		22.5	
ED_{50}(range) 155(76.0 - 460)					
ED_{90}(range) 930(450 - 2700)					
Resistance factor I_{90} 0.98		Isobolar Units			
	30.0 + 0.3	5		-	77.4 ± 7.9
	100.0 + 0.3	5		-	69.2 ± 4.4
N	300.0 + 0.3	5	1	-	24.7 ± 9.1
	600.0 + 0.3	5		-	3.3 ± 2.2
	Ø	10		22.5	
ED_{50}(range) 95.0(50.0 - 195)					
ED_{90}(range) 400(205 - 800)					
Resistance factor I_{90} 0.42		Isobolar Units			

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS - TABLE 182

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME ERYTHROMYCIN +

OR NUMBER .FLOXACRINE..... PARASITE (SUB)SPECIES ..P. berghei.....

FORMULATION ..Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0 + 0.5	5		-	22.1 ± 14.2
	100.0 + 0.5	5		-	4.5 ± 1.6
N	300.0 + 0.5	5	1	-	2.0 ± 0.9
	600.0 + 0.5	5		-	1.3 ± 1.2
	∅	10		22.5	
ED_{50}(range) 7.5(3.5 - 19.0)					
ED_{90}(range) 70.0(33.0 - 180)					
Resistance factor I_{90} 0.07		Isobolar Units			
	30.0 + 1.0	5		-	0
	100.0 + 1.0	5		-	0
N	300.0 + 1.0	5	1	-	0
	600.0 + 1.0	5		-	0
	∅	10		22.[illegible]	
ED_{50}(range) < 30					
ED_{90}(range) < 30					
Resistance factor I_{90}<0.03		Isobolar Units			

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDE)

TABLE 183

COMPOUND NAME OR NUMBER ..FLOXACRINE..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION ..Tween 80 1 H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..>1:0.. MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0·1	5		-	80·4 ± 2·3
	0·3	5		-	64·5 ± 5·1
N	0·5	5	1	-	28·3 ± 8·7
	1·0	5		-	1·0 ± 0·5
	Ø	10		35·7	
ED_{50}(range) 0·25(0·16 - 0·42)					
ED_{90}(range) 0·6(0·36 - 0·97)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS

(BLOOD SCHIZONTOCIDES)

TABLE 1 S 1

COMPOUND NAME

OR NUMBER ..PRIMAQUINE..... PARASITE (SUB)SPECIES ..P. berghei....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >.5.0. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		–	87.5 ± 3.8
	1.0	5		–	83.6 ± 2.5
N	3.0	5	1	–	53.0 ± 11.2
	5.0	5		–	8.1 ± 4.2
	Ø	10		35.7	
ED_{50}(range) 1.6(0.8 - 4.3)					
ED_{90}(range) 6.0(3.0 - 16.0)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 185

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME FLOXACRINE +

OR NUMBER PRIMAQUINE..... PARASITE (SUB)SPECIES .P. berghei.....

FORMULATION .Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0.3	5		-	86.2 ± 1.8
	0.3 + 0.3	5		-	74.9 ± 2.5
N	0.5 + 0.3	5	1	-	43.8 ± 6.0
	1.0 + 0.3	5		-	0.01 ± 0.01
	Ø	10		35.7	
ED_{50}(range) 0.25(0.14 - 0.5)					
ED_{90}(range) 0.4(0.22 - 0.8)					
Resistance factor I_{90}					
	0.1 + 1.0	5		-	81.7 ± 4.7
	0.3 + 1.0	5		-	54.1 ± 5.4
N	0.5 + 1.0	5	1	-	20.6 ± 9.0
	1.0 + 1.0	5		-	0.3 ± 0.1
	Ø	10		35.7	
ED_{50}(range) 0.2(0.15 - 0.36)					
ED_{90}(range) 0.45(0.31 - 0.75)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS

(BLOOD SCHIZONTOCIDES)

TABLE 183

COMPOUND NAME FLOXACRINE +

OR NUMBER PRIMAQUINE ..... PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0.1 + 3.0	5		-	47.6 ± 10.1
	0.3 + 3.0	5		-	8.8 ± 8.2
N	0.5 + 3.0	5	1	-	0
	1.0 + 3.0	5		-	0
	Ø	10		35.7	
ED_{50}(range) 0.13 (0.08 - 0.21)					
ED_{90}(range) 0.2 (0.13 - 0.33)					
Resistance factor I_{90}					
	0.1 + 10.0	5		-	10.8 ± 7.2
	0.3 + 10.0	5		-	0.01 ± 0.01
N	0.5 + 10.0	5	1	-	0
	1.0 + 10.0	5		-	0
	Ø	10		35.7	
ED_{50}(range) 0.06 (0.04 - 0.07)					
ED_{90}(range) 0.1 (0.07 - 0.12)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 187

COMPOUND NAME Primaquine +

OR NUMBER Floxacrine ..... PARASITE (SUB)SPECIES P. berghei ....

FORMULATION Tween 80/H_2O .. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 0.1	5		–	86.2 ± 1.8
	1.0 + 0.1	5		–	81.7 ± 4.7
N	3.0 + 0.1	5	1	–	47.6 ± 10.1
	10.0 + 0.1	5		–	10.8 ± 7.2
	Ø	10		35.7	
ED_{50}(range) 1.6(0.9 - 3.1)					
ED_{90}(range) 7.2(4.2 - 14.0)					
Resistance factor I_{90}					
	0.3 + 0.3	5		–	74.9 ± 2.5
	1.0 + 0.3	5		–	54.1 ± 5.4
N	3.0 + 0.3	5	1	–	8.8 ± 8.2
	10.0 + 0.3	5		–	0.01 ± 0.0
	Ø	10		35.7	
ED_{50}(range) 0.65(0.44 - 1.4)					
ED_{90}(range) 1.8(1.2 - 3.8)					
Resistance factor I_{90}					

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 188

COMPOUND NAME PRIMAQUINE +

OR NUMBER FLOXACRINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 0.5	5		-	43.8 ± 6.0
	1.0 + 0.5	5		-	20.6 ± 9.0
N	3.0 + 0.5	5	1	-	0
	10.0 + 0.5	5		-	0
	Ø	10		35.7	
ED_{50}(range) 0.4(0.24-0.73)					
ED_{90}(range) 0.78(0.47-1.4)					
Resistance factor I_{90}					
	0.3 + 1.0	5		-	0.01 ± 0.01
	1.0 + 1.0	5		-	0.3 ± 0.1
N	3.0 + 1.0	5	1	-	0
	10.0 + 1.0	5		-	0
	Ø	10		35.7	
ED_{50}(range) < 0.3					
ED_{90}(range) < 0.3					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 183

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER FLOXACRINE ..... PARASITE (SUB)SPECIES P. berghei .....

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >1.0... MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	80.4 ± 2.3
	0.3	5		-	64.5 ± 5.1
N	0.5	5	1	-	28.3 ± 8.7
	1.0	5		-	1.0 ± 0.5
	Ø	10		35.7	
ED_{50}(range) 0.25(0.16-0.42)					
ED_{90}(range) 0.6(0.36-0.97)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 190

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..CHLOROQUINE..... PARASITE (SUB)SPECIES ..P. berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..>10.0 MG/KG X 4..

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		–	68.7 ± 4.8
	1.0	5		–	66.6 ± 6.3
N	3.0	5	1	–	23.5 ± 2.7
	10.0	5		–	0.01 ± 0.01
	Ø	10		35.7	
ED_{50}(range) 1.4(1.1 - 2.2)					
ED_{90}(range) 2.7(2.1 - 4.1)					
Resistance factor I_{90}					
ED_{50}(range)					
ED_{90}(range)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 191

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME FLOXACRINE +

OR NUMBER CHLOROQUINE ..... PARASITE (SUB)SPECIES P. berghei .....

FORMULATION Tween 80 / H_2O . ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0.3	5		-	78.6 ± 8.3
	0.3 + 0.3	5		-	45.7 ± 4.2
N	0.5 + 0.3	5	1	-	20.6 ± 8.0
	1.0 + 0.3	5		-	4.3 ± 3.5
	Ø	10		35.7	
ED_{50}(range) 0.22 (0.12 - 0.3)					
ED_{90}(range) 0.7 (0.4 - 0.95)					
Resistance factor I_{90}					
	0.1 + 1.0	5		-	75.5 ± 2.2
	0.3 + 1.0	5		-	50.9 ± 4.5
N	0.5 + 1.0	5	1	-	11.2 ± 4.3
	1.0 + 1.0	5		-	1.1 ± 0.9
	Ø	10		35.7	
ED_{50}(range) 0.22 (0.14 - 0.33)					
ED_{90}(range) 0.49 (0.31 - 0.74)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 192

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME FLOXACRINE +

OR NUMBER CHLOROQUINE..... PARASITE (SUB)SPECIES ..P. berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0·1 + 3.0	5		–	35·7 ± 4·1
	0·3 + 3.0	5		–	26·0 ± 2·4
N	0·5 + 3.0	5	1	–	1·2 ± 0·6
	1·0 + 3.0	5		–	0·4 ± 0·2
	Ø	10		35·7	
ED_{50}(range) 0·08(0·04-0·17)					
ED_{90}(range) 0·26(0·15-0·56)					
Resistance factor I_{90}					
	0·1 + 10·0	5		–	0·06 ± 0·05
	0·3 + 10·0	5		–	0
N	0·5 + 10·0	5	1	–	0
	1·0 + 10·0	5		–	0
	Ø	10		35·7	
ED_{50}(range) < 0·1					
ED_{90}(range) < 0·1					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS

(BLOOD SCHIZONTOCIDES)

TABLE 193

COMPOUND NAME CHLOROQUINE +

OR NUMBER FLOXACRINE..... PARASITE (SUB)SPECIES ...P. berghei.....

