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Experimental hut evaluation of the pyrrole insecticide chlorfenapyr on bed nets for the control of *Anopheles arabiensis* and *Culex quinquefasciatus*

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Summary

OBJECTIVE To determine the efficacy of chlorfenapyr against *Anopheles arabiensis* and *Culex quinquefasciatus* in East Africa and to identify effective dosages for net treatment in comparison with the commonly used pyrethroid deltamethrin.

METHODS Chlorfenapyr was evaluated on bed nets in experimental huts against *A. arabiensis* and *C. quinquefasciatus* in Northern Tanzania, at application rates of 100–500 mg/m^2.

RESULTS In experimental huts, mortality rates in *A. arabiensis* were high (46.0–63.9%) for all dosages of chlorfenapyr and were similar to that of deltamethrin-treated nets. Mortality rates in *C. quinquefasciatus* were higher for chlorfenapyr than for deltamethrin. Despite a reputation for being slow acting, >90% of insecticide-induced mortality in laboratory tunnel tests and experimental huts occurred within 24 h, and the speed of killing was no slower than for deltamethrin-treated nets.

CONCLUSIONS Chlorfenapyr induced low irritability and knockdown, which explains the relatively small reduction in blood-feeding rate. Combining chlorfenapyr with a more excito-repellent pyrethroid on bed nets for improved personal protection, control of pyrethroid-resistant mosquitoes and pyrethroid resistance management would be advantageous.

keywords chlorfenapyr, mosquito nets, *Anopheles, Culex*

Introduction

Pyrethroid-treated nets are the primary tool for preventing malaria in Africa (Armstrong-Schellenberg *et al.* 2000; Curtis *et al.* 2003). This technology is threatened by the development and rapid spread of pyrethroid resistance in the *Anopheles gambiae* and *A. funestus* species complexes in several parts of Africa (Vulule *et al.* 1994, 1999; Chandre *et al.* 1999; Hargreaves *et al.* 2000; N'Guessan *et al.* 2007a). There is an urgent need to identify alternative insecticides, which meet criteria for vector control and show no cross-resistance to pyrethroids (Zaim & Guillet 2002). Such insecticides have been developed by pesticide manufacturers for the agricultural sector, where market size provides greater potential rewards and profitability than the public health sector.

A typical example is fipronil, a phenylpyrazole insecticide, which is effective against veterinary pests (Postal *et al.* 1995) and which has some activity against mosquitoes (Ali *et al.* 1998) but shows cross-resistance to dieldrin in *A. stephensi* and hence was not developed further (Kolaczinski & Curtis 2001).

Some novel insecticides that have shown encouraging results against mosquito larvae are chlorfenapyr, hydramethylnon, indoxacarb and imidacloprid. Diafenthiuron and chlorfenapyr also have potential for adult mosquito control (Paul *et al.* 2006). Chlorfenapyr, a pyrrole, is a relatively new pro-insecticide which is now widely used for control of veterinary and agricultural pests (Lovell *et al.* 1990; Sheppard & Joyce 1998). This insecticide, developed in 1988 (Tracy *et al.* 1994) and commercialised by BASF Corporation for agricultural pest control, has a unique mechanism of action involving the uncoupling of oxidative phosphorylation in the mitochondria as the primary target site (Black *et al.* 1994). Owing to this, chlorfenapyr seems unlikely to show cross-resistance to conventional neurotoxic insecticides. Laboratory tests with a discriminating concentration of chlorfenapyr resulted in full mortality in the susceptible, *kdr* and *Ace-1^R* strains of *A. gambiae sensu stricto*, indicating no cross-resistance to

these pyrethroid and organophosphate resistance mechanisms (N'Guessan *et al.* 2007b). N'Guessan observed that 100 and 250 mg/m^2 dosages of chlorfenapyr had significantly better impact on the *kdr* strain than field rates of permethrin (500 mg/m^2), deltamethrin (25 mg/m^2) or lambdacyalothrin (18 mg/m^2) under similar conditions in tunnel tests (WHO 2006). Thus, we conducted further investigations towards the development of chlorfenapyr as an alternative to pyrethroid insecticides for net treatment. This study focused on determining efficacy against *A. arabiensis* and *Culex quinquefasciatus* in East Africa and identifying effective dosages for net treatment in comparison with the commonly used pyrethroid deltamethrin.

