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Chemotherapeutic reactions of *Chandlerella hawkingi*, the filarial parasite of the Indian jungle crow, *Corvus macrorhynchos* (Wagler)

R. K. CHATTERJEE AND A. B. SEN

Central Drug Research Institute, Lucknow, U.P., India

1. A high percentage of Indian jungle crows (*Corvus macrorhynchos* Wagler), found in and around Lucknow, harbour a natural filarial infection *Chandlerella hawkingi*. The microfilariae of this species are sheathed and show nocturnal periodicity.

2. Fourteen compounds active against other kinds of filariae, especially against *Litomosoides carinii*, were tested against *Ch. hawkingi* in jungle crows to find whether this infection would be suitable for routine filarial chemotherapy. This is apparently the first report of systematic screening of antifilarial compounds against an avian filariasis.

3. Tartar emetic (10 mg/kg intravenously, daily for 6 days) and arsenamide (5 mg/kg intraperitoneally, daily for 6 days) proved to be effective in killing adult worms. Trivalent tryparsamide, though effective, was toxic in the doses tried. Diethylcarbamazine and other compounds tested were ineffective.

4. The chemotherapeutic susceptibilities of *Ch. hawkingi* differ considerably from those of *L. carinii* and *Wuchereria bancrofti*.

Indian jungle crows (*Corvus macrorhynchos* Wagler), found in and around Lucknow, harbour a natural filarial infection *Chandlerella hawkingi* (Chatterjee, Sen & Bhattacharya, 1965). The percentage of naturally infected birds is high, so it was thought worth while to study whether this infection could be utilized for screening potential anti-filarial compounds. Accordingly this paper reports the chemotherapeutic reaction of *Ch. hawkingi* to some known antifilarial drugs.

Methods

The jungle crows were obtained through a local dealer. The intensity of infection in each bird was assessed by examining 5 mm^3 of peripheral blood drawn from a wing vein at 22.00 hr. Birds showing fifty or more microfilariae (" long form ") per 5 mm^3 of blood were used for screening. Two birds were used for each drug at each dose level and each bird received injections intraperitoneally daily for 6 consecu-

tive days. Blood smears from these birds were taken at 22.00 hr on the seventh day after treatment, and were examined for microfilariae. The birds were then killed to assess the effects of the drugs on the adult worms. For this purpose the worms were removed from the heart (right auricle and right ventricle) and kept in saline at 40° C in an incubator for 15 min ; they were then examined for motility under a dissecting microscope.

The drugs and the maximum dose of each used in these experiments are listed below.

Arsenicals

1. Acetarsone (May & Baker), 10 mg/kg intraperitoneally daily for 6 days.

2. Tryparsamide (B.P. 1968), 500 mg/kg intraperitoneally daily for 6 days.

3. " Trivalent tryparsamide " (disodium N-phenylglycinamide-*p*-arsenodithioglycollate), 50 mg/kg intraperitoneally daily for 6 days.

4. Neoarsphenamine (3:3′-diamino-4:4′-dihydroxyarsenobenzene-N-methylene sulphoxylate), 60 mg/kg intraperitoneally daily for 6 days.

5. Arsenamide [(*p*-carbamylphenylarsylenedithio) diacetic acid], 5 mg/kg intraperitoneally daily for 6 days.

6. Melarsoprol (Mel B) (B.P. 1968), 15 mg/kg intraperitoneally daily for 6 days.

Antimonials

7. " Msb " (sodium *p*-melaminylphenyl stibonate), 100 mg/kg intraperitoneally daily for 6 days.

8. Potassium antimonyl tartrate (tartar emetic) (B.P. 1968), 10 mg/kg intravenously daily for 6 days.

9. Neostibosan (diethylamine-*p*-aminophenyl-stibonate), 100 mg/kg intraperitoneally for 6 days.

Others

10. Diethylcarbamazine (B.P. 1968), 150 mg/kg intraperitoneally daily for 6 days and 50 mg/kg orally daily for 6 days.

11. Suramin (B.P. 1968), 40 mg/kg intraperitoneally daily for 10 days.

12. BAC 20 (eicosane 1:20-*bis*(aminocinnolinium) iodide) (Allen & Hanbury), 2 mg/kg intraperitoneally daily for 6 days.

13. BIQ 20 (eicosane 1:20-*bis*(isoquinolinium) iodide) (Allen & Hanbury), 0.3 mg/kg intraperitoneally daily for 6 days.

14. Cyanine 863 (1′-ethyl-3:6-dimethyl-2-phenyl-4-pyrimido-2′-cyanine), 2 mg/kg intraperitoneally daily for 6 days.

Results

" Trivalent tryparsamide " killed adult worms but had no effect of microfilariae. At the dosage used it was also toxic to the host. Arsenamide (six daily doses of 5 mg/kg) also killed the adult worms but had no appreciable action on the larvae. The other arsenicals tested were inactive.

