# Oral pharmacological treatments for parasitic diseases of rainbow trout Oncorhynchus mykiss. II: Gyrodactylus sp.

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ABSTRACT: A total of 24 drugs were evaluated as regards their efficacy for oral treatment of gyrodactylosis in rainbow trout Oncorhynchus mykiss. In preliminary trials, all drugs were supplied to infected fish at 40 g per kg of feed for 10 d. Twenty-two of the drugs tested (aminosidine, amprolium, benznidazole, bithionol, chloroquine, diethylcarbamazine, flubendazole, levamisole, mebendazole, metronidazole, niclosamide, nitroxynil, oxibendazole, parbendazole, piperazine, praziquantel, ronidazole, secnidazole, tetramisole, thiophanate, toltrazuril and trichlorfon) were ineffective. Triclabendazole and nitroscanate completely eliminated the infection. Triclabendazole was effective only at the screening dosage (40 g per kg of feed for 10 d), while nitroscanate was effective at dosages as low as 0.6 g per kg of feed for 1 d.

KEY WORDS: Gyrodactylosis · Rainbow trout Treatment · Drugs

#### INTRODUCTION

The monogenean genus Gyrodactylus is widespread, though some individual species have a restricted distribution. Gyrodactyloses affect numerous freshwater species including salmonids, cyprinids and ornamental fishes, as well as marine fishes including gadids, pleuronectids and gobiids. Outbreaks of gyrodactylosis have been reported from farmed Pleuronectes platessa (McKenzie 1970).

In natural environments, massive infections by Gyrodactylus species are rare. A notable exception is G. salaris, which causes high mortality among salmon in Norwegian rivers (Heggberget & Johnsen 1982, Johnsen & Jensen 1992, Mo 1994). Among farmed fishes, gyrodactyloses are more common, and initially minor outbreaks can become a serious problem in a short time.

Gyrodactylus species are parasites of the fins, gills, eyes and body. Mo (1994) states that the epidermal lesions arising in gyrodactyloses are chiefly due either

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to the hooks of the opisthohaptor or to ulceration as a result of feeding by the parasite. The latter is the most serious.

Transmission takes place largely as a result of direct contact between live fishes, though other pathways (contact between a live fish and a dead fish, or with free-living parasites present in the substrate, or with drifting parasites in the water) may also be important (Bakke et al. 1992).

Various methods have been described for the control of gyrodactylosis, all based on pharmacological bath treatments (Mehlhorn et al. 1988, Schmahl et al. 1989, Santamarina et al. 1991, Tojo et al. 1992, 1993a, b, Tojo 1993). The aim of the present study was to investigate possible oral pharmacological treatments of gyrodactylosis in rainbow trout. A total of 24 drugs were tested at high dosages (40 g per kg of feed, for 10 d). Oral treatments have a number of advantages, including ease of administration and the fact that there is no need to handle the fish. Here we continue the screening study of possible oral pharmacological treatments of parasitoses in rainbow trout initiated with hexamitosis (Tojo & Santamarina 1998).

Drug	Brand name	Form	Manufacture
Aminosidine	Gabbrocol	Sol. inject.	Vetern S.P.A.
Amprolium	Prolsal	Powder	Iteve
Benznidazole	p.p.	Powder	Roche
Bithionol	p.p.	Powder	Syva
Chloroquine	p.p.	Powder	Cidan
Diethylcarbamazine	p.p.	Powder	Cidan
Flubendazole	p.p.	Powder	Esteve
Levamisole	p.p.	Powder	Ovejero
Mebendazole	p.p.	Powder	Esteve
Metronidazole	Flagyl	Powder	Rhone Mérieu
Niclosamide	Fugotenil	Pills	Uriach
Nitroxynil	p.p	Powder	Ovejero
Nitroscanate	Lopatol 500	Pills	Ciba-Geigy
Oxibendazole	p.p.	Powder	Syva
Parbendazole	p.p.	Powder	Smith Kline
Piperazine	p.p.	Granulate	Sobrino
Praziquantel	Droncit	Pills	Bayer
Ronidazole	p.p.	Powder	Sobrino
Secnidazole	p.p.	Powder	Rhone Merieu
Tetramisole	p.p.	Powder	Ovejero
Thiophanate	p.p.	Powder	Uriach
Toltrazuril	p.p.	Powder	Bayer
Trichlorfon	Neguvon	Powder	Bayer
Triclabendazole	p.p.	Powder	Ciba-Geigy

