

Evaluation of florfenicol in Atlantic salmon, *Salmo salar* L.: efficacy against furunculosis due to *Aeromonas salmonicida* and cold water vibriosis due to *Vibrio salmonicida*

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Abstract

Two replicated controlled trials were conducted to determine the efficacy of florfenicol against *Aeromonas salmonicida* and *Vibrio salmonicida* infections in Atlantic salmon, *Salmo salar* L., smolts kept in 25‰ salt water. Infection with *A. salmonicida* was treated with florfenicol, oxolinic acid, oxytetracycline, trimethoprim/sulphadiazine or flumequine, whereas the *V. salmonicida* infection was treated with florfenicol or oxolinic acid only. *A. salmonicida* infection was induced by the introduction of cohabitant fish previously inoculated intraperitoneally. Medication started simultaneously in all test tanks on the first day of specific mortality among test fish. *V. salmonicida* infection was induced by intraperitoneal inoculation of all test fish. Medication started 1 day after infection. Medicated feeds were produced by coating the antibacterials on standard feed pellets, and administered twice daily for 10 consecutive days. With the dose used in the present trials, florfenicol was highly effective in reducing specific mortalities due to both infections. It was slightly more effective than oxolinic acid and trimethoprim/sulphadiazine against *A. salmonicida* infection. There was no significant difference between florfenicol and oxolinic acid in reducing specific mortalities due to *V. salmonicida*.

Introduction

Furunculosis caused by *Aeromonas salmonicida* is a severe and widespread disease among salmonids in

both fresh water and sea water, and Atlantic salmon, *Salmo salar* L., is the most susceptible species. There have been many attempts to produce effective vaccines against the disease during the last 50 years, and in 1992 the introduction of oil-adjuvanted vaccines gave encouraging results from the field (Press & Lillehaug 1995; Midtlyng, Reitan & Speilberg 1996).

Cold water vibriosis is caused by *Vibrio salmonicida* (Egidius, Wiik, Andersen, Hoff & Hjeltne 1986), occurring mainly in Atlantic salmon. Disease outbreaks are most frequent during the winter period (Poppe, Håstein & Salte 1985). Cold water vibriosis has created huge problems in Norway and the Faroe Islands, and outbreaks have also been reported in Scotland (Bruno, Hastings, Ellis & Wootten 1985) and the east coast of North America (Sørum, Myhr, Zwicker & Lillehaug 1993). After the introduction of effective vaccines, the disease has been brought under control, although there are still outbreaks in the northernmost regions of Norway, possibly due to a higher infection pressure in these areas (Press & Lillehaug 1995).

Substantial development of resistance against quinolones, trimethoprim/sulphonamide combinations and tetracyclines in *V. salmonicida* and *A. salmonicida* (Hjeltne, Andersen & Egidius 1987; Olsen & Skeie 1988; Husevåg, Lunestad, Johannessen, Enger & Samuelsen 1991; Høie 1991; Inglis, Frerichs, Millar & Richards 1991) has led to a need for new antimicrobial drugs for the control of bacterial diseases in fish. New agents with enhanced bioavailability compared with those currently in use are also interesting from an

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environmental point of view, as they could contribute to a reduction in the environmental impacts of antibacterial agents.

Florfenicol, a broad-spectrum antibacterial agent, is a fluorinated derivative of thiamphenicol, a chloramphenicol analogue in which the *p*-nitro group of the aromatic ring is substituted with a sulphonylmethyl group. *In vitro* studies with the compound have shown potent activity against several fish pathogenic bacterial species, including *A. salmonicida* and *Vibrio anguillarum* (Inglis & Richards 1991). Pharmacokinetic studies of florfenicol in Atlantic salmon in sea water at 11 °C demonstrated that plasma concentrations remained above the minimum inhibitory concentrations (MICs) of 0.8 µg ml⁻¹ reported for *A. salmonicida* and *V. salmonicida* for 36–40 h following a single oral dose of 10 mg florfenicol kg⁻¹ (Martinsen, Horsberg, Varma & Sams 1993).