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 0.1	5		-	78.6 ± 8.3
	1.0 + 0.1	5		-	75.5 ± 2.2
N	3.0 + 0.1	5	1	-	35.7 ± 4.1
	10.0 + 0.1	5		-	0.06 ± 0.05
	Ø	10		35.7	
ED_{50}(range) 1.8 (1.2 - 2.6)					
ED_{90}(range) 3.6 (2.5 - 5.2)					
Resistance factor I_{90}					
	0.3 + 0.3	5		-	45.7 ± 4.2
	1.0 + 0.3	5		-	50.9 ± 4.5
N	3.0 + 0.3	5	1	-	26.0 ± 2.4
	10.0 + 0.3	5		-	0
	Ø	10		35.7	
ED_{50}(range) 1.3 (0.9 - 2.2)					
ED_{90}(range) 2.6 (1.8 - 4.3)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 191

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME CHLOROQUINE +

OR NUMBER .FLOXACRINE..... PARASITE (SUB)SPECIES .P. berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 0.5	5		-	20.6 ± 8.0
	1.0 + 0.5	5		-	11.2 ± 4.3
N	3.0 + 0.5	5	1	-	1.2 ± 0.6
	10.0 + 0.5	5		-	0
	Ø	10		35.7	
ED_{50}(range) 0.17 (0.08 - 0.33)					
ED_{90}(range) 0.7 (0.33 - 1.3)					
Resistance factor I_{90}					
	0.3 + 1.0	5		-	4.3 ± 3.5
	1.0 + 1.0	5		-	1.1 ± 0.9
N	3.0 + 1.0	5	1	-	0.4 ± 0.2
	10.0 + 1.0	5		-	0
	Ø	10		35.7	
ED_{50}(range) 0.03 (<0.01 - 0.06)					
ED_{90}(range) 0.2 (0.05 - 0.4)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

