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Studies on Chemotherapy of Parasitic Helminths (XI), *In Vitro* Effects of Various Drugs on the Motor Activity of Adult *Schistosoma japonicum*

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It was suggested in a previous paper that detecting and determining the *in vitro* effects of drugs may be useful for the development of anthelminthics against *Schistosoma japonicum* as well as other helminths (Terada *et al.*, 1982a). It was also reported that such effects can be studied by the visual observation method that we recently developed (Sano *et al.*, 1981).

Though niclosamide has been exclusively used as an antitape-worm drug (Rollo, 1975), the drug showed unexpectedly a broad anthelminthic activity against nematodes, trematodes, and cestodes in our *in vitro* experiment (Sano *et al.*, 1982a). Thus, it is one of approaches for the development of anthelminthics for *S. japonicum* to examine an antischistosomal activity of known drugs including insecticides, herbicides, and anthelminthics. Crude extracts from various plants have been used traditionally against the acute and chronic schistosomiasis (Kouso Shin-igakuin ed., 1977), besides chemically synthesized anthelminthics (Rollo, 1975). Therefore, it is an another approach to examine the antischistosomal effects of isolated compounds from plants including those used traditionally.

In the present study, therefore, effects of various compounds including known anthelminthics and plant extracts on the motor activity of adult *S. japonicum* were examined by the visual observation method as one of basic studies for the development of more effective and less toxic anthelminthics against this parasite.

Materials and Methods

Worm collecting and experiments on drug effects on the motor activity of adult *S. japonicum* by the visual observation method were as described in previous papers (Sano *et al.*, 1981; Terada *et al.*, 1982a). The following agents were examined.

1. Known anthelminthics: niclosamide [Bayer], aminosidine [Kyowahakko], 1,4-bis-(trichloromethyl)-benzene (Hetol), phenylene-1,4-diisothiocyanate (Jonit) [Hoechst], hexylresorcinol, piperazine dihydrochloride,

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Table 1 Effects of various known anthelminthics on the motor activity of adult *S. japonicum*

Drug	Concentration (g/ml)	N*	Motility at		
			1 hr	3 hr	24 hr
No drugs		27	4.0±0.0†	4.0±0.0	4.0±0.0
Bithionol	10^{-5}	3	4.0±0.0	4.0±0.0	3.7±0.3
	3×10^{-5}	3	1.7±0.2	1.2±0.2	0.5±0.5
	10^{-4}	3	0.0±0.0	0.0±0.0	0.0±0.0
Niclosamide	10^{-7}	10	3.9±0.1	3.9±0.1	3.8±0.1
	10^{-6}	10	2.5±0.2	1.7±0.3	0.6±0.2
	10^{-5}	3	0.0±0.0	0.0±0.0	0.0±0.0
	10^{-4}	3	0.0±0.0	0.0±0.0	0.0±0.0
Aminosidine	10^{-4}	3	4.0±0.0	3.7±0.3	3.3±0.3
Joint	10^{-4}	3	4.0±0.0	4.0±0.0	2.3±0.9
Hetol	10^{-4}	3	4.0±0.0	3.7±0.3	3.3±0.3
Hexylresorcinol	1.9×10^{-5}	6	3.9±0.4	4.0±0.4	2.9±0.6
	1.9×10^{-4}	6	0.7±0.2	0.0±0.0	0.0±0.0
Dithiazanine	10^{-7}	3	4.0±0.0	4.0±0.0	4.0±0.0
	10^{-6}	3	3.0±0.0	2.5±0.0	3.2±0.4
	10^{-5}	3	1.5±0.0	1.7±0.2	0.0±0.0
	10^{-4}	3	0.0±0.0	1.5±0.0	0.0±0.0
Av-B_{1a}	2.5×10^{-8}	3	4.0±0.0	4.0±0.0	4.0±0.0
	2.5×10^{-6}	6	3.8±0.2	4.0±0.0	4.0±0.0
Ivermectin	5×10^{-7}	3	4.0±0.0	4.0±0.0	4.0±0.0
	10^{-5}	3	4.0±0.0	3.7±0.3	4.0±0.0
Piperazine	1.8×10^{-5}	3	4.0±0.0	4.0±0.0	4.0±0.0
	1.8×10^{-4}	4	4.0±0.0	4.0±0.0	4.0±0.0
Mebendazole	3×10^{-5}	3	4.0±0.0	4.0±0.0	4.0±0.0
	10^{-4}	3	1.8±1.2	0.5±0.5	0.0±0.0
Thiabendazole	10^{-4}	3	4.0±0.0	3.7±0.3	3.7±0.3
Pyrantel	10^{-4}	3	4.0±0.0	4.0±0.0	3.0±0.0
Pyruvinium	10^{-4}	6	3.7±0.2	3.0±0.0	0.7±0.2
Diethylcarbamazine	10^{-5}	3	4.0±0.0	4.0±0.0	4.0±0.0
	10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0