The objective of the present study was to assess the efficacy of florfenicol at a dosage of 10 mg kg⁻¹ daily for 10 consecutive days, compared with other antibacterial compounds and an unmedicated diet, for the treatment of furunculosis and cold water vibriosis in Atlantic salmon employing laboratory challenges of *A. salmonicida* and *V. salmonicida*.

Materials and methods

The study with *A. salmonicida* is referred to as experiment 1 and with *V. salmonicida* as experiment 2.

Animal data

The experimental fish were non-vaccinated Atlantic salmon smolts. They were delivered from two local hatcheries which are both surveyed regularly by the regional veterinary officer and where neither *A. salmonicida* nor *V. salmonicida* have been detected. The farms employed a 100% flow-through system of fresh water. A pool of uniform fish was formed by removing any fish of extreme size and any that were not clinically normal.

The fish were transported to the testing laboratory, VESO Vikan AkvaVet, in a transportation tank containing 400 l of fresh water. There, they were released into fibre-glass tanks and quarantined for a minimum period of 4 weeks. Prior to the experiment, the fish were netted out of the quarantine tanks in groups of 10 and distributed to the test tanks.

The fish in experiment 1 had an average weight of 37 ± 5.7 g (average ± SD, *n* = 50) at delivery and originated from Bjøråa Edelfisk A/S, Kongsmoen, Norway. After the quarantine period they were randomly allocated to each of 18 fibre-glass tanks until each contained 100 fish. The total volume of each test tank was 180 l. Tanks were blocked in six replicate groups of three tanks each. Four hundred extra fish were moved to a fibre-glass tank with a total volume of 400 l for use as cohabitants and replacement fish.

The fish in experiment 2 had an average weight of 53 ± 3.6 g (average ± SD, *n* = 50) at delivery and originated from Kvernviklaks A/S, Salsnes, Norway. After the quarantine period they were randomly allocated to each of six fibre-glass tanks until each tank contained 100 fish. The total volume of each test tank was 400 l. Tanks were blocked in two replicate groups of three tanks each. One extra tank contained 300 fish for use in a pre-challenge test and as replacements.

After redistribution to the test tanks the fish were acclimatized to the new tanks for 40 and 22 days for experiments 1 and 2, respectively. Fish that died during the acclimatization period were replaced until 2 days prior to challenge. The biomass of each tank was determined by weighing the fish in a bucket filled with water 1 week prior to challenge. The water quality was 25‰ sea water (pH 8.2) at 12 °C in experiment 1 and 10 °C in experiment 2, supplied at a rate of 0.8 l kg fish⁻¹ min⁻¹ in a full flow-through system. Oxygen content was kept above 7 mg l⁻¹.

The water quality was monitored throughout the whole test period by use of a programmable logical steering (PLS) unit (Satt-Con 31, Alfa-Laval Automasjon, Skedsmo, Norway). Temperature, pH, salinity and oxygen content of the water were recorded and logged every hour throughout the whole experimental period. All effluent water was treated with sodium hypochlorite before the water was released into the sewage pipe.

Photoperiod was on a regime of 9 h daylight, 3 h twilight, 9 h darkness and 3 h dawn throughout the study.

Challenge

Experiment 1 – *Aeromonas salmonicida*

A. salmonicida VI-88/09/03175 (culture collection, Central Veterinary Laboratory, Oslo) was used.

Preparation of the challenge inoculum was performed as described by Nordmo & Ramstad (1997). Cohabitants were recruited from the same tank where they had been kept for acclimatization. A total of 180 fish were injected intraperitoneally (i.p.) with 10^4 CFU of *A. salmonicida* each. This challenge dose was expected to induce acute furunculosis with 100% mortality during the following 7–10 days (unpublished data). Their adipose fins were clipped, and they were distributed to the test tanks one by one in a random manner, the allocation being decided by ballot. A total of 10 cohabitants were added to each of the 18 tanks containing 100 test fish.