5.6 DRUG INTERACTION ISOBOLOGRAMS

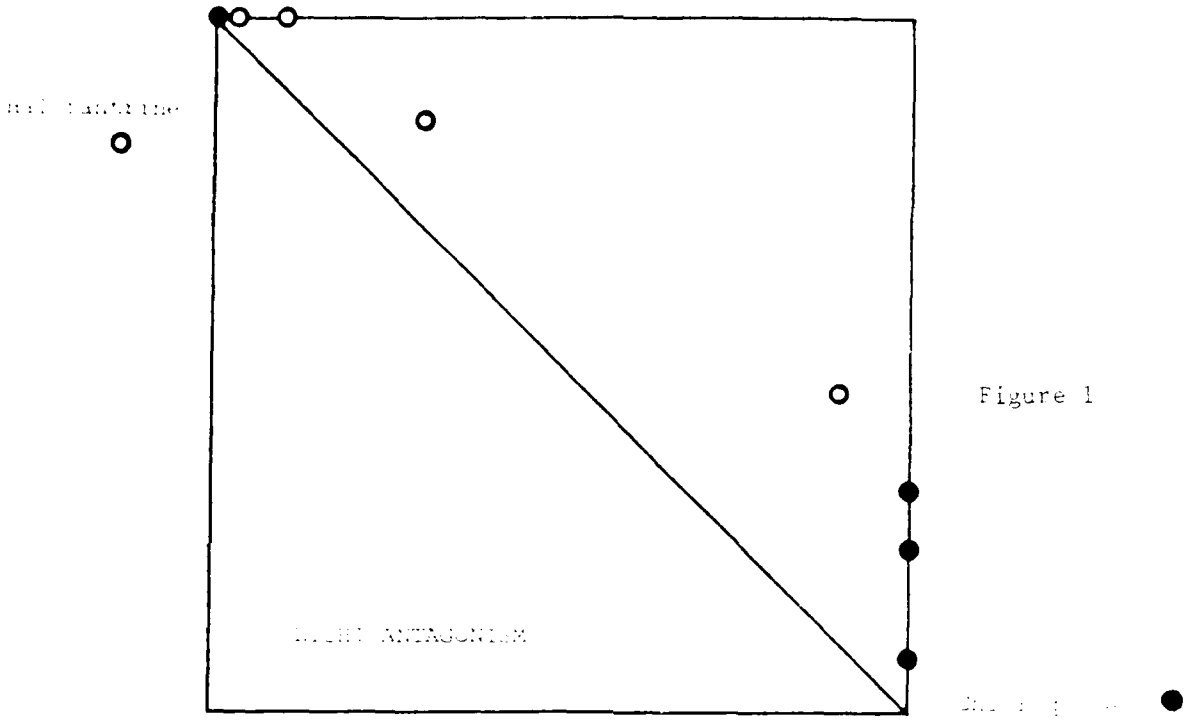


Figure 1

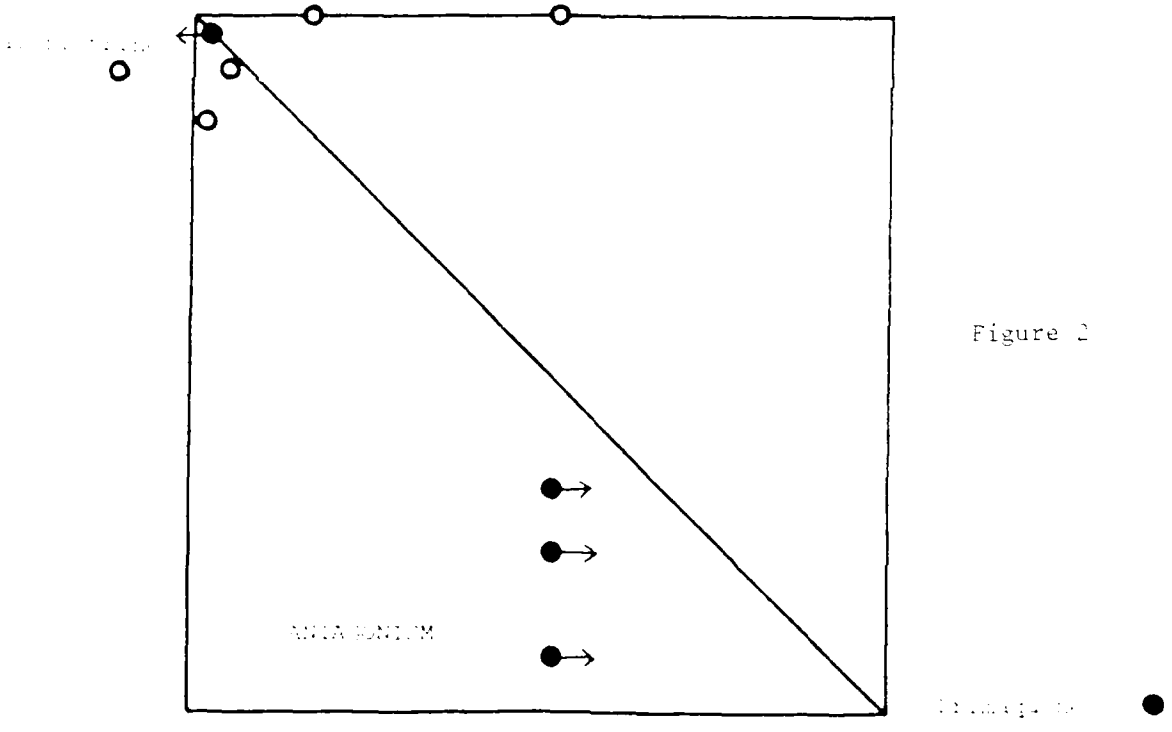


Figure 2

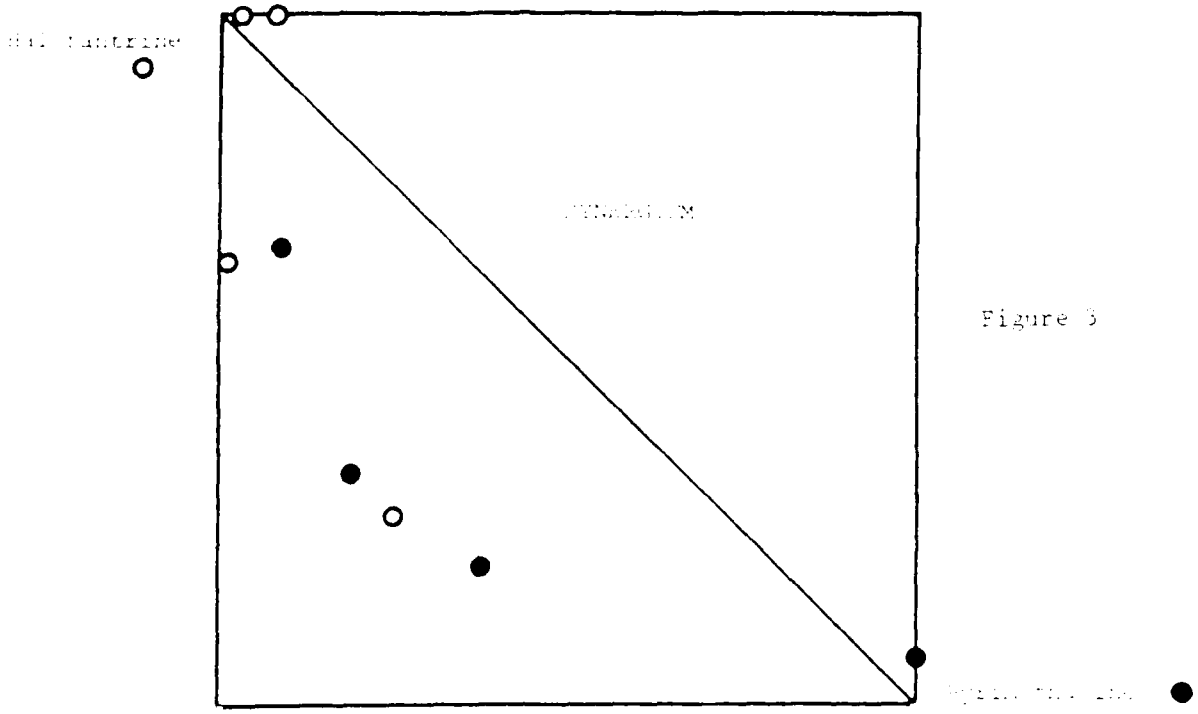


Figure 3

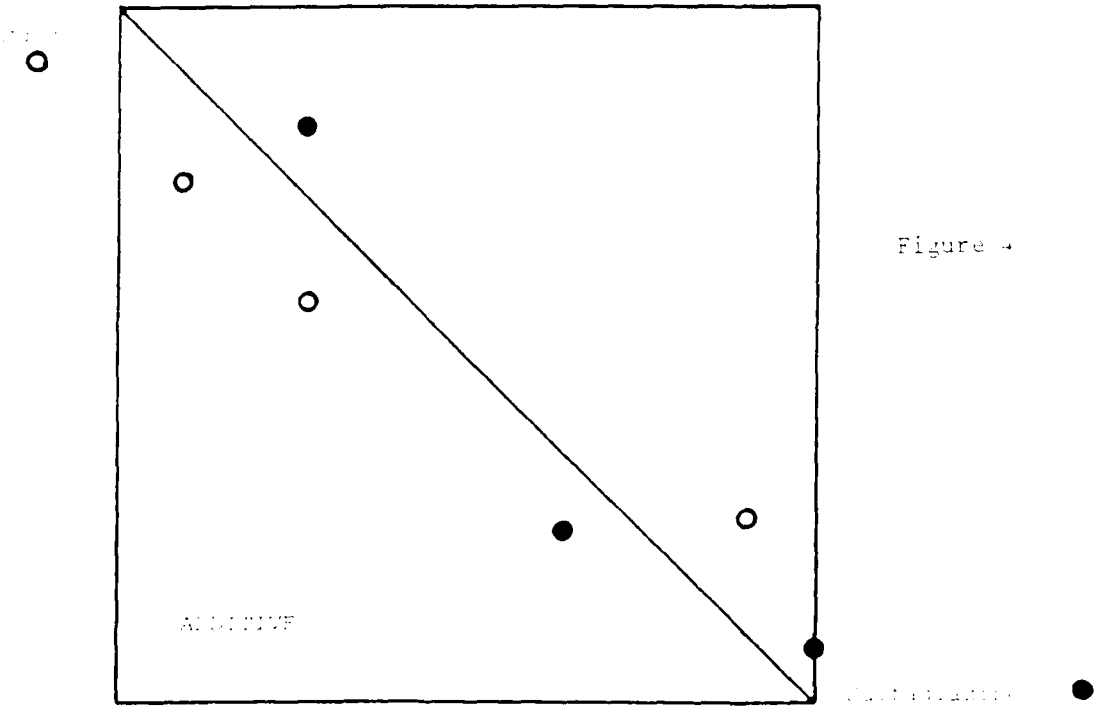


Figure 4

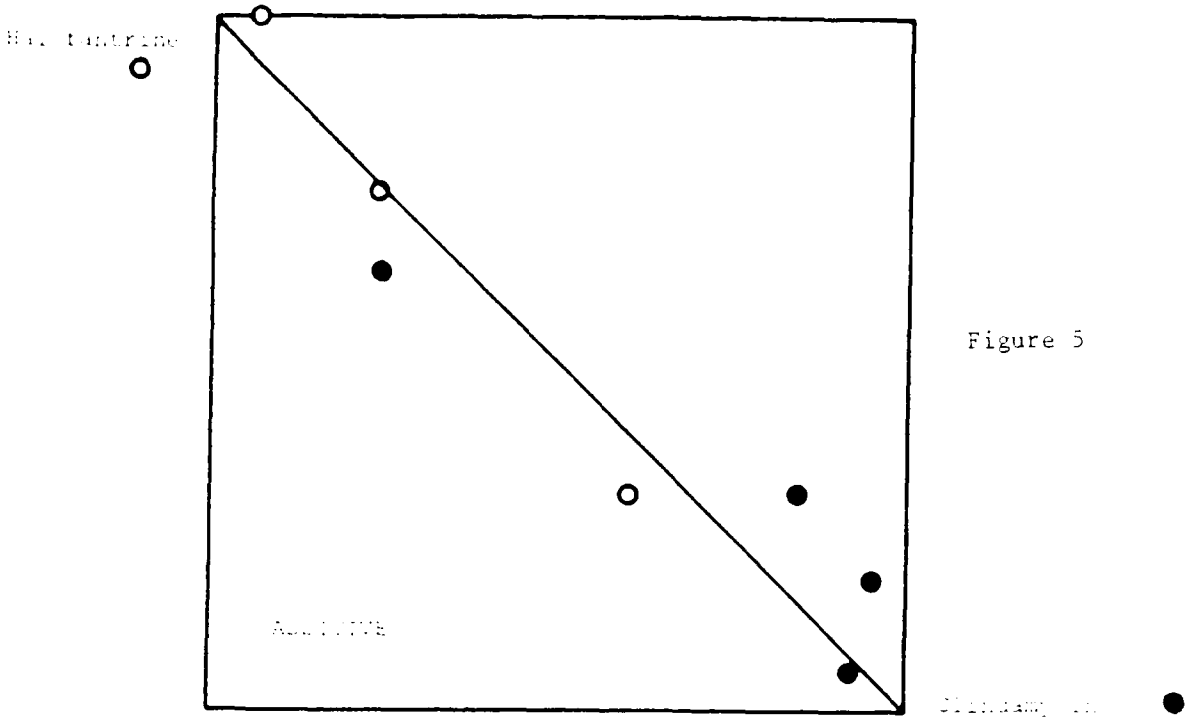