*: Number of experiments, †: All values are shown as mean ± S.E.

thiabendazole [Wako], dithiazanine iodide [Eizai], avermectin Bıa (Av-Bıa), ivermectin [Merck], mebendazole [Janssen Pharmaceutica N.V.], pyrantel tartrate [Pfeizer], pyruvinium pamoate [Sankyo], diethylcarbamazine citrate, bithionol [Tanabe].

2. Known insecticides and herbicides: All drugs including S-benzyldiisopropylphosphorothiolate (IBP), *o-sec*-butylphenylmethylcarbamate (BPMC), *m*-tolyl methylcarbamate (MTMC) were kindly offered from Kumiaikagaku.

3. Compounds isolated from various plants: tuberostemonine [*Stemona tuberosa*], matrine, oxymatrine, N-methylcytisine [*Sophora flavescens*], emodine, physcion, resveratrol, polydatin [*Polygonum cuspidatum*], trans-3-(3,4-dimethoxyphenyl)-4-[(E)-3, 4-dimethoxystyryl] cyclohex-1-one (Comp. A), cis-3-(3,4-dimethoxyphenyl)-4-[(E)-3,4-dimethoxystryl] cyclohex-1-one (Comp. B) [*Zingiber cassumunar*], 3-hydroxy-6, 7-methylenedioxy-5-methoxyflavanone (PN-II), rel-(1R, 6S, 7S, 8S)-5-methoxy-7-phenyl-8-[6,4-methoxy-2-pyronyl]-1-(E)-styryl-2-oxa-bicyclo (4, 2, 0) octa-4-ene-3-one (PN-III), pinosylvin [*Polygonum nodosum*], pinocembrin, cardamonin, 1, 7-

Table 2 Effects of various known insecticides and herbicides on the motor activity of adult *S. japonicum*

Drug	Concentration (g/ml)	N*	Motility at		
			1 hr	3 hr	24 hr
No drugs		14	4.0±0.0†	3.9±0.1	3.9±0.1
Malathion	3.3×10^{-5}	4	3.8±0.3	3.8±0.3	3.9±0.1
	10^{-4}	3	4.0±0.0	4.0±0.0	3.3±0.4
Fenthion	2.8×10^{-5}	4	3.8±0.3	3.8±0.3	3.6±0.6
	10^{-4}	3	6.2±0.2	5.2±1.1	3.5±0.5
Fenitrothion	2.8×10^{-5}	4	4.0±0.4	4.0±0.4	4.0±0.0
	10^{-4}	3	5.0±1.0	4.0±1.0	3.7±0.3
Propaphos	3×10^{-5}	6	3.6±0.3	3.6±0.3	4.2±0.4
	10^{-4}	3	2.2±0.3	1.5±0.0	2.3±1.0
Chlorfenvinphos	3.6×10^{-5}	4	5.0±1.0	4.3±0.3	4.4±0.6
	10^{-4}	3	2.2±0.2	2.0±0.3	2.3±0.7
Tetrachlorvinphos	3.7×10^{-5}	4	4.5±0.3	3.8±0.3	3.8±0.3
	10^{-4}	3	1.7±0.2	1.5±0.0	2.3±0.2
Diazinon	3×10^{-5}	4	5.3±0.9	4.0±0.0	3.9±0.1
	10^{-4}	3	2.5±0.0	1.5±0.0	1.2±0.7
Methidathion	2.7×10^{-5}	4	3.6±0.4	4.0±0.4	3.9±0.1
	10^{-4}	3	5.8±0.3	3.0±0.0	4.0±0.0
Chlorpyriphosmethyl	3.2×10^{-5}	4	4.0±0.0	4.1±0.1	4.0±0.0
	10^{-4}	3	6.0±0.0	3.3±0.3	1.5±0.8
IBP	2.9×10^{-5}	4	3.8±0.3	3.3±0.3	3.9±0.1
	10^{-4}	3	5.3±0.2	3.0±0.0	4.0±0.0
Edifenphos	3.1×10^{-5}	4	4.0±0.0	4.0±0.0	3.9±0.1
	10^{-4}	3	2.7±0.2	2.7±0.2	2.7±0.2
BPMC	2×10^{-5}	4	4.0±0.0	3.3±0.3	3.9±0.1
	10^{-4}	3	1.8±0.3	2.0±0.0	2.8±0.2
MTMC	1.7×10^{-5}	4	3.8±0.3	3.6±0.4	3.8±0.1
	10^{-4}	3	2.2±0.2	2.3±0.2	3.3±0.3
Carbaryl	2×10^{-5}	4	3.4±0.4	3.3±0.3	3.8±0.3
	10^{-4}	3	1.5±0.0	2.3±0.2	3.0±0.0
Benthiocarb	2.6×10^{-5}	3	4.3±0.3	4.3±0.3	4.0±0.0
	10^{-4}	3	3.0±0.0	3.0±0.0	4.0±0.0
Orthobencarb	2.6×10^{-5}	3	4.0±0.6	3.3±0.3	4.0±0.0
	10^{-4}	3	3.0±0.0	3.0±0.0	4.0±0.0