Table 1. Drugs used in the study, showing manufacturer, brand name and form of presentation. p.p.: pure product

## MATERIALS AND METHODS

**Fish.** Rainbow trout *Oncorhynchus mykiss* Walbaum (weighing 16 g at the start of the experiments) were obtained from a local fish farm (Piscifactorías Coruñesas S.A., Carballo, A Coruña, Spain) and acclimatized for at least 36 h before assay in a 350 l tank with aeration and continuous flow of water (15  $\pm$  1°C, pH 6.5  $\pm$  0.5) from a nearby spring. Fish were fed daily with a commercial feed.

Infestation. All fish used in the trials showed highintensity infestation by Gyrodactylus sp., in some cases as a result of natural infections, and in other cases following experimental infestation in the laboratory. Parasite-free fish were experimentally infected by holding them for 15 to 20 d in a 350 l tank that also contained fish showing high-intensity infestation (400 uninfected fish to 100 infected fish). Twenty fish were then sampled at random for determination of infestation intensity (see below). Since infestation intensity was high in only 10 of the 20 fish, the experimental infestation period was extended by 7 d, after which time infestation intensity was again determined in 10 randomly sampled fish. At this time all 10 fish showed high-intensity infestation, and the assays were thus commenced.

Determination of infestation intensity. Fish were anaesthetized by bathing in MS-222 (Sandoz,  $0.05 \ g \ l^{-1}$ )

until respiration became weak. A mucus sample was then taken by gently scraping fins and body surface. The sample was mixed with 3 drops of water on a slide, coverslipped and examined with a light microscope (40×). Infestation intensity was recorded on a 5-point scale, after examination of a sample area of 24  $\times$ 32 mm, as follows: 'minimal' (+/-), only 1 individual of *Gyrodactylus* sp. detected in the sample; 'low' (+), more than 1 individual of Gyrodactylus sp. detected in the sample, the average number per microscope field being less than 10; 'moderate' (++), average number of individuals per microscope field 10 to 50; 'high' (+++), average number of individuals per microscope field >50; 'zero' (-), Gyrodactylus sp. not detected in the sample.

**Drugs and assay design.** The drugs tested in the study are listed in Table 1. Each drug was assayed in 20 infested fish maintained in an 80 l tank with a continous flow (5 l min<sup>-1</sup>). A simultaneous control assay (also of 20 fish; identical treatment, but without drugs) was performed for each drug. Tank conditions

(water source, flow, aeration, pH, temperature, light/dark cycle) were identical to those during the acclimatization period, except that water temperature dropped to as low as 12°C on a few occasions in the secnidazole assay, and rose to as high as 18°C on a few occasions in the bithionol assay. The treated fish received feed containing 40 g of drug per kg of feed for 10 d. The weight of food supplied to each tank on each day was equivalent to 2% of the total body weight of the fish in that tank. Note that this procedure does not guarantee that all fish received the same dose of drug. Throughout the assay period the fish were monitored regularly to ensure that they were eating the food, and to check for signs of toxicity. Twenty-four hours after the end of the assay, fish were anaesthetized for determination of infestation intensity as above. Drug found to be effective at the screening dosage were subsequently tested at lower dosages (see 'Results').