Figure 5

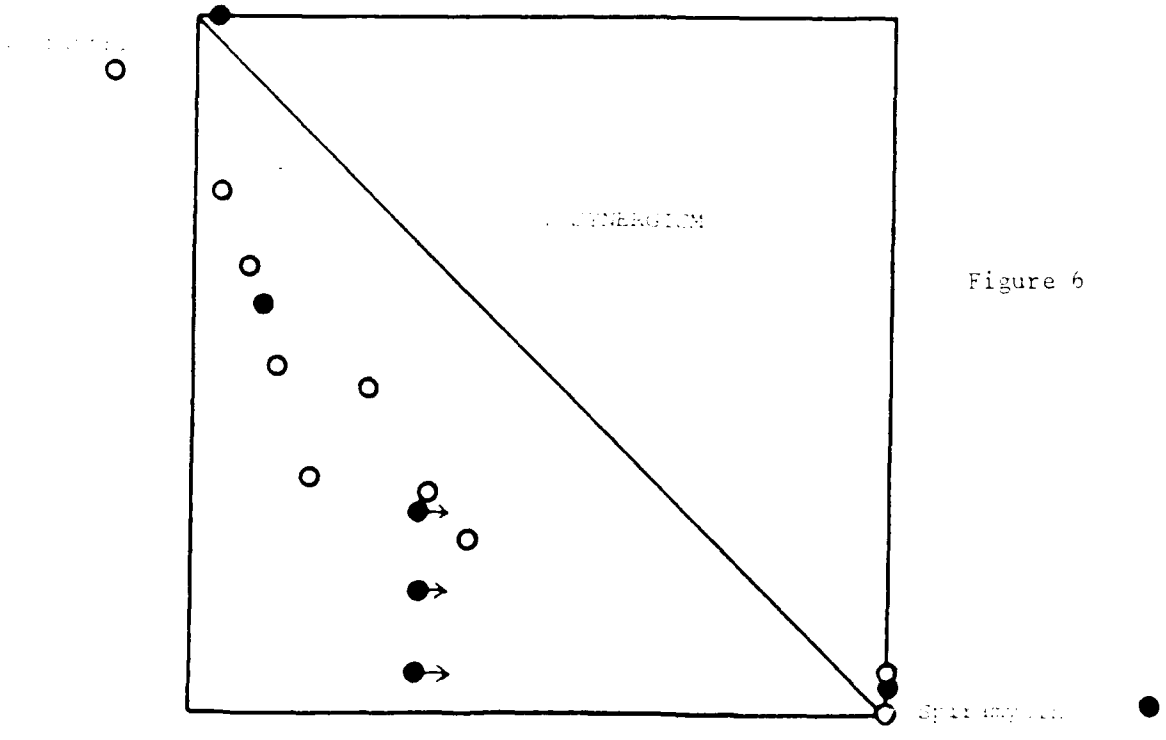


Figure 6

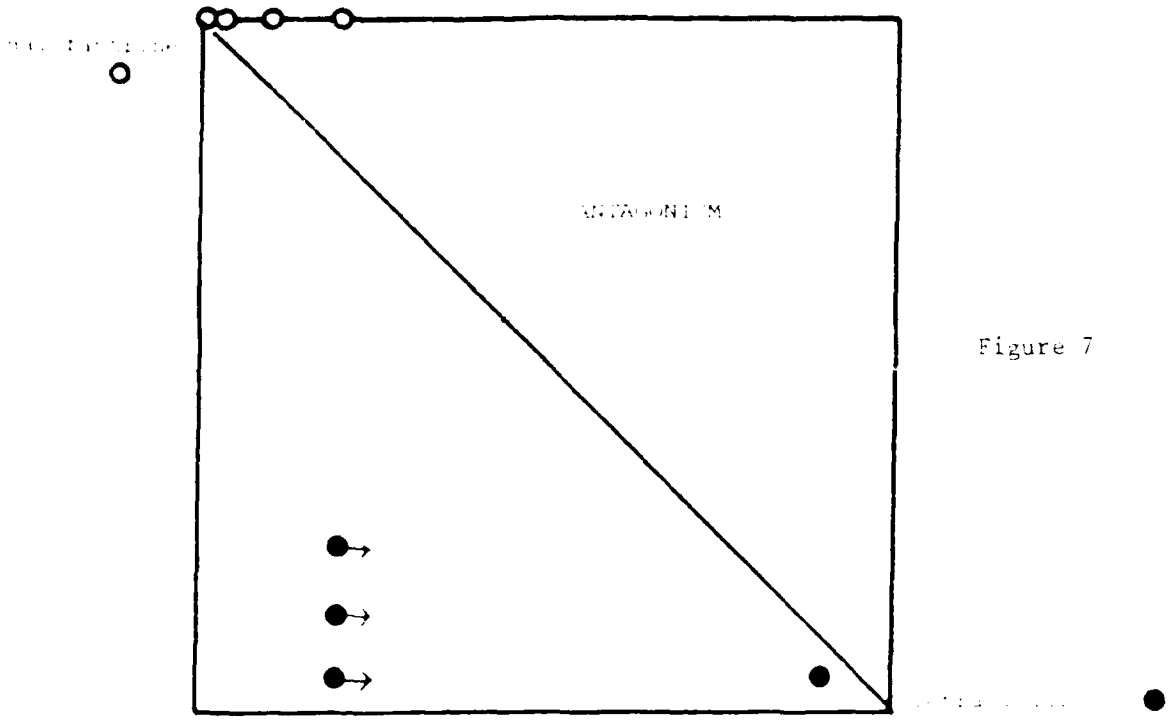


Figure 7

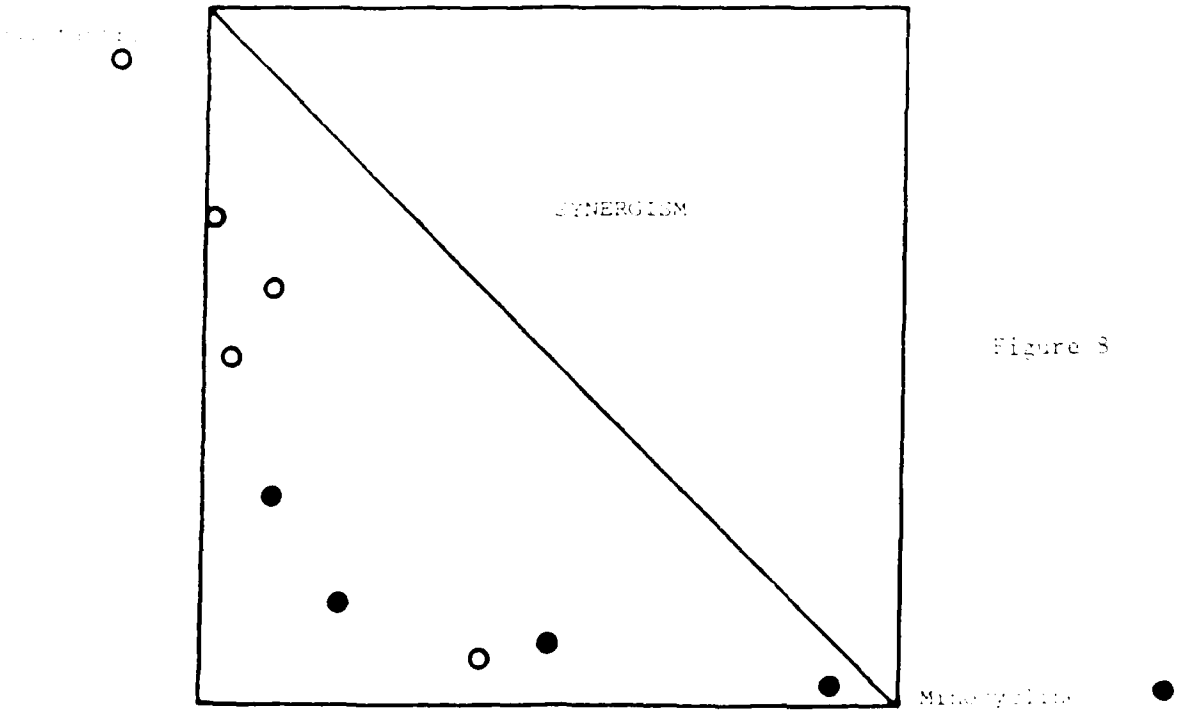


Figure 8

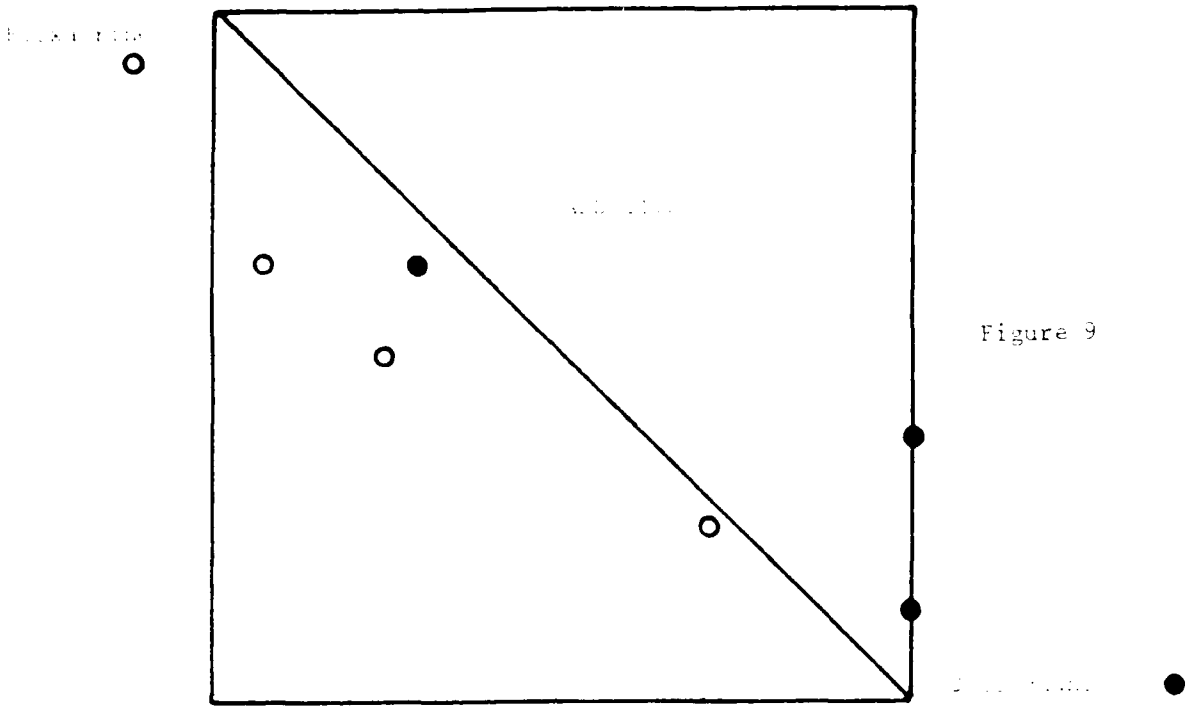


Figure 9

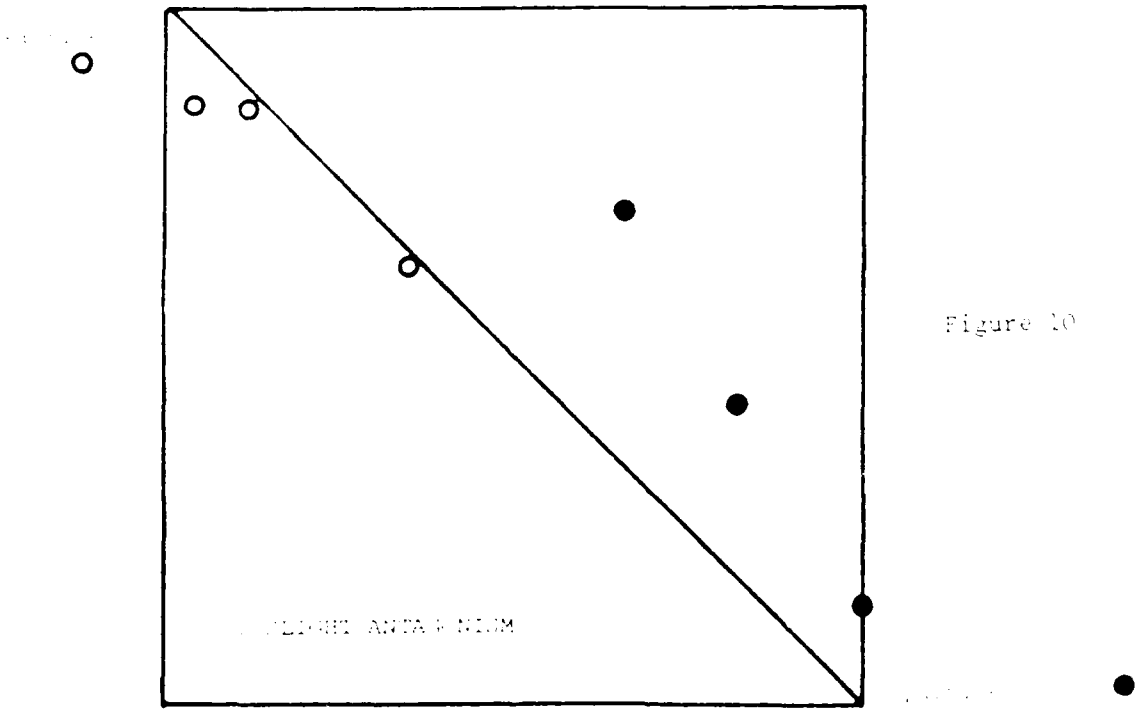