Materials and methods

Study area

Evaluation of chlorfenapyr-treated nets was carried out under laboratory and experimental hut conditions at the Kilimanjaro Christian Medical Centre, Moshi, in Northern Tanzania. The laboratory studies involved contact bioassays and tunnel tests (WHO 2006). Experimental hut studies took place in an area of rice irrigation at Mabogini field station in Lower Moshi (Kulkarni *et al.* 2007). The only man-biting mosquitoes found in significant numbers in Lower Moshi are *A. arabiensis* and *C. quinquefasciatus* (Ijumba *et al.* 2002).

Test materials were rectangular nets made of polyester and impregnated with chlorfenapyr at various dosages (100, 250, 500 mg/m^2) or with deltamethrin at a standard dosage (25 mg/m^2).

Evaluation techniques

Mosquito net was subjected to WHO cone bioassay before proceeding with tunnel tests or experimental hut trials. Sugar-fed, 5-day-old laboratory-reared *A. arabiensis* (Dondotha) were tested on each net according to standard procedures (WHO 2006). A total of 30 mosquitoes in three replicates of 10 mosquitoes were exposed on each treatment for 3 min before transfer to paper cups with sugar solution for 24- and 72-h mortality counts.

Standard WHO resistance tests were carried out by exposing wild caught *C. quinquefasciatus* and *A. arabiensis* mosquitoes to insecticide test papers in WHO test kits. Exposure was for 1 h and mortality was scored after 24 h holding (WHO 2006).

All treatments plus control were subjected to a tunnel test (WHO 2006). The equipment consists of a square glass cylinder (60 × 25 × 25 cm) with three chambers: bait chamber, middle chamber and releasing chamber. The release and middle chambers were separated by a paper divide with a 16 cm^2 window. The middle and bait chambers were separated by test netting material with nine 1 cm diameter holes supported by a wooden frame. Mosquitoes released into the tunnel are attracted by host odour into the middle chamber, and have the opportunity to enter the bait chamber through holes in the netting. The system represents a miniaturised room with access to a host occupying a torn-treated net. Three replicates of approximately 50 mosquitoes were tested as precursor to experimental hut trials. Non-blood-fed 5- to 8-days old *A. arabiensis* (Dondotha) were released into each tunnel at 18:00 and recovered at 8:00. Mosquitoes were then removed and scored as live or dead and unfed or blood fed. Live mosquitoes were held and delayed mortality scored after 24 and 72 h.

Experimental hut evaluation was carried out at Mabogini field station, Moshi, Northern Tanzania in three experimental huts constructed according to a design described by Smith (1965) and Smith and Webley (1969). Some slight modifications were made involving reduction of eave space, addition of cardboard and hessian cloth ceiling, concrete floor surrounded by a water filled moat, and improved screening of the veranda. The working principle of these huts has been described by Curtis *et al.* (1996) and Mosha *et al.* (2008).

Two separate trials, each lasting for 16 nights, were conducted:

- *Chlorfenapyr dosage rate evaluation: 12 February–3 March 2006*. Treatments of 100, 250, 500 mg/m^2 chlorfenapyr plus untreated control were rotated between three huts every 4 days, with one treatment being excluded during each rotation. During this time, *A. arabiensis* were abundant while *C. quinq*uefasciatus were very infrequently captured in the experimental huts.
- *Comparison of chlorfenapyr with deltamethin: 7 March–26 March 2006*. The high dosage of 500 mg/m^2 was dropped and the remaining dosages of 100 and 250 mg/m^2 were compared with the pyrethroid deltamethrin (25 mg/m^2). *Anopheles arabiensis* numbers were still high and the number of *C. quinquefasciatus* had increased to a reportable level.