The test was divided into premedication, medication and post-medication periods. The premedication period lasted from the introduction of cohabitants to the start of medication. Medication started in all test tanks on the first day (day 1) of specific mortality among test fish in any of the test tanks. The premedication, medication and post-medication periods lasted for 10, 10 and 14 days, respectively.

Experiment 2 – *Vibrio salmonicida*

V. salmonicida strain NCMB 2262 (culture collection, Central Veterinary Laboratory, Oslo) was used. Preparation of the challenge inoculum was performed as described by Nordmo, Sevatdal & Ramstad (1997). A challenge dose of 10^6 CFU fish⁻¹ injected i.p. was selected, based on an induction of a cumulative mortality of at least 70% during a 3 week period in a pre-challenge test. Medication started in all test tanks at 1 day post-inoculation. The test was divided into a medication and a post-medication period that lasted for 10 and 14 days, respectively.

Medication

Standard medicated pellets from T. Skretting A/S, Stavanger, Norway, were used. They were produced by coating ordinary feed pellets, used as unmedicated diet, with the test products.

The following feeds were used:

- unmedicated diet: Tess Edel, 3.0 mm pellet;
- florfenicol: Floraqpharma vet., 2 g kg⁻¹ feed;
- oxolinic acid: Oxolinsyre vet. 5 g kg⁻¹ feed;
- oxytetracycline: Oksytetracyklin vet. 10 g kg⁻¹ feed;

- trimethoprim/sulphadiazine: Skrettoprim-sulfa vet. 15 g kg⁻¹ feed;
- flumequine: Flumequine vet. 5 g kg⁻¹ feed.

The content of drug in medicated feeds was analysed by T. Skretting A/S. The unmedicated control feed was analysed for the presence of antimicrobial agents by the College of Veterinary Medicine, Oslo.

Treatment regimes

All groups were fed twice a day at 08.00 h and 15.00 h. The feeding ratio was 1% body weight day⁻¹ with the unmedicated diet during the pre- and post-medication periods. Average fish weights of 48.5 g in experiment 1 and 53.5 g in experiment 2 were the basis for calculating the amount fed from the challenge date and during the rest of the trial.

During the medication period, fish were fed twice a day, at 08.00 h and 15.00 h, at a feeding ratio of 0.5% body weight day⁻¹ for unmedicated, florfenicol, oxolinic acid, trimethoprim/sulphadiazine and flumequine groups, and 1.0% body weight day⁻¹ for the oxytetracycline groups divided equally between the two meals. The higher rate of feeding of the oxytetracycline groups was recommended by the feed manufacturer.

The following daily dosage rates of antibacterials were used for 10 consecutive days: florfenicol, 10 mg kg fish⁻¹ day⁻¹; oxolinic acid, 25 mg kg fish⁻¹ day⁻¹; oxytetracycline, 100 mg kg fish⁻¹ day⁻¹; trimethoprim/sulphadiazine, 5 mg trimethoprim and 25 mg sulphadiazine kg fish⁻¹ day⁻¹; and flumequine, 25 mg kg fish⁻¹ day⁻¹.

Each diet was given a letter code, decided by ballot, and the study was run blind to the study director and technical assistants. The amount fed was adjusted daily according to the number of deaths on the previous day.

Observation and examination

During the medication and post-medication periods, all dead fish were examined for gross pathology and bacteriologically for the presence of the challenge organism. Kidney smears from fish challenged with *A. salmonicida* were plated on TYA (tryptone yeast agar, Difco, Detroit, MI, USA). The plates were incubated at 22 °C for 4 days. Isolates of *A. salmonicida* were identified as typical colonies producing brown pigment, which by microscopy

showed non-motile aggregating bacteria (Austin & Austin 1987), and reacted positively by agglutination with the latex test BioNor AQUA Mono As (BioNor, Skien, Norway) (Romalde, Magariños, Fouz, Bandin, Nuñez & Toranzo 1995).