### RESULTS

Of the 24 drugs tested, 22 were not effective (i.e. did not completely eliminate infestation); the results for these drugs are listed in Table 2. The results for the 2 effective drugs (nitroscanate and triclabendazole) are listed in Table 3; both eliminated infestation in all 20

Table 2. Results of the assays that proved ineffective. For each drug (in all cases administered at 40 g per kg of feed for 10 d), infestation intensity 24 h post-treatment infection intensity (as evaluated by examination of body scrapings; see text) is shown for each of the 20 fish included in the assay for that drug. Infestation intensity: +++, high; ++, moderate; +, low; +/-, minimal; -, zero (i.e. no *Gyrodactilus* sp. detected in body scrapings); nd: not determined; D: fish died during experiment

Drug	Trout number																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Aminosidine	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	n
Amprolium	++	+	+	+	+	+	+	+	+	+	+	+	+	+	_	_	-	-	-	-
Benznidazole	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	++	++	+-
Bithionol	++	++	++	++	++	++	++	++	+	+	+	+	+	+/-	+/-	+/-	+/-	+/-	_	-
Chloroquine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Diethylcarbamazine	++	++	++	+	+	+	+	+	+	+/-	+/-		-	_	-	-	-	nd	nd	n
Flubendazole	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	+
Levamisole	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	-	-
Mebendazole	+	+	+	+		_	_	_	_	_	-	_	-	_	_	_	-	-	-	-
Metronidazole	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	+
Niclosamide <sup>a,b</sup>	+	+	+	+	+	+	+	+	+	+	+	+	+	_	-	_	D	D	nd	n
Nitroxynil	+	+	+	+	+	+	+	+	+	+	+	+	+	_	-	_	-	_	D	n
Oxibendazole	++	++	+	+	+	+	+	+	+	+	+/-	+/-	+/-	+/-	+/-	_	_	-	_	-
Parbendazole	+	+	+	+	+	+	_	-	_	-	_	_	-	_	-	_	_	nd	nd	n
Piperazine <sup>b</sup>	+++	+++	+++	+++	++	++	++	++	++	++	++	++	++	+	+	+	+	_	_	_
Praziquantel	++	++	++	+	+	+	+	+	+	+/-	+/-	_	-	-	_	-	-	-	nd	n
Ronidazole	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	++	++	n
Secnidazole	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	++	++	++	++	++	+
Tetramisole	++	+	+	+	+	+	+	+	+	+	+	+	+	+	_	_	-	-	-	-
Thiophanate	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	Γ
Toltrazuril	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+
Trichlorfon b	+++	++	++	+	+/-	+/-	_	_	_	-	_	_	_	_		_	_	_	_	_

fish included in each assay. Triclabendazole was effective at doses as low as 40 g per kg feed for 10 d, and nitroscanate at doses as low as 0.6 per kg feed for 1 d. Neither of the 2 effective drugs had evident toxic effects.

#### DISCUSSION

The benzimidazole group is that group which has been most extensively investigated for the treatment of fish helminthioses. We tested 5 drugs from this

Table 3. Results of the assays that proved effective. For each drug, infestation intensity 24 h post-treatment infection intensity (as evaluated by examination of body scrapings and of trout; see text) is shown for each of the 20 fish included in the assay for that drug. Results of control assays are also shown. Infection intensity: +++, high; ++, moderate; +, low; +/-, minimal; -, zero (i.e. no Gyrodactylus spp. detected in body scrapings); nd: not determined; D: fish died during experiment

9	Dose	Days								Trout number												
	(g kg- <sup>1</sup>	)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Nitroscanate	40	10	_	-	_	-	-	-	_	-	-	-	-	-	-	-	_	_	_	_	_	_
	-	-	+++	+++	+++	+++	++	++	++	++	++	++	++	++	++	++	+	+	+	+/	+/-	+/-
	6.25	2	_	_	-	_	-	_	_	-	-	_		-	_	-	-	_	-	-	_	-
	-	-	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	+
	6.25	1	-	_	_	_	_	_	_	-	_	_	_	_	_	_	_	_	_	_		-
	_	_	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	+	+	+
	0.63	1	_	_	-	_	-	_	_	-	_	_	-	_	_	_	_	-	_	_	_	_
	-	-	+++	++	++	++	++	++	++	++	++	++	++	++	++	++	++	+	+	+	-	-
Triclabendazole	40	10	_	_	_	_	_	_	_	_	_	_	_	_	-	_	_	-	_	_	_	_
		_	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	++	++	+
	40 ª	5	+++	+++	+++	+++	++	+	+	+	+	+	+	+	+	+/-	+/-	+/-	+/-		-	_