Figure 10

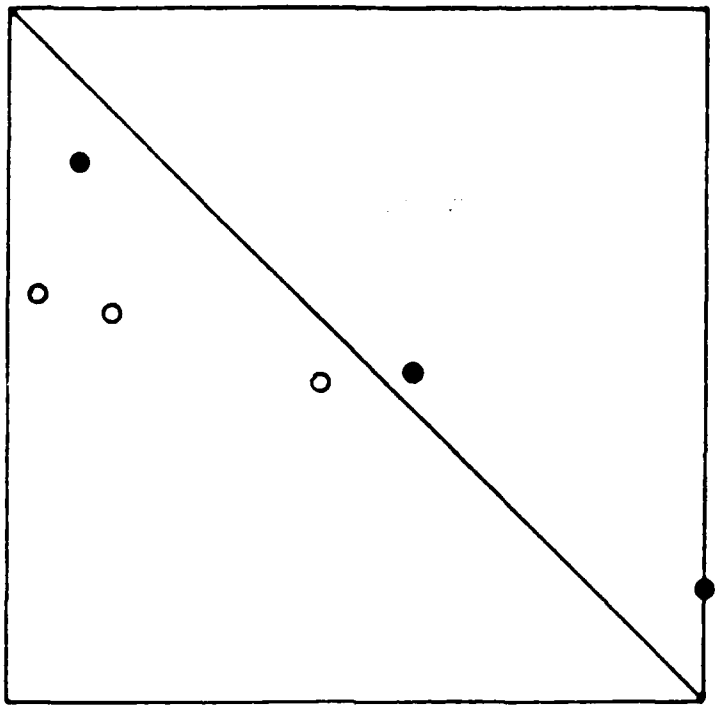


Figure 11

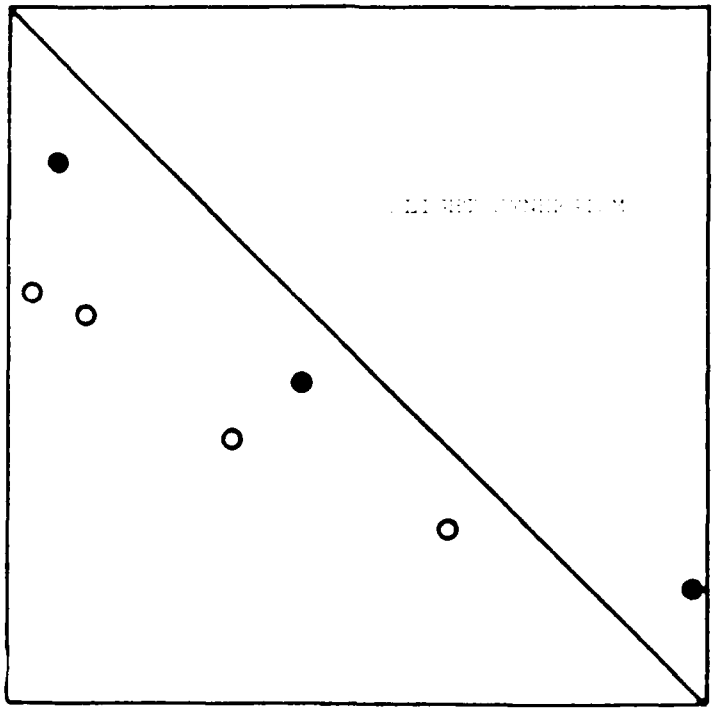


Figure 12

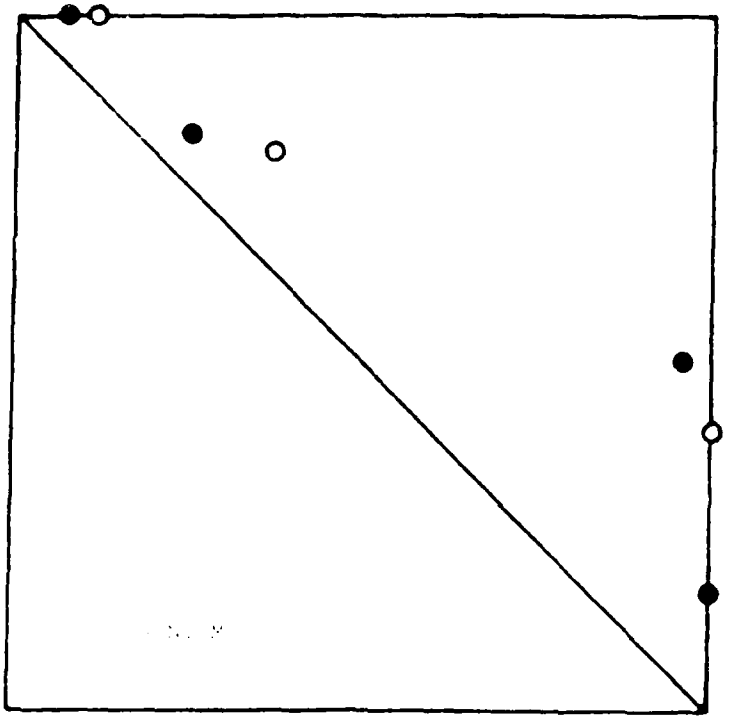


Figure 1b

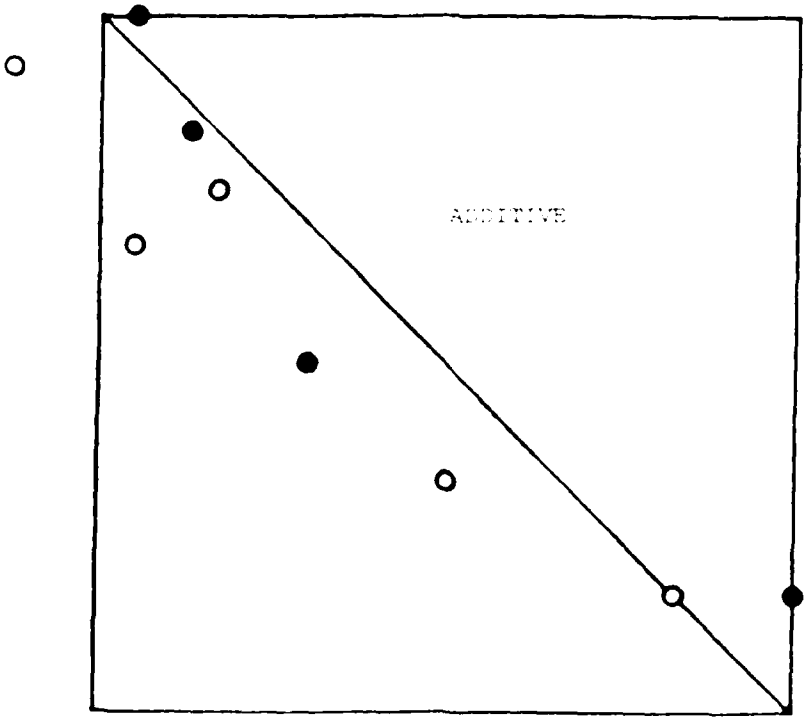
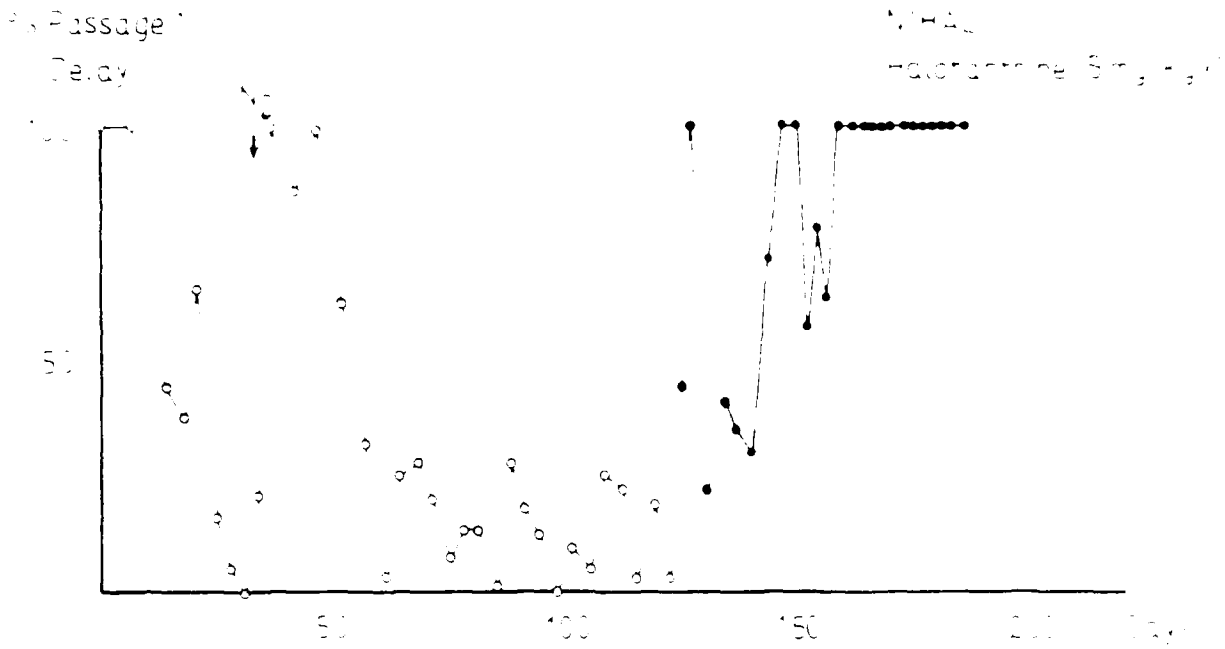


Figure 1c