TABLE 1. *Summary of chemotherapeutic reactions of different filarial parasites to known antifilarials*

Sample	Drugs	*Ch. hawkingi*		*W. bancrofti*		*D. witei*		*O. volvulus*		*Loa loa*		*A. perstans*		*D. immitis*		*L. carinii*	
		Worms	mf.	Worms	mf.	Worms	mf.	Worms	mf.	Worms	mf.	Worms	mf.	Worms	mf.	Worms	mf.
1	Diethylcarbamazine	−	−	?	+	−	−	−	+	+	+	?	−	+	+	−	+
2	Cyanine 863	−	−	−	+*	−	−							−	+	−	+
3	Suramin	−	−	−	−	−	−	+	−	−	−	−	−			−	−
4	BAC 20	−	−			−	−									+	−
5	BIQ 20	−	−													+	−
6	MSb	−	−													+	+†
7	Tartar emetic	+	−	+	−			−	−					−	−	+	−
8	Neostibosan	−	−	+	−			+	−	+	−			−	−	+	−
9	Neoarsphenamine	−	−	+	−											+	−
10	Arsenamide	+	−	+	+			+	−			+	−	+	−	+	−
11	Tryparsamide	−	−											−	−	+	−
12	Trivalent tryparsamide	+	−													+	−
13	Mel B	−	−	?	?—			−	+								

+, Active; −, inactive, * Produces slight diminution in numbers of microfilariae; † Kills infective larvae.

Compiled from this work and from Findlay (1950); Hawking (1950); Hawking, Sewell & Thurston (1950); Hawking & Terry (1959); Kershaw & Williamson (1952); Schitzer & Hawking (1963); Worms, Terry & Terry (1961).

Potassium antimonyl tartrate killed the adult worms when given intravenously at a dose of 10 mg/kg for 6 days and the number of circulating microfilariae decreased slightly. The other antimonial drugs were ineffective.

Diethylcarbamazine at a dose of 150 mg/kg daily for 6 days had no effect on adult worms or microfilariae. A daily intraperitoneal dose of 200 mg/kg was toxic to the crows and none survived the third injection. Suramin, the quaternary ammonium compounds, BAC 20 and BIQ 20, and the cyanine dye, Cyamine 863 were all ineffective in the doses tried.

Discussion

Chandlerella hawkingi is found in many Indian jungle crows and is similar to human filarial infections in having nocturnal periodicity, sheathed microfilariae and in showing the adhesion phenomenon (Sen, Chatterjee & Bhattacharya, 1965). The response of different species of filarial worms to a drug quite often differs and the present investigation was undertaken to study whether the chemotherapeutic response of *Ch. hawkingi* is close enough to that of human infections to be reliable for routine screening of potential antifilarial compounds.

Table 1 summarizes the activity of the antifilarial drugs on *Ch. hawkingi* and on other species of filarial worms. Diethylcarbamazine, the most effective compound available for human filariasis, is inactive against the adult worms of *Ch. hawkingi, Litomosoides carinii, Dipetalonema witei* and *D. perstans* (Hawking, 1950; Schnitzer & Hawking, 1963). No record is available of the effects of this drug on other bird filariae. The mode of action of diethylcarbamazine on mammalian microfilariae is peculiar in that it exerts no direct lethal action on the larvae but sensitizes them so that they become susceptible to phagocytosis by fixed macrophages of the reticuloendothelial system in the liver (Hawking, Sewell & Thurston, 1950). The microfilariae of *Ch. hawkingi* are not affected in this way. Cyanine 863 has a direct filaricidal action against *L. carinii* but, apart from producing a temporary fall in the microfilaria count, has no action against *W. bancrofti*. Suramin is active against the adult worms of *Onochocera volvulus* only. BAC 20 and BIQ 20 are active against adults of *L. carinii* (Hawking & Terry, 1959) but are too irritant for administration to man. MSb is effective as a prophylactic in cotton rats exposed to infective mites (Kershaw & Williamson, 1952), but this type of experiment could not be studied in the jungle crows because the full life cycle was not established in the laboratory. As in the case of *W. bancrofti* and *L. carinii*, potassium antimonyl tartrate killed adult worms of *Ch. hawkingi*, but neostibosan, which is active against the adults of *W. bancrofti, O. volvulus, Loa loa* and *L. carinii*, was ineffective against adults of *Ch. hawkingi*. Of the arsenicals, only arsenamide and trivalent tryparsamide were active against the adults of *Ch. hawkingi*. Thus it can be concluded that, as in the case of *Dipetalonema witei*, the chemotherapeutic reactions of *Ch. hawkingi* do not correspond as closely to those of human *W. bancrofti* as do those of *L. carinii*.

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