*: Number of experiments, †: All values are shown as mean ± S.E.

diphenyl-1, 3-heptadiene-5-one (AK-5) [*Alpinia katsumadai*], cacalol [*Cacalia adenostyloides*], croomine [*Croomia heterosepala*], poriolide, isoporiolide [*Leucothoe keiskei*].

4. Drugs combined with praziquantel: sodium antimonyl tartrate (Stibnal) [Banyu], niridazole [Ciba], hycanthone methanesulfonate [Sterling-Winthrop], oxamniquine [Pfeizer] and praziquantel [Bayer]. Trans-5-amino-3-[2-(5-nitro-2-furyl)-vinyl]-1,2,4-oxadiazole (SQ-18506) and 4-isothiocyano-4′-nitro-diphenylamine (CGP-4540) were kindly provided by Dr. E. Bueding, School of Medicine, The Johns Hopkins University.

Statistical analysis (Student's *t*-test) was carried out as to the combined effects of drugs with praziquantel in Table 4.

Results

In the text and tables, the concentration of all compounds is shown as g/ml.

Table 3 Effects of compounds isolated from various plants on the motor activity of adult *S. japonicum*

Compound	Concentration (g/ml)	N*	Motility at		
			1 hr	3 hr	24 hr
No drugs		30	4.0±0.0†	4.0±0.0	3.9±0.1
Tuberostemonine	10^{-4}	5	4.2±0.2	4.0±0.3	3.6±0.2
	2×10^{-4}	3	4.0±0.0	4.0±0.0	3.7±0.3
Matrine	10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0
	2×10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0
Oxymatrine	10^{-4}	5	4.4±0.7	3.9±0.2	3.6±0.2
N-Methylcytisine	10^{-4}	6	3.3±0.3	3.8±0.2	3.5±0.2
Poriolide	10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0
Poriolide+Isoporiolide	10^{-4}	3	3.0±0.0	3.0±0.0	3.7±0.3
Croomine	10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0
Resveratrol	10^{-4}	3	3.0±0.0	3.0±0.0	2.7±0.2
Polydatin	10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0
Physcion	10^{-4}	3	4.0±0.0	3.7±0.3	4.0±0.0
Emodine	10^{-5}	3	2.0±0.3	2.0±0.3	3.2±0.4
	10^{-4}	3	0.5±0.0	0.5±0.0	0.2±0.2
Comp. A	10^{-4}	3	4.0±0.0	4.0±0.0	3.3±0.3
Comp. B	10^{-4}	3	4.0±0.0	4.0±0.0	3.0±1.0
PN-II	10^{-4}	3	4.0±0.0	3.7±0.3	3.0±0.0
PN-III	10^{-4}	3	4.0±0.0	4.0±0.0	4.0±0.0
Pinosylvin	10^{-5}	3	4.0±0.0	4.0±0.0	4.0±0.0
	10^{-4}	3	3.0±0.0	2.3±0.3	0.0±0.0
Cacalol	10^{-5}	3	4.0±0.0	4.0±0.0	4.0±0.0
	10^{-4}	3	1.8±0.3	0.5±0.0	1.0±0.0
Pinocembrin	10^{-4}	3	3.7±0.3	3.7±0.3	2.0±0.0
Cardamonin	10^{-5}	3	4.0±0.0	4.0±0.0	4.0±0.0
	3×10^{-5}	3	1.2±0.6	1.0±0.5	0.5±0.0
	10^{-4}	3	1.0±0.5	0.0±0.0	0.0±0.0
AK-5	10^{-4}	3	4.0±0.5	2.5±0.5	1.8±0.4

*: Number of experiments, †: All values are shown as mean ± S.E.