5.7 ACQUISITION OF RESISTANCE GRAPHS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Delay
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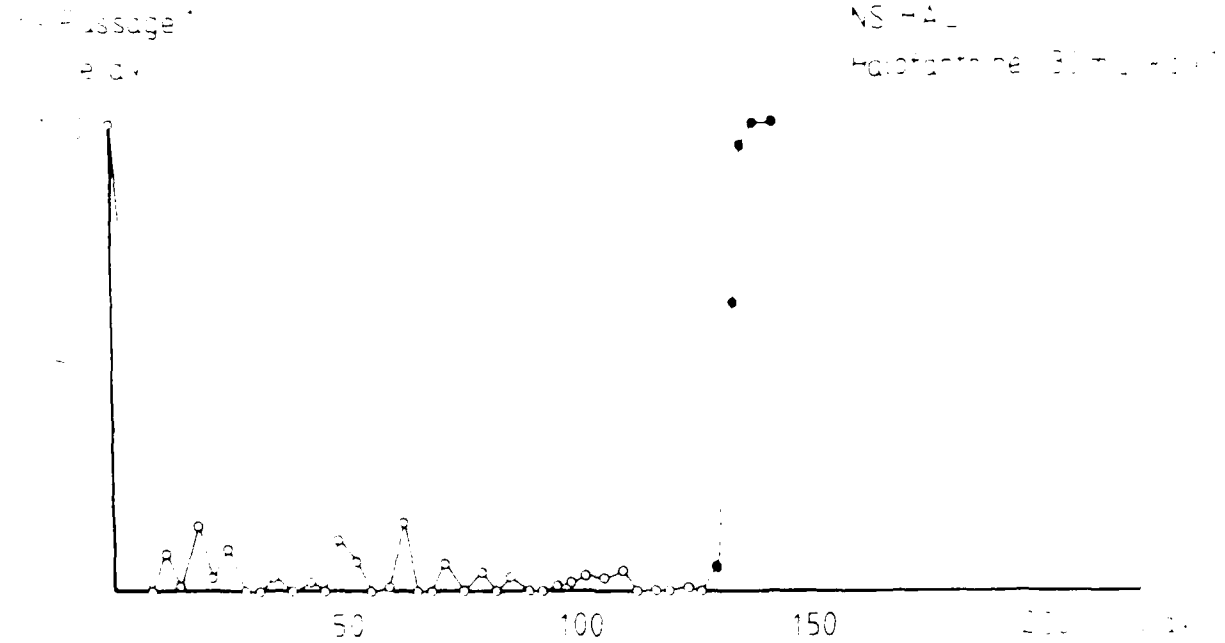
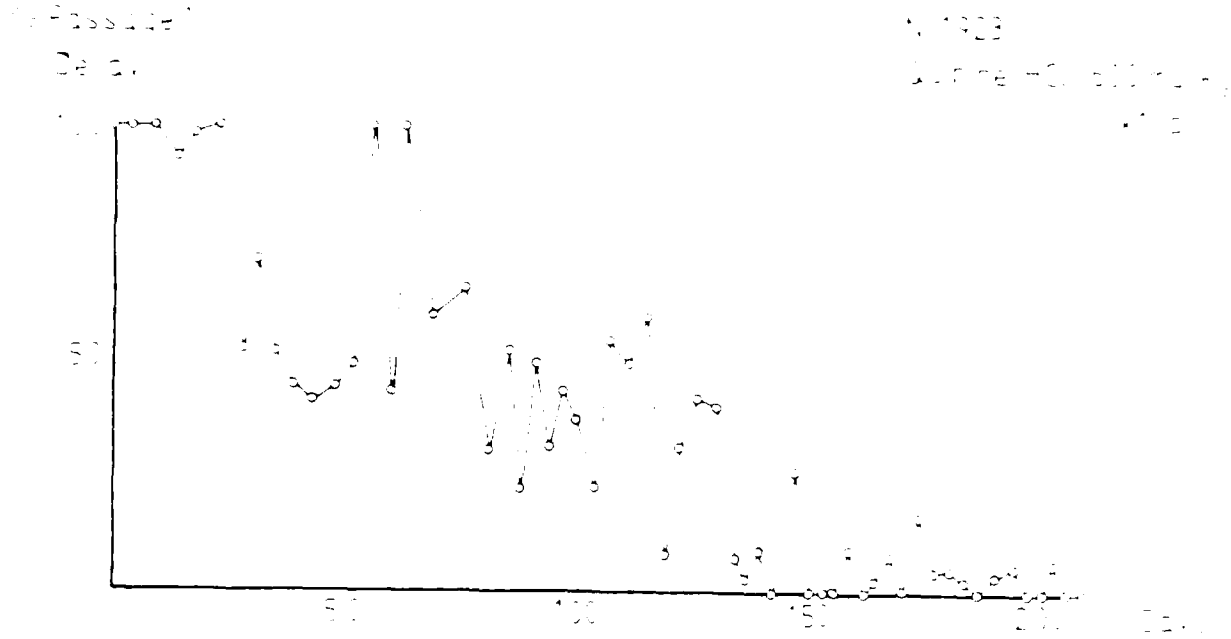
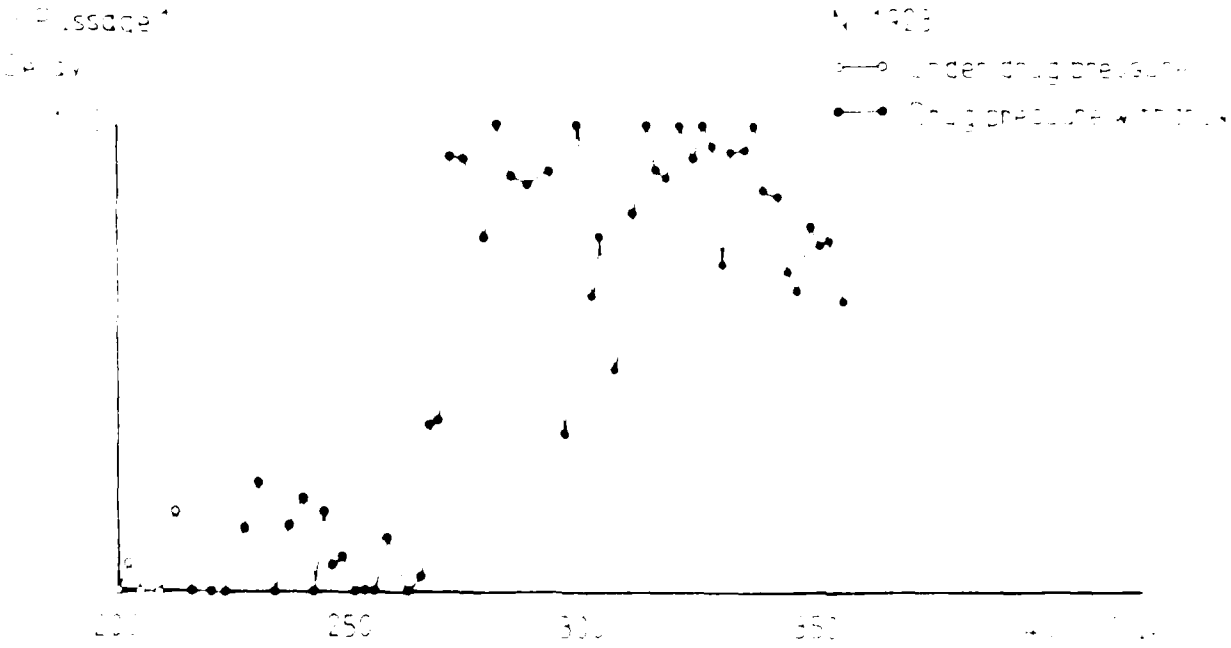
100
150