During each trial, three recently treated nets (2–3 days before) plus an untreated net were rotated through each of the three huts. Each net had six 4 cm diameter holes, two on the long side and one on the short side of the net, to simulate the condition of a worn net. Sleepers were rotated between huts on successive nights to reduce any bias

because of differences in individual attractiveness to mosquitoes. The direction of two open verandas was routinely changed from East–West to North–South orientation with each treatment rotation in order to minimise the potential confounding factor of preferential escape route through the eaves towards external light at sunrise.

Mosquitoes were collected in the morning at 06:00 from inside the net, window (exit) traps, and ceiling, walls and floors of the verandas and room. The collected mosquitoes were kept for species identification, determination of abdominal condition and mortality counts. All members of the *A. gambiae* complex identified by morphological characteristics were assumed to be *A. arabiensis* based on previous cytotaxonomic and PCR identification results (Ijumba *et al.* 2002; Kulkarni *et al.* 2006) and our own cytotaxonomic examination results of some mosquito samples.

All live mosquitoes were held in paper cups and provided with 10% glucose solution. Mortality counts were carried out after 24- and 72-h holding periods for calculation of delayed mortality rates.

Data processing and analysis

The number of mosquitoes in the two veranda traps was multiplied by two to adjust for the unrecorded escapes through the two open verandas, which are left unscreened to allow routes for entry of wild mosquitoes via the gaps under the eaves. The data was double entered and analysed to show the effect of each treatment in terms of: (1) insecticide-induced exiting rates – percentage of total mosquitoes collected from veranda and exit traps; (2) blood-feeding inhibition – percentage of unfed mosquitoes from treated hut relative to percentage from control; and (3) overall mortality – total number of mosquitoes found dead immediately and after holding for 24 or 72 h. Assessment of these outcome variables between treatments relative to the control was analysed by logistic regression using STATA 8.0 Statistical software.

Toxicology

Chlorfenapyr has a WHO toxicological classification III: an LD50 oral toxicity in rats of >400 mg/kg body weight, acute dermal toxicity >2000 mg/kg and inhalation toxicity of 1.9 mg/l. Chlorfenapyr is placed in the category of 'slightly hazardous' to humans (Tomlin 2000), similar to many insecticides used in public health.

A risk assessment of the use of chlorfenapyr on nets was undertaken by BASF toxicologists [BASF unpublished observation: *Exposure and health risks associated to the treatment and subsequent use of long-lasting impregnated mosquito nets (LLIN) treated with chlorfenapyr*] using the WHO generic risk assessment model (WHO 2004). Potential exposure to chlorfenapyr was evaluated using assumptions, parameters and default values defined in the WHO model, which refers to user-treated bed nets. The calculated exposure levels to chlorfenapyr for the relevant age groups (adult, child and newborn) are all below the corresponding relevant dermal and systemic acute reference doses or acceptable exposure levels for repeated exposure. Exposure was deemed acceptable based on the conservative scenarios from the WHO model, indicating safe use of the chlorfenapyr-treated nets for the intended use.

Ethical clearance

Informed consent was obtained from all volunteers recruited to the experimental hut studies. The study was approved by ethics committees of LSHTM and NIMR (Ref: NIMR/HQ/R.8a/Vol. X/86).

Results

Contact bioassays and resistance tests

Nets treated with dosages of chlorfenapyr of 100–500 mg/m^2 induced mortality rates in *A. arabiensis* that ranged from 54.2% with the lowest to 68.5% with the highest concentration (Figure 1). There was little increase in final mortality with dosages above 250 mg/m^2. There was delayed mortality of 15–25% between 24 and 74 h. Deltamethrin (25 mg/m^2) caused higher mortality (100%) than chlorfenapyr.

Anopheles arabiensis showed 100% mortality on deltamethrin test papers in resistance tests. *Culex quinquefasciatus* showed 80% mortality on permethrin and 96% mortality on deltamethrin test papers (n = 100 mosquitoes per test).