Verification of *V. salmonicida* infection was performed by plating kidney smears on blood agar plates with 2% NaCl (Central Veterinary Laboratory, Oslo). The plates were incubated at 15 °C for 4 days. Isolates of *V. salmonicida* were identified as typical small, smooth, greyish non-haemolytic colonies which by microscopy showed motility (Egidius *et al.* 1986) and which reacted positively by agglutination with the latex test BioNor AQUA Mono Vs (BioNor, Skien, Norway).

Only fish positive with respect to the challenge organisms were included in the results as specific mortalities.

Statistical analysis

Treatments were compared on the basis of specific mortality at the end of the medication period and at the end of the study. The Kaplan–Meier survival function (Matthews & Farewell 1988a) was used to estimate the likelihood of survival. This model takes into account the fact that, as fish die, the group is reduced, making further deaths less likely. The Cox model was used to estimate the risk ratio (Matthews & Farewell 1988b). The risk ratio is the ratio between the risk of dying at any time in two groups, i.e. if the risk ratio is high, fish in one group will die earlier than in the other. The Kaplan–Meier plot illustrates the proportion of fish still alive at any time. Differences between parallel tanks were adjusted for in the Cox model by entering each tank as an independent variable, in addition to the treatment variable.

Results

Experiment 1 – *Aeromonas salmonicida*

Mortality data are presented in Table 1. Mortalities among the test fish started 10 days post-introduction of cohabitant fish.

Mortalities in all five medicated groups were significantly lower ($P < 0.0001$) than in the unmedicated group both at the end of medication (day 10) and at the end of the trial (day 25). The risk ratio (ratio of the chance of death) between unmedicated and medicated groups varied from 2.5

(oxolinic acid) to 4.0 (florfenicol), with a ratio of 3.0 (95% CI, 2.4–3.7) when comparing the unmedicated group with all treatment groups. Analysing for the 10 days of medication (days 1–10) compared to the post-medication period (days 11–25) separately shows that the risk ratios change from 2.0 (1.6–2.6) to 17.9 (10.2–31.4).

The florfenicol treatment was more effective than the oxolinic acid ($P = 0.039$) and trimethoprim/sulphadiazine treatments ($P = 0.037$, Table 2). There was also a tendency for better efficacy of florfenicol compared with all the drugs tested as shown in the Kaplan–Meyer survival function distribution in Fig. 1.

A comparison of survival in tanks with the same treatment demonstrated significant differences between tanks ($P = 0.0012$). After adjusting for this effect, the differences between medicated and unmedicated groups were still highly significant ($P < 0.0005$). The difference between the florfenicol and oxolinic acid/trimethoprim-sulphadiazine groups was, however, no longer significant ($P = 0.2$).

Fish that died during the medication period showed few external signs of disease, but later, during the post-medication period, the gross pathology was typical of findings described for chronic furunculosis (Munro & Hastings 1993): dominated by furuncles, darkening and petechiation at fin bases, and lethargy. The major findings in the body cavities were bloody fluid accumulations and petechiation. *A. salmonicida* was re-isolated from 96.3% of fish that died during the medication and post-medication periods.

Experiment 2 – *Vibrio salmonicida*

Mortality data are presented in Table 3.

The challenge resulted in an outbreak of cold water vibriosis in all test tanks with mortalities starting 6 or 7 days post-inoculation. The overall number of mortalities for both treated and untreated tanks was 304 (51%), and *V. salmonicida* was re-isolated from all fish. Fish in the unmedicated groups lost appetite 4–5 days post-inoculation and became totally anorexic during the next 2–3 days.