1. Effects of various known anthelminthics on the motor activity of adult *S. japonicum* (Table 1)

Among 15 drugs examined, only niclosamide had an effect comparable to those of known effective antischistosomal drugs. This compound (10^{-6}–10^{-4}) spastically inhibited the motor activity and caused spastic paralysis in the worms.

In higher concentrations, some drugs such as bithionol (3×10^{-5}–10^{-4}), dithiazanine (10^{-5}–10^{-4}), hexylresorcinol (1.9×10^{-4}) and mebendazole (10^{-4}) were rather effective, while the rests had little effect.

2. Effects of various known insecticides and herbicides on the motor activity of adult *S. japonicum* (Table 2)

In general, all of tested insecticides and herbicides showed little or slight effects on the motor activity of the worm even at the concentration of 10^{-4}.

Some compounds including fenthion (10^{-4}), fenitrothion (10^{-4}), chlorfenvinphos (3.6×10^{-5}), diazinon (3×10^{-5}), methidathion (10^{-4}), chlorpyriphosmethyl (10^{-4}) and IBP (10^{-4}) stimulated the motor activity slightly and transiently. On the other hand, some drugs such as propaphos (10^{-4}), chlorfenvinphos (10^{-4}), tetrachlorvinphos (10^{-4}), diazinone (10^{-4}), edifenphos (10^{-4}), BPMC

Table 4 Effects of combination of praziquantel with various compounds on the motor activity of adult *S. japonicum*

Compound	Concentration (g/ml)	N*	Motility at 1 hr	Motility at 3 hr	Motility at 24 hr	N	Motility at 1 hr	Motility at 3 hr	Motility at 24 hr
I. Combination with praziquantel (10^{-7} g/ml)							Without combination		
(Praziquantel)	10^{-7}	16	1.8±0.2†	1.6±0.2	1.8±0.2				
Stibnal	$3\times^{-7}$	4	1.5±0.0	1.3±0.5	1.0±0.0§	6	3.8±0.3	2.3±0.2	2.1±0.2
CGP-4540	2.7×10^{-6}	4	1.8±0.1	1.8±0.1	0.0±0.0§	10	4.0±0.0	3.5±0.3	2.3±0.6
Niridazole	10^{-5}	4	2.0±0.0	2.0±0.0	2.8±0.1‡	3	4.0±0.0	4.0±0.0	1.8±0.2
Hycanthone	4.5×10^{-6}	4	2.0±0.0	2.2±0.3	0.5±0.3§	6	3.8±0.2	2.4±0.4	3.8±0.5
Oxamniquine	10^{-4}	4	1.8±0.1	1.5±0.0	1.3±0.1	3	3.3±0.3	3.0±0.0	1.2±0.2
SQ-18506	10^{-5}	4	2.0±0.0	2.5±0.3‡	2.0±0.0	3	4.0±0.0	4.0±0.0	0.2±0.2
Bithionol	10^{-5}	4	1.5±0.3	1.3±0.7	0.8±0.4‡	3	4.0±0.0	4.0±0.0	3.7±0.3
Niclosamide	10^{-7}	6	1.9±0.2	1.9±0.2	1.8±0.1	10	3.9±0.1	3.9±0.1	3.8±0.1
	10^{-6}	10	1.0±0.2§	0.5±0.1§	0.4±0.1	10	2.5±0.2	1.7±0.3	0.6±0.2
Dithiazanine	10^{-5}	4	1.8±0.1	1.1±0.2	0.0±0.0	3	1.5±0.0	1.7±0.2	0.0±0.0
Pinosylvin	10^{-5}	4	2.8±0.3‡	2.8±0.1§	3.0±0.0§	3	4.0±0.0	4.0±0.0	4.0±0.0
Cacalol	10^{-5}	4	2.3±0.3	2.3±0.3	3.0±0.0§	3	4.0±0.0	4.0±0.0	4.0±0.0
Cardamonin	10^{-5}	4	1.6±0.1	1.0±0.2‡	1.6±0.3	3	4.0±0.0	4.0±0.0	4.0±0.0
Emodine	10^{-5}	4	1.9±0.2	1.6±0.1	1.5±0.3	3	2.0±0.3	2.0±0.0	3.2±0.4
II. Combination with praziquantel (10^{-8} g/ml)									
(Praziquantel)	10^{-8}	8	3.4±0.2	3.9±0.1	3.9±0.1				
Niclosamide	10^{-7}	6	3.8±0.2	3.8±0.2	3.8±0.2	10	3.9±0.1	3.9±0.1	3.8±0.1
	10^{-6}	6	2.0±0.3	1.3±0.2	0.3±0.1	10	2.5±0.2	1.7±0.3	0.6±0.2