group (flubendazole, mebendazole, oxibendazole, parbendazole and triclabendazole). The benzimidazole most widely used against monogeneans is mebendazole, generally administered by immersion (Székely & Molnár 1987, Buchmann & Bjerregaard 1990, Székely & Molnár 1990, Mellergaard 1991, Tojo 1993). Immersion treatment with mebendazole is also widely used against cestodes (Boonyaratpalin & Rogers 1984, Alarcón & Castro 1988, Sanmartín et al. 1989) and nematodes (Taraschewski et al. 1988). Despite their widespread use, however, mebendazole treatments are often less than 100% effective. Toxicity is rarely observed: in bath treatment, low concentrations and/or brief exposures are well tolerated, while oral treatment with doses of 150 mg kg-1 have effects of varying severity, depending on species (Taraschewski et al. 1988, Sanmartín et al. 1989). Other drugs from this group, such as albendazole, fenbendazole, flubendazole, oxfendazole, oxibendazole, parbendazole and thiabendazole, have been tested for bath treatment against Gyrodactylus sp. infections of Oncorhynchus mykiss; of these drugs, only fenbendazole was 100% effective, while the others were ineffective or only partially effective; toxic effects varied between the different drugs (Tojo et al. 1992, Tojo 1993). In the present study, neither flubendazole, mebendazole, oxibendazole nor parbendazole, administered orally at 40 g per kg of feed for 10 d, were 100% effective against the Gyrodactylus sp. infection. None of these drugs showed signs of being toxic to the fish. However, triclabendazole was 100% effective. Previous studies have found that immersion exposure to triclabendazole at 25 mg l<sup>-1</sup> for 12 h is 100% effective and does not have evident toxic effects (Tojo et al. 1992, Tojo 1993). In the present study, triclabendazole was 100% effective, and likewise lacked side-effects, when administered orally at 40 g per kg of feed for 10 d. Treatment at the same dosage for 5 d was not sufficient to eliminate infection, though most of the parasites showed reduced mobility. This result highlights the importance of a sufficient treatment period when using benzimidazoles.

A possible explanation for our findings with triclabendazole is that the drug in fact acts externally, having passed into the water through the faeces of the treated fish. However, this possibility can almost certainly be ruled out, since the concentration of the drug in the tank would have been at most 0.16 mg l<sup>-1</sup> (even without considering replacement of the water); a previous study has indicated that exposure to at least 25 mg l<sup>-1</sup> for at least 12 h is necessary for elimination of parasites (Tojo et al. 1992).

Despite the above results, oral treatment with triclabendazole is unlikely to be an economically viable option, since the required dosage (40 g per kg of feed for 10 d) implies use of large amounts of the drug. We tested one probenzimidazole, thiophanate. Drugs of this group have been little studied as regards effectiveness against fish helminthioses. The 3 drugs from this group which have been studied to date (netobimin, febantel and thiophanate) have all proved ineffective, regardless of mode of administration (Sanmartín et al. 1989, Santamarina et al. 1991, Tojo 1993). Thiophanate is ineffective against gyrodactylosis both in bath treatment (Santamarina et al. 1991, Tojo 1993) and when administered orally at 40 g per kg of feed for 10 d (present results).

We tested 2 phenol derivatives, bithionol and nitroxynil. The phenol derivatives niclofolan and nitroxynil have previously been shown to be effective for bath treatment of gyrodactylosis in rainbow trout at 0.2 mg  $1^{-1}$  for 3 h and at 50 mg  $1^{-1}$  for 3 h respectively; however, both drugs also had severe toxic effects (Santamarina et al. 1991, Tojo et al. 1993a). Bithionol was tested by Buchmann et al. (1992) against Pseudodactylogyrus spp. and has been recommended by Herwig et al. (1979) against Bothriocephalus spp. and Echinorhynchus spp. We have previously tested bithionol for bath treatment of gyrodactylosis in rainbow trout, finding it effective and without evident toxic effects when exposure was to 20 mg l<sup>-1</sup> for 3 h; however, higher concentrations had clear toxic effects (Santamarina et al. 1991). In the present study, neither bithionol nor nitroxynil were effective when administered orally at 40 g per kg of feed for 10 d. In neither case did we observe signs of toxicity; this is in accordance with a previous study in which bithionol was administered at the same dose to rainbow trout infected with Ichthyophthirius multifiliis (Tojo 1993)