In the tunnel tests, there was a non-linear relationship between dosage and passage rates through the chlorfenapyr-treated netting, with proportionately more mosquitoes penetrating the 250 mg/m^2 treatment than the lower or higher dosage treatments. Blood-feeding inhibition showed the same trend, as only mosquitoes that penetrated the netting could feed (Figure 2). Mortality rates with all treatments ranged between 96% and 100% after 72 h (Figure 3). Almost all mortality occurred during the first 24 h.

Experimental hut trials

A summary of the results of chlorfenapyr treatments ranging from 100 to 500 mg/m^2 for *A. arabiensis* is shown

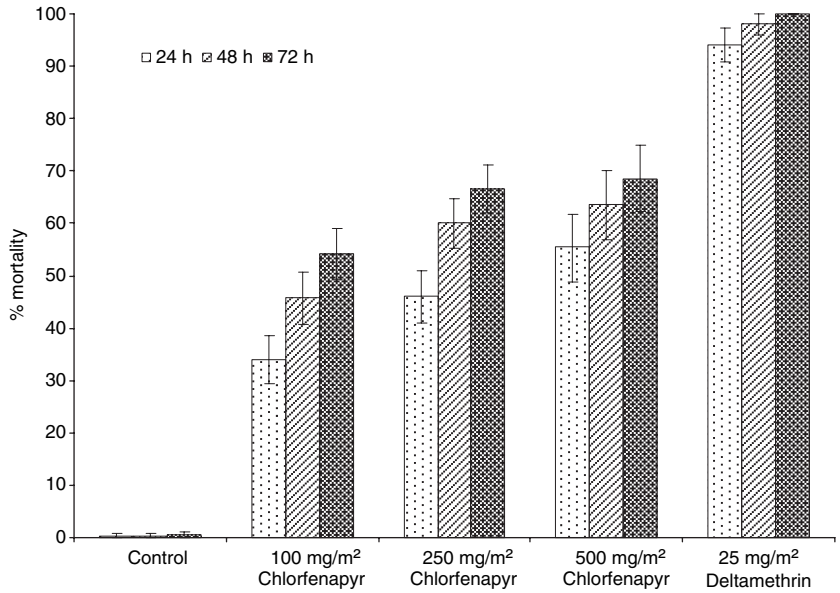

Figure 1 Mortality of *Anopheles arabiensis* 24, 48 and 72 h after exposure to chlorfenapyr or deltamethrin in cone bioassay tests.

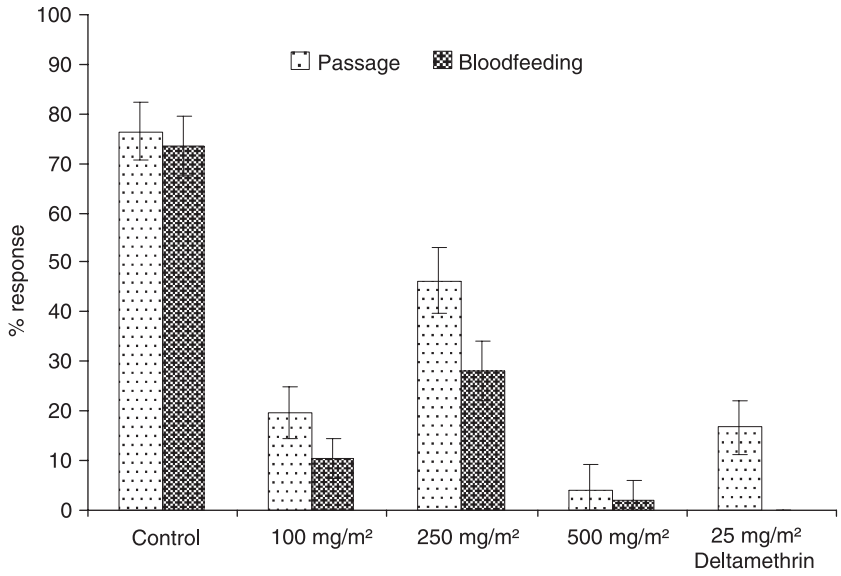

Figure 2 Behavioural responses of *Anopheles arabiensis* (Dondotha) in tunnel tests to chlorfenapyr- or deltamethrin-treated netting.