Mortalities in both medicated groups were significantly lower ($P < 0.0001$) than in the unmedicated group both at the end of medication (day 10) and at the end of the study (day 25). The risk ratio between unmedicated diet and active treatments was 5.9 (95% CI, 4.3–8.3) for florfenicol and 4.5 (3.3–6.3) for oxolinic acid at the end of

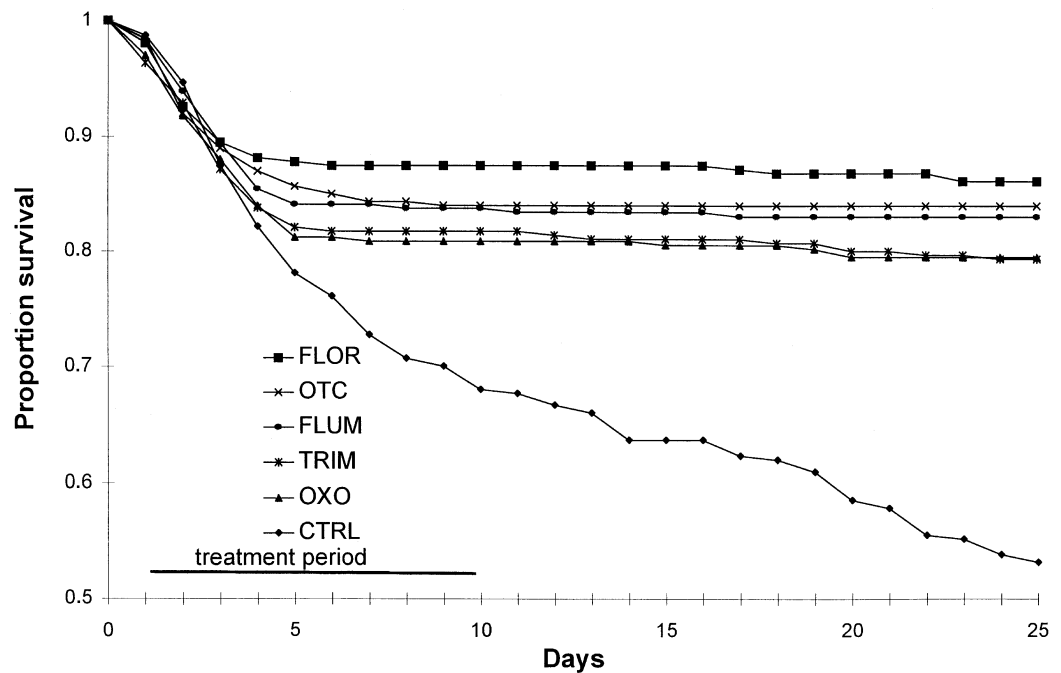


Figure 1 Kaplan–Meier survival function distribution following challenge of Atlantic salmon with *Aeromonas salmonicida* and treatment with five different drugs. FLOR, florfenicol; OTC, oxytetracycline; FLUM, flumequine; TRIM, trimethoprim/sulphadiazine; OXO, oxolinic acid; CTRL, unmedicated diet.

Table 1 Mortality data from an *in vivo* efficacy trial with diets containing florfenicol, oxolinic acid, oxytetracycline, trimethoprim/sulphadiazine, flumequine or no medication in Atlantic salmon challenged with *Aeromonas salmonicida*

Treatment (dose kg ⁻¹ day ⁻¹ for 10 days)	n	Cumulative specific mortalities				95% CI
		10 days post-challenge (end of medication)		25 days post-challenge (end of trial)		
		No.	(%)	No.	(%)	
Florfenicol, 10 mg	297	37	(12.5)	41	(13.8)	10.1–18.3
Oxolinic acid, 25 mg	294	56	(19.1)	60	(20.4)	16.0–25.5
Oxytetracycline, 100 mg	300	48	(16.0)	48	(16.0)	12.0–20.6
Trimethoprim/sulphadiazine, 5 mg + 25 mg	298	54	(18.1)	61	(20.5)	16.0–25.5
Flumequine, 25 mg	296	48	(16.2)	50	(16.9)	12.8–21.7
Unmedicated diet	297	95	(32.0)	139	(46.8)	41.0–52.7