Passage
50
100
150




250

F.7 FIVE DAY TEST DATA (NEW RESISTANT LINES)

TABLE 195

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	N		N/HAL		N1923		NS		NS/HAL							
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
HALOFANTRINE	SC	0.5	1.3	3.6	2.8	>100	>77	0.4	1.6	560	350						
CHLOROQUINE	SC	0.8	3.1	7.0	2.3	>60	>19	4.7	42.0	»100	»2.4						
PRIMAQUINE	SC	1.5	5.8	10.5	1.8	18.5	3.2	3.4	7.0	16.0	2.3						
MEFLOQUINE	SC	1.6	2.8	9.0	3.2	>60	>21	4.4	10.0	»60	»10						
QUININE	SC	45.0	85.0	210	2.5	>600	>7.1	46.0	190.0	»600	»3.2						

ED mg/kg x 4 MTD maximum tolerated dose

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 196

[illegible]

COMPOUND NAME

OR NUMBER HALOFANTRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >30 MG/KG X 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	0.1	5		-	94.8 ± 5.2
	0.3	5		-	91.4 ± 2.0
N	1.0	5	1	-	51.6 ± 14.1
	3.0	5		-	0.1 ± 0.1
	Ø	10		20.9	
ED_{50}(range) 0.5 (0.1 - 1.3)					
ED_{90}(range) 1.3 (0.4 - 3.5)					
Resistance factor I_{90} 1.0					
	0.3	5		-	84.3 ± 3.9
	1.0	5		-	74.2 ± 9.6
N/HAL	3.0	5	1	-	44.4 ± 13.1
Pass. 31	10.0	5		-	0.1 ± 0.1
	30.0	5		-	0.02 ± 0.01
	Ø	10		23.9	
ED_{50}(range) 1.1 (0.4 - 2.8)					
ED_{90}(range) 3.6 (1.1 - 9.0)					
Resistance factor I_{90} 2.8					

Principal Investigator: Professor W. Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS -TABLE 197

BLOOD SCHIZONTOCIDES

COMPOUND NAME

OR NUMBER CHLOROQUINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >100 MG/KG X 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	82.8 ± 4.1
	0.3	5		-	80.1 ± 5.7
N	1.0	5	1	-	52.1 ± 7.6
	3.0	5		-	24.3 ± 8.5
	Ø	10		20.9	
ED_{50}(range) 0.8(0.2 - 2.1)					
ED_{90}(range) 3.1(0.9 - 8.5)					
Resistance factor I_{90} 1.0					
	1.0	5		-	91.4 ± 3.9
	3.0	5		-	53.6 ± 8.9
N/HAL	10.0	5	1	-	0.8 ± 0.3
Pass. 31	30.0	5		-	0.08 ± 0.08
	Ø	10		23.9	
ED_{50}(range) 2.7(1.4 - 3.9)					
ED_{90}(range) 7.0(3.6 - 10.3)					
Resistance factor I_{90} 2.3					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

BLOOD SCHIZONTICIDE

COMPOUND NAME
OR NUMBER PRIMAQUINE PARASITE SUB-SPECIES P. berghei

FORMULATION Tween 80 | H_2O ROUTE OF ADMINISTRATION : SC/~~IP, PO, IV~~

MAXIMUM TOLERATED DOSE (MTD) >60.0 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% (100)
	0.1	5		-	92.5 ± 3.6
	0.3	5		-	93.1 ± 2.4
N	1.0	5	1	-	63.0 ± 5.1
	3.0	5		-	34.4 ± 4.0
	10.0	5		-	0
	Ø	10		20.9	
ED_{50} (range) 1.5 (1.1 - 2.2)					
ED_{90} (range) 5.8 (4.1 - 8.4)					
Resistance factor I_{90} 1.0					
	1.0	5		-	77.6 ± 4.8
	3.0	5		-	68.1 ± 8.0
N/HAL	10.0	5	1	-	14.7 ± 7.8
Pass 31	30.0	5		-	0.3 ± 0.07
	60.0	5		-	0.03 ± 0.01
	Ø	10		23.9	
ED_{50} (range) 2.9 (1.6 - 6.0)					
ED_{90} (range) 10.5 (5.6 - 23.0)					
Resistance factor I_{90} 1.8					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS - Page 199

[illegible]

COMPOUND NAME

OR NUMBER ..MEFLOQUINE..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >60... MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	100 ± 7.1
	1.0	5		-	85.9 ± 2.3
N	3.0	5	1	-	17.4 ± 5.2
	10.0	5		-	0
	Ø	10		20.9	
ED_{50}(range) 1.6(0.5 - 2.2)					
ED_{90}(range) 2.8(0.9 - 3.7)					
Resistance factor I_{90} 1.0					
	1.0	5		-	87.5 ± 3.8
	3.0	5		-	73.8 ± 6.3
N/HAL	10.0	5	1	-	25.8 ± 4.8
Pass. 31	30.0	5		-	0.1 ± 0.08
	60.0	10		-	0
	Ø	10		23.9	
ED_{50}(range) 3.4(2.2 - 6.5)					
ED_{90}(range) 9.0(5.8 - 18.0)					
Resistance factor I_{90} 3.2					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

COMPOUND NAME
CR NUMBER ..QUININE..... PARASITE (SUB)SPECIES ..P. berghei.....

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : ~~SC IP~~ PO ~~IV~~

MAXIMUM TOLERATED DOSE (MTD) >600.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR % / Control PR %
	10·0	5		-	98·2 ± 2·7
	30·0	5		-	61·3 ± 7·3
N	100·0	5	1	-	36·1 ± 7·8
	300·0	5		-	0
	Ø	10		25·3	
ED_{50}(range) 45·0 (23·0 - 90·0)					
ED_{90}(range) 85·0 (43·0 - 175)					
Resistance factor I_{90} 1·0					
	30·0	5		-	86·1 ± 3·5
	100·0	5		-	48·9 ± 7·5
N/HAL	300·0	5	1	-	13·3 ± 3·3
Pass. 31	600·0	5		-	0·02 ± 0·01
	Ø	10		23·9	
ED_{50}(range) 90·0 (55·0 - 180)					
ED_{90}(range) 210 (125 - 420)					
Resistance factor I_{90} 2·5					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS - TABLE 201

BLOCK SCHIZONTICIDE

COMPOUND NAME

OR NUMBER ..HALOFANTRINE..... PARASITE (SUB)SPECIES ..P. yoelii.....

FORMULATION ..Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) .>100 MG/KG X .4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR%
	0.1	5		-	86.1 ± 2.6
	0.3	5		-	67.6 ± 6.1
NS	1.0	5	1	-	36.5 ± 10.5
	3.0	5		-	1.6 ± 0.6
	10.0	5		-	0.02 ± 0.01
	30.0	5		-	0
	Ø	10		24.4	
ED_{50}(range) 0.4(0.3 - 1.0)					
ED_{90}(range) 1.6(0.9 - 3.5)					
Resistance factor I_{90} 1.0					
	3.0	5		-	98.8 ± 3.0
	10.0	5		-	90.0 ± 4.1
NS/HAL	30.0	5	1	-	87.3 ± 2.4
Pass. 35	100.0	5		-	46.4 ± 9.8
	Ø	10		10.2	
ED_{50}(range) 85.0(48.0 - 118)					
ED_{90}(range) 560(320 - 780)					
Resistance factor I_{90} 350					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

COMPOUND NAME

DR NUMBER ...CHLOROQUINE..... PARASITE SUBSPECIES ..P. yoelii.....