in Table 1. An average of 41.8 females per hut were collected from the huts and verandahs each morning. Numbers collected were similar in untreated control and insecticide-treated huts. Significantly fewer mosquitoes were found inside the holed chlorfenapyr 100 mg- and 500 mg-treated nets than inside the holed untreated nets. Significantly higher exiting rates of *A. arabiensis* (80.2%) were recorded with the 500 mg/m^2 dosage, while exiting rates with all other dosages were not significantly different from the control. Significant blood-feeding inhibition was not observed for any dosage. High mortality of *A. arabiensis*, ranging between 58.5% and 63.9%, was recorded 72 h after exposure to chlorfenapyr. Most mortality occurred within the first 24 h. Delayed mortality between 24 and 72 h was about 5%.

For the comparison of the efficacy of chlorfenapyr and deltamethrin against *A. arabiensis* and *C. quinquefasciatus*, refer to Tables 2 and 3. An average of 26.0 *A. arabiensis*

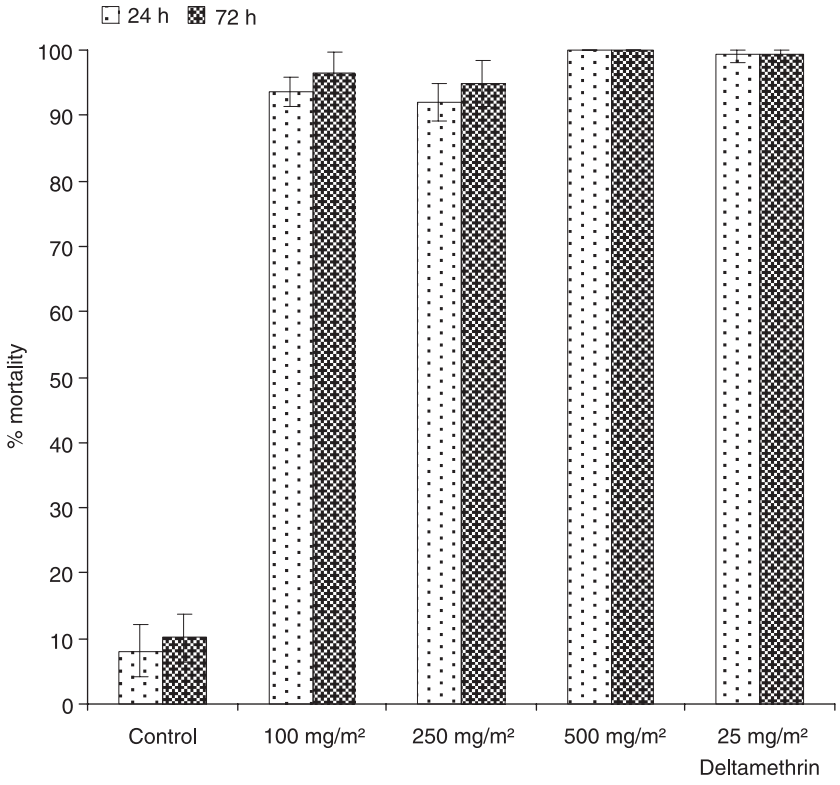

Figure 3 Mortality of *Anopheles arabiensis* (Dondotha) in tunnel tests to chlorfenapyr- or deltamethrin-treated netting.