Table 2 Comparison of efficacy of diets containing florfenicol vs oxolinic acid, oxytetracycline, trimethoprim/sulphadiazine and flumequine for the treatment of Atlantic salmon challenged with *Aeromonas salmonicida*

Florfenicol vs:	Whole test period		Days 1–10		Days 11–25	
	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Oxolinic acid	1.53 (1.02–2.29)	0.039	1.58 (1.03–2.41)	0.034	1.10 (0.27–4.38)	0.898
Oxytetracycline	1.17 (0.77–1.79)	0.463	1.30 (0.84–2.01)	0.238	0.00 (0.00–1.56)	0.124
Trimethoprim/ sulphadiazine	1.53 (1.03–2.29)	0.037	1.50 (0.98–2.29)	0.063	1.88 (0.55–6.43)	0.315
Flumequine	1.24 (0.81–1.88)	0.324	1.31 (0.85–2.03)	0.221	0.53 (0.10–2.87)	0.457

Table 3 Mortality data from an *in vivo* efficacy trial with diets containing florfenicol, oxolinic acid or no medication in Atlantic salmon challenged with *Vibrio salmonicida*

Treatment (dose kg ⁻¹ day ⁻¹ for 10 days)	n	Cumulative specific mortalities				95% CI
		10 days post-challenge (end of medication)		25 days post-challenge (end of trial)		
		No.	(%)	No.	(%)	
Florfenicol, 10 mg	200	40	(20.0)	48	(24.0)	18.1–30.2
Oxolinic acid, 25 mg	200	45	(22.5)	62	(31.0)	24.8–37.5
Unmedicated diet	200	135	(67.5)	194	(97.0)	94.2–99.0

Table 4 Risk ratio for groups of Atlantic salmon challenged with *Vibrio salmonicida* and medicated with either florfenicol or oxolinic acid. Separate analyses are made for the medication period (days 1–10) and for the whole test period

	Whole test period		Days 1–10	
	Risk ratio	P-value	Risk ratio	P-value
Florfenicol	7.7 (5.5–11.1)	< 0.0001	5.9 (4.3–8.3)	< 0.0001
Oxolinic acid	5.6 (4.0–7.7)	< 0.0001	4.5 (3.3–6.3)	< 0.0001

medication (day 10). At the end of the observation period, the risk ratios were 7.7 (5.5–11.1) and 5.6 (4.0–7.7) for florfenicol and oxolinic acid, respectively (Table 4).

The florfenicol treatment reduced mortality slightly more than the oxolinic acid (Fig. 2), but the difference was not statistically significant ($P = 0.15$).

A comparison of survival in parallel tanks demonstrated a significant difference in mortality for the florfenicol ($P = 0.047$) and the unmedicated diet ($P = 0.036$) groups, but not for the oxolinic acid group ($P = 0.41$). These differences were taken into account when analysing for differences between treatment regimes.

The clinical and gross pathology showed very few external signs typical of natural cold water vibriosis (Hjeltnes & Roberts 1993). The most dominant finding was red swelling in the abdominal wall at the site of injection and ascites in some of the fish.

The analysis of the medicated feed demonstrated a content of active substance within those limits set by the manufacturer of the feed in both experiments. No substances of antimicrobial activity were detected in the unmedicated diets. All the medicated feed was accepted by the fish in all groups and appeared to be well tolerated.

Discussion

The mortality rates of the florfenicol groups were highly significantly lower compared with the unmedicated groups in both the *A. salmonicida* and *V. salmonicida* experiments. Florfenicol gave results equal to or better than the other treatments. Based on its different mode of action to currently used antimicrobials, florfenicol should have utility on farms where drug-resistant strains of bacteria have emerged.