*: Number of experiments, †: All values are shown as mean ± S.E.
Significant difference from control (single treatment with praziquantel 10^{-7}): ‡ $P<0.05$, § $P<0.01$.
In the case of inhibition, asterik was put on the figures which were significantly different both from single treatment with praziquantel (10^{-7}) and also from single treatment with a given drug.

(10^{-4}), MTMC (10^{-4}) and carbaryl (10^{-4}) caused a slight inhibition on the motor activity transiently or sustainedly.

3. Effects of compounds isolated from various plants on the motor activity of adult *S. japonicum* (Table 3)

Among 20 compounds examined, five showed some inhibitory effects on the motor activity of the worms; emodine (10^{-5}–10^{-4}) and cardamonin (3×10^{-5}–10^{-4}) were rather effective and pinosylvin (10^{-4}), cacalol (10^{-4}), and AK-5 (10^{-4}) were very slightly effective.

4. Effects of combination of praziquantel with various compounds on the motor activity of adult *S. japonicum* (Table 4)

By the combination of various drugs with praziquantel, the contractive effects of praziquantel (10^{-7}) were stimulated significantly by some drugs such as Stibnal (3×10^{-7}, at 24 hr), CGP-4540 (2.7×10^{-6}, at 24 hr), hycanthone (4.5×10^{-6}, at 24 hr), bithionol (10^{-5}, at 24 hr), niclosamide (10^{-6}, at 1 and 3 hr), and cardamonin (10^{-5}, at 3 hr). On the other hand, the effects of praziquantel (10^{-7}) were inhibited significantly by some other drugs including niridazole (10^{-5}, at 24 hr), SQ-18506 (10^{-5}, at 3 hr), pinosylvin (10^{-5}, at 1, 3, and 24 hr), and cacalol (10^{-5}, at 24 hr).

Discussion

In vitro effects of various known compounds such as insecticides, herbicides, and anthelminthics excluding antischistosomal drugs on adult *S. japonicum* were examined.

In the previous paper (Terada *et al.*,

1982a), we reported that cholinesterase inhibitors such as eserine, metrifonate, and dichlorvos remarkably inhibited the motor activity of adult *S. japonicum*, and also stated that the cholinergic mechanism may function as an inhibitory one in *S. japonicum* as well as *S. mansoni*. However, all of 14 insecticides and 2 herbicides tested showed only slight effects even at the concentration of 10^{-4}, though most of these compounds are known as cholinesterase inhibitors.

Among 15 anthelminthics tested, niclosamide was the only compound which showed comparable effects to those of known effective antischistosomal drugs (Terada *et al.*, 1982a). This compound caused spastic paralysis in adult *S. japonicum* at concentrations of 10^{-6} or more. The mode of action of niclosamide against *S. japonicum* as well as other worms such as *Dipylidium caninum* and *Diplogonoporus grandis* was similar to that of praziquantel (Sano *et al.*, 1982a, 1982b). On the other hand, these two drugs differed each other in that the effect of praziquantel after the short exposure such as 30 to 60 min was rapidly reversed by washing with Tyrode's solution, while that of niclosamide was not reversed by washing (Thomas and Andrews, 1977; Sano *et al.*, 1982a, 1982b; Terada *et al.*, 1982b). Thus, it is possible that niclosamide has *in vivo* effects against tissue parasites. However, niclosamide was reported to be singularly less toxic when administered orally (Gönnert and Schraufstätter, 1960; Abdallah and Saif, 1961), and has been exclusively used as an anthelminthic for intestinal cestodes (Rollo, 1975). Therefore, it is necessary to study the *in vivo* effects including the efficacy and toxicity of this drug after parenteral administration.