and 3.5 *C. quinquefasciatus* females were collected from the room and verandahs of each hut per day. Fewer mosquitoes were collected from inside chlorfenapyr 250 mg and deltamethrin-treated nets than inside untreated nets. As in the previous trial, nets treated with 100 or 250 mg/m^2 chlorfenapyr showed no significant difference in exiting rate compared with the untreated control. Exiting rates between deltamethrin and chlorfenapyr did not differ significantly. A similar trend is observed for *C. quinquefasciatus*. There were higher exiting rates with the deltamethrin treatment but, possibly as a result of the low numbers collected, no treatment showed an exiting rate significantly different from the control. In contrast to the previous trial, blood-feeding rates of *A. arabiensis* were significantly lower in the huts with chlorfenapyr-treated nets than in huts with untreated nets. There were no significant differences in feeding rate between the different concentrations of chlorfenapyr. The level of blood-feeding inhibition associated with deltamethrin treatment was no different from that of

Table 1 Summary of results obtained for *Anopheles arabiensis* in experimental huts with three different doses of chlorfenapyr

	Untreated net	Chlorfenapyr 100 mg/m^2	Chlorfenapyr 250 mg/m^2	Chlorfenapyr 500 mg/m^2
Total females caught	511	468	487	540
Females caught/night	42.6	39.0	40.6	45.0
24 h Mortality (%)	5.3^a (3.6–7.6)	58.3^b (53.8–62.7)	56.1^b (51.6–60.4)	54.3^b (50.0–58.4)
Corrected for control	–	56.0	53.6	51.7
72 h Mortality (%)	5.3^a (3.6–7.6)	63.9^b (59.4–68.1)	61.6^{bc} (57.2–65.8)	58.5^c (54.3–62.6)
Corrected for control	–	61.9	59.5	56.2
Blood feeding (%)	26.8^a (23.1–30.8)	26.1^a (22.3–30.2)	26.3^a (22.6–30.4)	26.5^a (22.9–30.4)
Blood-feeding inhibition (%)	–	2.6	1.9	1.1
Exiting rates (%)	73.6^a (69.6–77.2)	75.6^a (71.5–79.3)	72.5^a (68.3–76.3)	80.2^b (76.6–83.3)
% Caught in net	11.2^a (8.7–14.2)	4.5^b (2.9–6.8)	8.4^a (6.3–11.2)	3.1^b (2.0–5.0)

Numbers in the same row sharing a letter superscript do not differ significantly.

Table 2 Summary of results obtained for *Anopheles arabiensis* in experimental huts comparing two doses of chlorfenapyr and deltamethrin

	Untreated net	Chlorfenapyr 100 mg/m^2	Chlorfenapyr 250 mg/m^2	Deltamethrin 25 mg/m^2
Total females caught	321	422	265	238
Females caught/night	26.8	35.2	22.1	19.8
24 h Mortality (%)	3.4^a (1.9–6.1)	51.2^b (46.4–55.9)	42.3^c (36.5–48.3)	45.4^{bc} (39.2–51.7)
Corrected for control	–	49.5	40.3	43.5
72 h Mortality (%)	4.7^a (2.8–7.6)	56.9^b (52.1–61.5)	46.0^c (40.1–52.1)	49.6^{bc} (43.3–55.9)
Corrected for control	–	54.8	43.3	47.1
Blood feeding (%)	39.6^a (34.4–45.0)	25.1^b (21.2–29.5)	21.9^b (17.3–27.3)	22.3^b (17.4–28.0)
Blood-feeding inhibition (%)	–	36.6	44.7	43.7
Exiting rates (%)	81.9^a (77.3–85.8)	81.0^a (77.0–84.5)	85.7^a (80.9–89.4)	88.2^a (83.5–91.8)
% Caught in net	10.9^a (7.9–14.8)	7.8^{ab} (5.6–10.8)	4.5^b (2.6–7.8)	3.8^b (2.0–7.1)
Immediate mortality (% of total mortality)	0.0^a (0.0–0.0)	30.4^b (24.9–36.5)	35.2^b (27.3–44.1)	34.7^b (26.7–43.8)

Numbers in the same row sharing a letter superscript do not differ significantly.