The total dose of active substance used for florfenicol was 100 mg kg⁻¹, whereas the doses used for the other drugs were 250, 300 and 1000 mg kg⁻¹ for the quinolones, trimethoprim/sulphadiazine and oxytetracycline, respectively. Florfenicol has been demonstrated to have a very good bioavailability in Atlantic salmon ($F = 96.5\%$) (Martinsen *et al.* 1993). As antimicrobials for the treatment of bacterial infections in farmed salmon have to be administered via the oral route, there is always a risk of negative impact on the environment due to a deposition of excess feed and faeces containing the drug under the net pens (Husevåg *et al.* 1991). The high bioavailability and low doses used for florfenicol compared with other drugs may reduce the negative impact on the environment caused by drugs with low bioavailability.

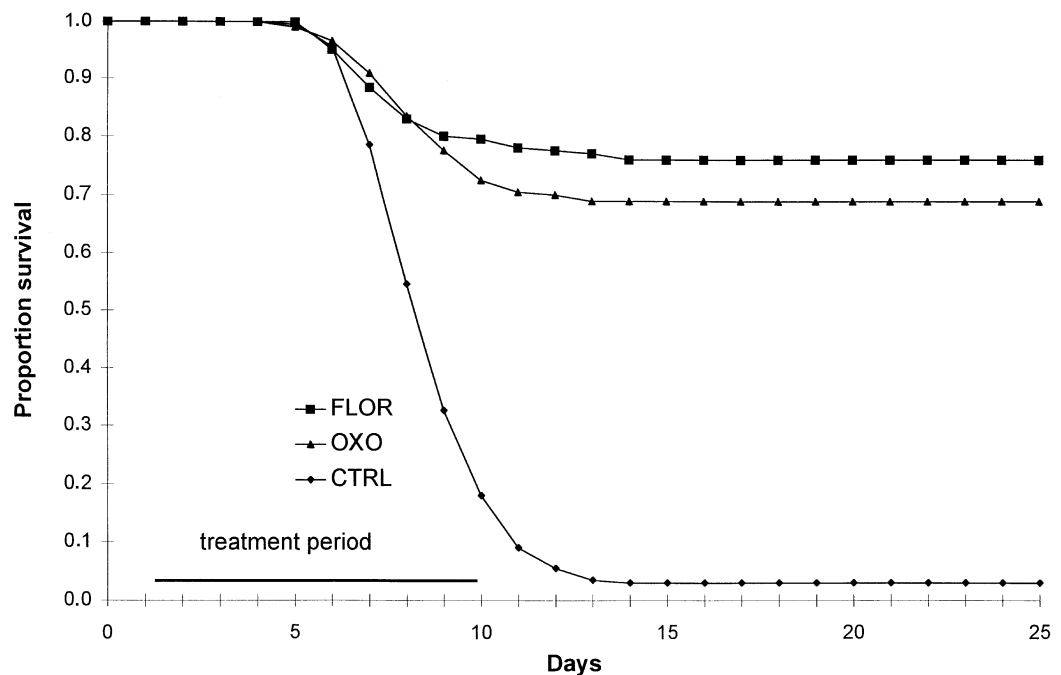


Figure 2 Kaplan–Meier survival function distribution following challenge of Atlantic salmon with *Vibrio salmonicida* and treatment with two different drugs. FLOR, florfenicol; OXO, oxolinic acid; CTRL, unmedicated diet.

In the present experiments, all drugs tested were administered for 10 consecutive days. Under field conditions, regimes with treatment on alternate days are commonly used for oxolinic acid and flumequine (Nordmo, Varma, Sutherland & Brokken 1994). For the quinolones (oxolinic acid and flumequine), the recommendations from feed manufacturers normally range from 100 to 150 mg kg⁻¹ daily for 6 days or on alternate days for a total of 8 or 10 days. For trimethoprim/sulphadiazine, the normal regime under field conditions would be to treat the fish for only 5–7 days. The reason for not using treatment regimes commonly used under field conditions according to the manufacturer's recommendations was the objective of comparing the efficacy of the drugs under comparable regimes.