FORMULATION ...Tween 80 | H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >100.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR % / control PR %
	1·0	5		-	81·1 ± 9·6
	3·0	5		-	54·9 ± 6·7
NS	10·0	5	1	-	24·9 ± 5·7
	30·0	5		-	18·0 ± 6·5
	60·0	5		-	9·4 ± 1·3
	Ø	10		24·4	
ED_{50}(range) 4·7(2·2 - 12·0)					
ED_{90}(range) 42·0(19·0 - 108)					
Resistance factor I_{90} 1·0					
	10·0	5		-	100
	30·0	5		-	100 ± 4·5
NS/HAL	60·0	5	1	-	86·1 ± 7·7
Pass 35	100·0	5		-	85·1 ± 2·4
	Ø	10		10·2	
ED_{50}(range) > 100					
ED_{90}(range) ≫100					
Resistance factor I_{90}≫2·4					

Principal Investigator: Professor W. Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TEST

[illegible]

COMPOUND NAME

OR NUMBER ...PRIMAQUINE..... PARASITE (SUB SPECIES) ...P.yoelii.....

FORMULATION ...Tween 80 / H_2O... ROUTE OF ADMINISTRATION : SC ~~[illegible]~~

MAXIMUM TOLERATED DOSE (MTD) >60.0 MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	91.0 ± 5.1
	3.0	5		-	78.0 ± 10.3
NS	10.0	5	1	-	7.0 ± 2.5
	30.0	5		-	0
	Ø	10		29.2	
ED_{50} (range) 3.4 (2.0 - 6.0)					
ED_{90} (range) 7.0 (4.1 - 12.6)					
Resistance factor I_{90} 1.0					
	3.0	5		-	92.2 ± 8.3
	10.0	5		-	79.3 ± 7.0
NS/HAL	30.0	5	1	-	0.2 ± 0.2
Pass 35	60.0	5		-	0.04 ± 0.02
	Ø	10		10.2	
ED_{50} (range) 7.0 (2.7 - 19.8)					
ED_{90} (range) 16.0 (6.0 - 44.0)					
Resistance factor I_{90} 2.3					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

COMPOUND NAME

CR NUMBER MEFLOQUINE PARASITE SUBSPECIES P. yoelii

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION

MAXIMUM TOLERATED DOSE MTD >60.0 MG/KG x 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PPR / Control PPR
	3.0	5		-	70.8 ± 5.0
	10.0	5		-	14.[illegible] ± 9.5
NS	30.0	5	1	-	0.07 ± 0.07
	100.0	5		-	0
	Ø	10		29.2	

ED_{50}(range) 4.4 (3.4-6.0)

ED_{90}(range) 10.0 (7.8-14.0)

Resistance factor I_{90} 1.0

	3.0	5		-	92.8 ± 9.8
	10.0	5		-	100.0 ± 3.0
NS/HAL	30.0	5	1	-	100.0 ± 3.0
Pass 35	60.0	5		-	94.3 ± 3.2
	Ø	10		10.2	

ED_{50}(range) ≫ 60

ED_{90}(range) ≫ 60

Resistance factor I_{90} ≫ 10

Principal Investigator: Professor W. Peter
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS — TABLE 205

[illegible]

COMPOUND NAME

OR NUMBER QUININE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : ~~[illegible]~~

MAXIMUM TOLERATED DOSE (MTD) >600 MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	100 ± 0.1
	10.0	5		-	77.8 ± 11.9
NS	30.0	5		-	67.3 ± 13.0
	100.0	5		-	52.6 ± 3.8
	300.0	5		-	9.1 ± 4.6
	600.0	5		-	0.2 ± 0.2
	Ø	10		19.6	
ED_{50} (range) 46.0 (11.0-95.0)					
ED_{90} (range) 190.0 (45.0-390)					
Resistance factor I_{90} 1.0					
	100.0	5		-	100 ± 2.3
	300.0	5		-	98.8 ± 1.3
NS/HAL	600.0	5		-	91.7 ± 5.5
Pass. 35	Ø	10		10.2	
ED_{50} (range) >600					
ED_{90} (range) >>600					
Resistance factor I_{90} >>3.2					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

COMPOUND NAME

CR NUMBER HALOFANTRINE PARASITE (SUBSPECIES) P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >30 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRR / Control PRR X100
	0.1	5		-	94.8 ± 5.2
	0.3	5		-	91.4 ± 2.0
N	1.0	5	1	-	51.6 ± 14.1
	3.0	5		-	0.1 ± 0.1
	Ø	10		20.9	
ED_{50}(range) 0.5 (0.1 - 1.3)					
ED_{90}(range) 1.3 (0.4 - 3.5)					
Resistance factor I_{90} 1.0					
	1.0	5		-	57.5 ± 6.2
	3.0	5		-	56.5 ± 16.3
N/1923	10.0	5	1	-	91.5 ± 3.1
(R.S. 56)	30.0	5		-	100 ± 2.2
	100.0	5		-	80.3 ± 11.8
	Ø	10		5.0	
ED_{50}(range) > 100					
ED_{90}(range) > 100					
Resistance factor I_{90} > 77					

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COMPOUND NAME

CR NUMBER CHLOROQUINE [illegible]

FORMULATION Tween 80 | H_2O ROUTE OF ADMINISTRATION ——

MAXIMUM TOLERATED DOSE MTD >100 MG/KG x 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated [illegible]
	0.1	5		–	82.8 ± 4.1
	0.3	5		–	80.1 ± 5.7
N	1.0	5	1	–	52.1 ± 7.6
	3.0	5		–	24.3 ± 8.5
	Ø	10		20.9	

ED_{50}(range)	0.8 (0.2 - 2.1)
ED_{90}(range)	3.1 (0.9 - 8.5)
Resistance factor I_{90}	

	3.0	5		–	94.5 ± 4.0
	10.0	5		–	91.8 ± 4.1
N/1923	30.0	5	1	–	91.8 ± 7.4
(Pass 56)	60.0	5		–	100 ± 5.5
	Ø	10		8.0	

ED_{50}(range)	> 60
ED_{90}(range)	> 60
Resistance factor I_{90}	> 19

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PRIMAQUINE ..... PARASITE SUBSPECIES Plasmodium

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE MTD >60 MG/KG x 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRS / Control PRS %
	0.1	5		–	92.5 ± 3.6
	0.3	5		–	93.1 ± 2.4
N	1.0	5	1	–	63.0 ± 5.1
	3.0	5		–	34.4 ± 4.0
	10.0	5		–	0
	Ø	10		20.9	
ED_{50} (range) 1.5 (1.1 – 2.2)					
ED_{90} (range) 5.8 (4.1 – 8.4)					
Resistance factor I_{90} 1.0					
	3.0	5		–	59.5 ± 14.2
	10.0	5		–	34.0 ± 13.4
N, 1923	30.0	5	1	–	9.5 ± 4.3
(Pass 56)	60.0	5		–	0.3 ± 0.[illegible]
	Ø	10		8.0	
ED_{50} (range) 6.8 (2.7 – 2.5)					
ED_{90} (range) 18.5 (7.2 – 34.0)					
Resistance factor I_{90} 3.2					

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COMPOUND NAME

CODE NUMBER MEFLOQUINE PARASITE [illegible] SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION [illegible]

MAXIMUM TOLERATED DOSE (MTD) >60 MG/KG X 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated [illegible] / Control [illegible]
	0.3	5		–	100 ± 7.1
	1.0	5		–	[illegible]
N	3.0	5	1	–	174 ± [illegible]
	10.0	5		–	0
	Ø	10		20.9	

ED_{50} range 1.6 (0.5 - 2.2)

ED_{90} range 2.8 (0.6 - 3.7)

Resistance factor I_{90} 1.0

	3.0	5		–	85.5 ± 7.4
	10.0	5		–	73.5 ± 13.0
N/1923	30.0	5	1	–	97.5 ± 4.6
(Pass 56)	60.0	5		–	100
	Ø	10		8.0	

ED_{50} range >60

ED_{90} range >60

Resistance factor I_{90} >21

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[illegible]

[illegible] QUININE ..... PARASITE SUB-SPECIES P. beighei ....

FORMULATION Tween 80 / H_2O .. ROUTE OF ADMINISTRATION : [illegible]

MAXIMUM TOLERATED DOSE (MTD) > 600 MG/KG (4)

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PRT / Control PRT (%)
	10.0	5		–	98.2 ± 2.7
	30.0	5		–	61.3 ± 7.3
N	100.0	5	1	–	36.1 ± 7.5
	300.0	5		–	0
	Ø	10		25.3	
ED_{50} (range) 45.0 (23.0 - 90.0)					
ED_{90} (range) 85.0 (43.0 - 175)					
Resistance factor I_{90} 1.0					
	100.0	5		–	85.0 ± 8.2
	300.0	5		–	76.5 ± 8.4
N11923	600.0	5	1	–	73.4 ± 23.1
(Pass 5e)	Ø	10		8.0	
ED_{50} (range) > 600					
ED_{90} (range) > 600					
Resistance factor I_{90} > 7.1					

Principal Investigator: Professor W. Peters

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