Additionally, effects of isolated compounds from various plants were examined. It was reported that crude extracts of some plants, such as *Stemona tuberosa, Sophora flavescens, Polygonum cuspidatum,* and *Cacalia adenostyloides* have been used traditionally as bactericides, insecticides or wormicides (Kouso Shin-igakuin ed., 1977). Especially, it was reported that crude extracts of *S. flavescens* could relive ascites in schistosomiasis japonica and had wormicidal effects against the worm (Kouso Shin-igakuin ed., 1977). Although emodine from *P. cuspidatum* and cacalol from *C. adenostyloides* showed slight effects in this experiment, matrine, oxymatrine, and N-methylcytisine, some of many components from *S. flavescens* had little effect on the motor activity of adult *S. japonicum*. On the other hand, cardamonin from *Alpina katsumadai* which has not been used traditionally as an anthelminthic was rather effective at the concentration of 3×10^{-5}. Thus, though promising compounds were not detected in the present study, further examinations should be carried out on compounds isolated from plants including those not used traditionally.

Praziquantel was reported to have a broad spectrum against plathelminths including *S. japonicum* in animal and clinical experiments (Gönnert and Andrews, 1977; Thomas and Andrews, 1977; Thomas and Gönnert, 1977; Webbe and James, 1977; Katz *et al.*, 1979; Santos *et al.*, 1979; Davis *et al.*, 1979; Rim and Yoo, 1979; Rim and Chang, 1980; Yokogawa *et al.*, 1980), and was the most effective in our *in vitro* experiments against adult *S. japonicum* (Terada *et al.*, 1982a). Since this drug seems to be the most promising one at present, we examined the combined effects of praziquantel with other drugs to make praziquantel more effective and less toxic. Among 13 compounds tested, some stimulated the contractive effects of praziquantel, though some others inhibited the effects of praziquantel. Though Stibnal, CGP-4540, hycanthone, and bithionol showed stimulatory effects only at 24 hr, niclosamide (10^{-6}) and cardamonin showed the effects at 1 and/or 3 hr. The combination with niclos-

amide may be most interesting from aspects such as *in vitro* efficacy and the irreversibility of the action, as mentioned above, and the blood concentration. Since niclosamide and praziquantel showed to have broad spectra against cestodes and trematodes (Sano *et al.*, 1982a; Terada *et al.*, 1982b), the combination of these two drugs probably increase the efficacy of these drugs against intestinal cestodes and trematodes. This combination may be also useful for the clinical therapy of tissue parasites including *S. japonicum* when the *in vivo* effects of niclosamide against these parasites are established.

Summary

As one of basic studies for the development of more effective and less toxic anthelminthics against *Schistosoma japonicum,* effects of various compounds including known anthelminthics and plant extracts on the motor activity of adult *S. japonicum* were examined. Among 31 known compounds such as insecticides, herbicides, and anthelminthics, only niclosamide had an effect comparable to those of known effective antischistosomal drugs. Among 20 compounds isolated from various plants, only two, emodine from *Polygonum cuspidatum* and cardamonin from *Alpina katsumadai*, showed inhibitory effects on the motor activity of the worms. Effects of combination of praziquantel, the most promising compound at present, with other drugs were examined. Among 13 tested compounds, niclosamide was the most interesting one with respect to the combination with praziquantel.

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寄生虫症の化学療法に関する研究（XI）
日本住血吸虫の自動運動に及ぼす各種薬物の影響

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より有効で，より安全性の高い抗日本住血吸虫薬の開発研究の一端として，日本住血吸虫の自動運動に及ぼす各種薬物の作用を肉眼的観察法により検討した．

1)　既知薬物の抗日本住血虫作用を検討した．抗住血吸虫薬以外の駆虫薬（15種），殺虫剤ないし殺菌剤(14種）および除草剤（2種）のうち既知抗日本住血吸虫薬に匹敵する作用を示したのは，niclosamide のみであった．

2)　経験的に生薬煎汁とし殺虫剤，駆虫薬として従来用いられてきた生薬などの成分20種のうち，イタドリ成分 emodine およびソウズク成分 cardamonin に日本住血吸虫の自動運動抑制作用が認められた．

3)　つぎに，現状で最も将来性ある抗日本住血吸虫薬と考えられる praziquantel と各種薬物との併用効果について検討したが，praziquantel との併用に関しても niclosamide が最も興味ある結果を与えた．