The relative percentage survival (RPS) (Amend 1981) for the florfenicol group compared with the unmedicated diet at the end of the experiments was 70% in the *A. salmonicida* challenge and 75% in the *V. salmonicida* challenge. In another therapeutic experiment against furunculosis in the same species, the relative survival was reported to be 82% (Inglis, Richards, Varma, Sutherland & Brokken 1991). Comparisons of RPS should, however, be made with caution as there are likely to be many variables between test systems (Nordmo & Ramstad 1997).

In the experiment with *V. salmonicida*, medication of the infected fish started 1 day post-inoculation, whereas the first mortality among fish that were given unmedicated feed started 6 days post-inoculation. The treatment must therefore be regarded as both prophylactic and therapeutic. The reason for starting medication at this early stage of the outbreak was based on experience from a similar study where medication started 5 days post-challenge (unpublished data). At this time, most of the fish had become anorexic, which made it impossible to administer medication via feed. During a natural outbreak of cold water vibriosis, it is unlikely that fish with disease signs will be cured, due to failure to ingest medicated feed. Treatment under field conditions will therefore also be of a prophylactic nature for those fish in the prodromal stage of the disease or not already infected.

In the two experiments reported, a cohabitation challenge model was chosen for *A. salmonicida*, whereas i.p. inoculation was chosen for *V. salmonicida*. Cohabitation challenge most closely mimics natural exposure, as it ensures that immune mechanisms located to the integument remain intact (Ingram 1980; Cipriano, Ford, Teska & Hale 1992). The reason for not choosing a bath or cohabitation challenge with *V. salmonicida* was based upon

previous experience of difficulties with inducing acute cold water vibriosis by these routes.

A valid use of the Cox model for statistical analysis requires that the deaths of different fish in the same tank are independent events, i.e. that the death of one fish does not impact upon others in the same tank. Further, the observed differences in mortality between parallel tanks may indicate that we were not able to set up an identical challenge environment in all the test tanks. In the cohabitation challenge with *A. salmonicida*, the *P*-value for the difference between parallel tanks was 0.0012, whereas in the i.p. challenge with *V. salmonicida* it was only 0.047 and 0.036 for the florfenicol and unmedicated diet groups, respectively, and not significant for the oxolinic acid group. An identical challenge environment must therefore be regarded as easier to establish in an i.p. challenge with *V. salmonicida* compared with a cohabitation challenge with *A. salmonicida*. However, it is considered unlikely that these variations in the reported studies with florfenicol will be so great that they invalidate the conclusions of the statistical analyses. Also, if dependencies should exist, the reported risk ratios will still be valid as the results apply to practical fish farming where many fish are kept in the same enclosed area.

Quinolones and oxytetracycline are known to complex with di- and trivalent cations (Ca^{2+} , Fe^{2+} , Mg^{2+} , Al^{3+}). These cations are important components of sea water as well as being present at various levels in feed pellets. Thus, both sea water and feed may impair the absorption and/or activity of quinolones and oxytetracycline (Martinsen 1993; Barnes, Hastings & Amyes 1995; Pursell, Samuelsen & Smith 1995). In the assessment of efficacy in laboratory tests, the choice of water quality may therefore be crucial for the relevance of the results to field conditions. The use of 25‰ salt water in the present study would imply that the results are applicable to normal rearing conditions in sea water. Also, field evaluations by Nordmo *et al.* (1994) in outbreaks of furunculosis confirmed the results obtained in the present laboratory tests, that florfenicol is highly effective in the treatment of furunculosis under commercial conditions.

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