Table 3 Summary of results obtained for *Culex quinquefasciatus* in experimental huts comparing two doses of chlorfenapyr and deltamethrin

	Untreated net	Chlorfenapyr 100 mg/m^2	Chlorfenapyr 250 mg/m^2	Deltamethrin 25 mg/m^2
Total females caught	61	47	28	32
Females caught/night	5.1	3.9	2.3	2.7
24 h Mortality (%)	1.6^a (0.2–10.7)	31.9^b (20.2–46.4)	17.9^{ab} (7.6–36.4)	12.5^a (4.8–28.9)
Corrected for control	–	30.8	16.6	11.1
72 h Mortality (%)	1.6^a (0.2–10.7)	31.9^b (20.2–46.4)	17.9^{ab} (7.6–36.4)	12.5^a (4.8–28.9)
Corrected for control	–	30.8	16.6	11.1
Blood feeding (%)	49.2^a (36.9–61.5)	23.4^b (13.5–37.5)	28.6^{ab} (15.0–47.6)	6.3^c (1.6–21.8)
Blood-feeding inhibition (%)	–	52.4	41.9	87.2
Exiting rates (%)	80.3^a (68.5–88.5)	78.7^a (64.8–88.2)	78.6^a (59.8–90.0)	96.9^a (80.9–99.6)

Numbers in the same row sharing a letter superscript do not differ significantly.

chlorfenapyr. Chlorfenapyr and deltamethrin treatments were associated with lower rates of blood feeding in *C. quinquefasciatus*, with deltamethrin producing significantly lower blood-feeding rates than any chlorfenapyr dosage.

Mortality rates in *A. arabiensis* were high across all dosages of chlorfenapyr relative to the control and there was no clear dosage effect. Mortality rates were similar to the previous trial. Mortality rates with the deltamethrin treatment were similar to the chlorfenapyr treatment and there was no evidence of delayed mortality being any less with deltamethrin. Immediate mortality rates (at the time of the morning collection) also did not differ between chlorfenapyr and deltamethrin. *Culex quinquefasciatus* mortality rates in the chlorfenapyr-treated huts were lower than for *A. arabiensis*, with the highest mortality (31.9%) occurring in the huts with the 100 mg/m^2-treated net. Chlorfenapyr-induced mortality was significantly higher than with the deltamethrin-treated net which killed only 12.5%. All chlorfenapyr-induced mortality in *C. quinquefasciatus* occurred within the first 24 h.

Discussion

The experimental hut trials demonstrate that chlorfenapyr has potential as a residual insecticide against mosquitoes on bed nets. Both hut trials, supported by tunnel tests, indicate that the lower chlorfenapyr dosages (100–250 mg/m^2) are no less effective than higher dosages against *A. arabiensis* and *C. quinquefasciatus*. Against termites, the effectiveness of chlorfenapyr as a barrier treatment is largely attributed to its non-repellent toxic activity and to its long half-life which is about one year in soil (Rust & Saran 2006). Against mosquitoes, N'Guessan *et al.* (2007b) observed that chlorfenapyr is non-irritant at low dosages but stimulates take-offs at higher dosages.

The significantly increased exiting rates from huts containing nets treated with 500 mg/m^2 chlorfenapyr suggests that some excito-repellency may occur with higher dosages under natural conditions. At lower dosages, mosquitoes express little or no irritability and presumably spend more time on the treated surface, thereby picking up a more toxic dose. The reduced passage of *A. arabiensis* through the net in the tunnel test at higher dosages is possibly an expression of irritability to chlorfenapyr. With its low volatility of 1.3×10^{-5} Pa, chlorfenapyr does not have the characteristics of a spatial repellent. We could not detect or test for of spatial repellency expressed as deterred entry into huts owing to fluctuations in mosquito abundance during the course of the trial and of our need to systematically leave out treatments in order to test four treatments in the three available huts.

The mortality of *A. arabiensis* occurring between 24 and 72 h after exposure in all tests (contact, tunnel and hut) can be explained by the slow toxic action of chlorfenapyr, which in turn is attributed to its unique mode of action involving disruption of oxidative phosphorylation in the mitochondria (Lovell *et al.* 1990). Despite this, over 90% of mortality in huts and tunnels occurred within the first 24 h. There was no significant difference between deltamethrin and the chlorfenpyr treatments in terms of immediate mortality in the huts. This is an encouraging result from the perspective of users who might prefer to see an effect of treatment on numbers resting in the huts or lying dead on the nets or floors. High mortality during the first 24 h may be attributed to the more prolonged contact with treated nets in huts as opposed to contact bioassay exposure times.