Two imidathiazoles were tested in the present study, levamisole and tetramisole. As with the phenol derivatives, the effectiveness of these drugs is often conditioned by toxicity. Levamisole has been used successfully, without evident toxicity, against nematodes, such as Anguillicola crassus in the eel  $(1 \text{ mg l}^{-1} \text{ for } 24 \text{ h})$ (Taraschewski et al. 1988). This drug has also been reported to be effective against monogeneans, including Diplozoon paradoxum and Gyrodactylus aculeati (Schmahl & Taraschewski 1987, Schmahl et al. 1989), and several species of the genus Pseudodactylogyrus (Buchmann et al. 1990b). However, we have previously found that levamisole concentrations effective against Gyrodactylus species (37 mg l<sup>-1</sup> for 3 h) are toxic to rainbow trout (Santamarina et al. 1991, Tojo 1993). We also found that tetramisole at 100 mg l<sup>-1</sup> for 3 h was less effective than levamisole, and likewise had toxic effects. In the present study, oral administration of these drugs at 40 g per kg of feed for 10 d had no evident toxic effects, but was not effective.

Piperazine and its derivatives are widely used for the treatment of helminthioses in livestock, and to date

have not been found to be effective against monogenean infections of fishes. In previous studies, ketoconazole, diethylcarbamazine, piperazine citrate and piperazine dihydrochloride all proved ineffective in bath treatment at 200 mg l<sup>-1</sup> for 3 h (Santamarina et al. 1991, Tojo et al. 1993a, b). In the present study, both diethylcarbamazine and piperazine dihydrochloride were ineffective. These results thus confirm that piperazine and its derivatives are not of value for treatment of gyrodactylosis. Furthermore, piperazine dihydrochloride appears to have reduced food consumption.

One salicylanilide was tested in the present study, niclosamide. The drugs in this group vary in their effectiveness against fish helminthioses, but are invariably toxic to fish. Rafoxanide is not active against Pseudodactylogyrus or Gyrodactylus species (Buchmann et al. 1990a, Tojo et al. 1993a), while toxicity varies depending on the fish species. Bath treatment with closantel at 0.25 mg l<sup>-1</sup> for 3 h is effective against Gyrodactylus species, but toxic for rainbow trout (Santamarina et al. 1991). Orally administered niclosamide has been recommended against various cestodes, namely Bothriocephalus, Proteocephalus, Corallobothrium and Khawia sinensis (Herwig et al. 1979, Moore et al. 1984, Sanmartín et al. 1989, Schmahl et al. 1989); in none of these studies was toxicity observed. This drug is also effective in immersion treatments for combating monogeneans, including various species of Gyrodactylus (Schmahl & Taraschewski 1987, Schmahl et al. 1989) and Pseudodactylogyrus (Buchmann et al. 1990a), although in the latter case lethal toxicity was observed. We have previously found that bath treatment with niclosamide at 1.5 mg l<sup>-1</sup> for 3 h is 100% effective against gyrodactylosis in rainbow trout, and has no evident toxic effects, whereas higher concentrations are toxic (Tojo et al. 1993a). In the present study, oral administration of niclosamide at 40 g per kg of feed for 10 d showed sings of toxicity and was not 100% effective, although a large proportion of parasites were killed. Furthermore, niclosamide appears to have reduced food consumption, leading to accumulation of large amounts of feed at the bottom of the tank.

Four nitroimidazoles (benznidazole, metronidazole, ronidazole and secnidazole) were tested in the present study. The drugs of this group are typically more effective against protozoa than helminths. The only previous study of effectiveness against monogeneans in fish is that of Tojo et al. (1993b), in which we tested dimetridazole, carnidazole, metronidazole, ronidazole and benznidazole in bath treatment against gyrodactylosis in rainbow trout. None of these drugs proved effective. In the present study, benznidazole, metronidazole, ronidazole and secnidazole (not tested previously against *Gyrodactylus* sp.) were ineffective when ad-

ministered orally at 40 g per kg of feed for 10 d. None of the 4 drugs showed evident toxicity.

Aminosidine and chloroquine are antiprotozoals that have been tested previously for bath treatment of gyrodactylosis at 200 mg  $l^{-1}$  for 3 h. In no case was activity detected (Tojo et al. 1993b). Similarly, in the present study neither of these drugs was effective.

Amprolium is a thiamine with antiprotozoal activity, though in a previous study no anti-monogenean activity was detected (Tojo et al. 1993b). In the present study, amprolium was ineffective.

Nitroscanate has previously been reported to be effective in immersion treatment against *Gyrodactylus* sp. in trout (Santamarina et al. 1991). In the present study, oral administration of this drug at 40 mg per kg of feed for 10 d was likewise 100% effective. Subsequent trials revealed that 100% effectiveness was maintained with only 0.63 g per kg of feed for 1 d only. Furthermore, no signs of toxicity were observed. This drug would therefore seem to be highly effective for the treatment of gyrodactylosis.

Praziquantel has been extensively tested against fish helminthioses, and in many cases has proved effective. It has been tested against monogeneans (Schmahl & Mehlhorn 1985, Moser et al. 1986, Buchmann 1987, Schmahl & Taraschewski 1987, Schmahl et al. 1989, Buchmann et al. 1990b, Székely & Molnár 1990, Santamarina et al. 1991), trematodes (Bylund & Sumari 1981, Moser et al. 1986, Schmahl et al. 1989, Lorio et al. 1990), cestodes (Moser et al. 1986, Sanmartín et al. 1989, Schmahl et al. 1989, Flores-Crespo et al. 1994) and nematodes (Moser et al. 1986). We have previously tested praziquantel for bath treatment of gyrodactylosis in rainbow trout, and were unable to eliminate the infection at concentrations of 10 mg l<sup>-1</sup> for 3 h, with higher concentrations proving lethally toxic (Santamarina et al. 1991). This drug was likewise ineffective in the present study.

Toltrazuril has been tested previously against monogenean infections of fishes (Schmahl & Melhorn 1988, Schmahl et al. 1989). In bath treatment of gyrodactylosis in rainbow trout, exposure to 200 mg  $\rm l^{-1}$  for 3 h was not effective (Tojo et al. 1993b). Likewise, in the present study oral treatment was ineffective; indeed, infection intensities remained very high at the end of the assay.

Trichlorfon (Neguvón) has been extensively studied as regards the treatment of fish helminthioses, including infections by *Pseudodactylogyrus* spp. (Imada & Muroga 1979, Buchmann et al. 1992) and *Anguillicola crassus* (Taraschewski et al. 1988). Its effectiveness varies widely. Goven et al. (1980) found that bath treatment at 25 mg l<sup>-1</sup> for 72 h was necessary to eradicate gyrodactylosis, and treatments for shorter periods were ineffective even when higher doses were used

(Goven & Armend 1982, Santamarina et al. 1991). Trichlorfon was not effective in the present study.

In conclusion, the results of the present study indicate that both triclabendazole and nitroscanate are effective as oral treatments for gyrodactylosis in farmed rainbow trout. Nitroscanate is effective at a relatively low dosage (0.6 g per kg of feed for 1 d). However, this dosage is likely to be prohibitively expensive. Gyrodactylosis can be effectively treated by bath treatment with nitroscanate at only 0.7 mg l<sup>-1</sup>. Oral treatment with nitroscanate may be administered in situations in which bath treatment is not possible (floating tanks, natural ponds, etc.).

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