A combination of low irritancy, low knockdown and the relatively slow-killing effect of chlorfenapyr explains why the rate of blood-feeding inhibition with chlorfenapyr-treated nets is less than what is commonly observed with pyrethroid-treated nets against susceptible populations. N'Guessan *et al.* (2007a), for example, recorded 96% reduction in blood-feeding with lambdacyhalothrin-treated nets against susceptible *A. gambiae* in northern Benin whereas we observed little or only partial reduction with chlorfenapyr. Blood-feeding inhibition with pyrethroids against other susceptible populations, for example in Ivory Coast, is not as pronounced as in N. Benin (Hougard *et al.* 2003). Species specific differences in response to pyrethroid may operate. In our trial, deltamethrin was only equivalent to chlorfenapyr in terms of feeding inhibition in *A. arabiensis*, a species known to differ in behaviour and geographic distribution to *A. gambiae* s.s. Resistance in *A. arabiensis* is not a factor affecting feeding inhibition as this species is fully susceptible to deltamethrin in Lower Moshi (Kulkarni MA, Mosha FW, Temu E, Rowland M, Rau ME & Drakely C, unpublished observation).

The second hut trial indicated that chlorfenapyr produces a killing effect comparable with that of deltamethrin against *A. arabiensis* and superior to that of deltamethrin against *C. quinquefasciatus* (*Culex* is partially resistant to deltamethrin in this population). This is encouraging and warrants further evaluation of the lower dosage (100 mg/m^2) of chlorfenapyr against *A. arabiensis* and *C. quinquefasciatus*. To optimise the personal protective effect of this insecticide it may be beneficial to produce a mixture with an insecticide having high excito-repellent action such as a pyrethroid (Lindsay *et al.* 1991, 1992; Miller *et al.* 1991; Curtis *et al.* 1992). This approach will not only contribute to increased overall efficacy but may also guard against development of chlorfenapyr resistance – as may be developing in some agricultural pests in Australia – by the pyrethroid component killing any chloroquine-resistant individual and *vice versa* (Gunning & Moores 2002; Herron *et al.* 2004). This is classic resistance management strategy through use of mixtures (Denholm & Rowland 1992). It is important to emphasise there is no reported resistance to chlorfenapyr in mosquito populations. Thus, the lower mortality rates observed with chlorfenapyr in *C. quinquefasciatus* compared with *A. arabiensis* may be due to behavioural differences that affect contact time with treated surfaces.

The reported negative cross-resistance action of chlorfenapyr to pyrethroids in some species of insect (Pimprale *et al.* 1997; Sheppard & Joyce 1998) places it as a good candidate for malaria vector control in areas with pyrethroid-resistant *A. gambiae* (Vulule *et al.* 1994; Chandre *et al.* 1999; N'Guessan *et al.* (2007a)) and *A. funestus* (Hargreaves *et al.* 2000). However, it is necessary to extend the residual activity of chlorfenapyr by developing a long-lasting formulation comparable with pyrethroid-based long-lasting insecticidal nets. Being a solid at ambient temperature (melting point of 100–101 °C) with low vapour pressure (5×10^{-3} mPa), and practically insoluble in water (0.12 mg/l), chlorfenapyr would appear to have the characteristics suitable for inclusion in long-lasting formulations (Rand 2004). A bi-treated net would have utility not only in areas of resistance but also in areas which are currently pyrethroid susceptible in order to delay the selection of pyrethroid resistance and to extend the useful life of pyrethroids. The characteristics of low excito-repellency and toxicity may combine to make chlorfenapyr a strong candidate for indoor residual spraying, provided adequate residual activity on interior cement and mud walls could be ensured.

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