

## REVIEW ARTICLE

# An assessment of the use of drug and non-drug interventions in the treatment of *Ichthyophthirius multifiliis* Fouquet, 1876, a protozoan parasite of freshwater fish

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## SUMMARY

Infection by the ciliate protozoan *Ichthyophthirius multifiliis* Fouquet, 1876 causes significant economic losses in freshwater aquaculture worldwide. Following the ban on the use of malachite green for treating food fish, there has been extensive research aimed at identifying suitable replacements. In this paper we critically assess drug and non-drug interventions, which have been tested for use or have been employed against this parasite and evaluate possibilities for their application in farm systems. Current treatments include the administration of formaldehyde, sodium chloride (salt), copper sulphate and potassium permanganate. However, purportedly more environmentally friendly drugs such as humic acid, potassium ferrate (VI), bronopol and the peracetic acid-based products have recently been tested and represent promising alternatives. Further investigation, is required to optimize the treatments and to establish precise protocols in order to minimize the quantity of drug employed whilst ensuring the most efficacious performance. At the same time, there needs to be a greater emphasis placed on the non-drug aspects of management strategies, including the use of non-chemical interventions focusing on the removal of free-swimming stages and tomocysts of *I. multifiliis* from farm culture systems. Use of such strategies provides the hope of more environmentally friendly alternatives for the control of *I. multifiliis* infections.

Key words: *Ichthyophthirius multifiliis*, whitespot, drug, treatment, ciliate, parasite.

## INTRODUCTION

The freshwater protozoan parasite of fish, *Ichthyophthirius multifiliis* Fouquet 1876, also known as 'fish whitespot', continues to impact wild and cultured fish populations worldwide and places an economic burden on global freshwater finfish aquaculture.

The ciliate protozoan *I. multifiliis* is one of the most important freshwater pathogens affecting the aquaculture and ornamental fish industries. In part, its impact stems from its low host specificity, allowing it to infect a wide range of fish species, including commercially important species such as channel catfish (*Ictalurus punctatus* Rafinesque 1818) and rainbow trout (*Oncorhynchus mykiss* Walbaum 1792) (see Valtonen and Koskivaara, 1994; Noble and Summerfelt, 1996; Buchmann and Bresciani, 1997; Rintamäki-Kinnunen and Valtonen, 1997; Matthews, 2005; Jørgensen *et al.* 2009). It has a direct life cycle, which is temperature dependent such that the warmer the water temperature the faster the life

cycle completes. The life cycle involves 4 different stages: (1) the trophont, which resides within the surface epithelium of gills, fins and other body surfaces; (2) the protomont, a free-swimming stage that exits the fish and settles on the substrate to become the encysted tomocyst stage (3) which in turn repeatedly divides by binary fission to produce tomites which are released to the water column. Tomites differentiate into the infective stage (4) the theront, which needs to find a host within a short window to successfully complete the life cycle by penetrating the epidermis and developing into the trophont stage before it dies (Lom and Dyková, 1992; Matthews, 2005). Theronts can survive for up to 92 h at low water temperatures; their survival being inversely proportional to the ambient water temperature (Wagner, 1960; Aihua and Buchmann, 2001).

On farms, the most common approaches to treat this ciliate is through the use of either short (e.g. 30 min–4 h in tanks, raceways and flow-through systems) or long (e.g. 7–15 days in pond culture) duration in-bath treatments which target the free-swimming stages of the parasite (i.e. protomonts and theronts). Of the other two stages, the trophont is protected lying underneath the host surface

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epithelium (Post and Vesely, 1983) whilst the tomocyst is protected by a resistant coat (Ewing *et al.* 1983) and as such, are rarely susceptible to treatment.

Historically, malachite green (MG) was commonly used for the control of *I. multifiliis* and a range of other fish diseases (Srivastava *et al.* 2004) due to its demonstrable efficacy, low cost, ready availability, high stability during storage and high solubility in water (Schnick, 1988; Henderson *et al.* 1997). This organic (triphenylmethane) dye was favoured for the control of *I. multifiliis* infections because of its high efficacy against both the free-swimming stages (protomonts and theronts) of the parasite and the feeding parasite stage (trophont) within the fish's epithelium (Wahli *et al.* 1993; Tieman and Goodwin, 2001; Buchmann *et al.* 2003). MG and its derivatives (mainly leucomalachite) also display well-documented ecotoxicological effects including cytotoxicity, carcinogenicity, mutagenicity, induction of chromosomal fractures, teratogenicity and respiratory toxicity (Culp and Beland, 1996; Srivastava *et al.* 2004). Malachite green and its derivatives are also known to be highly persistent in the environment, bio-accumulating in the ecosystem and fish tissues (Henderson *et al.* 1997). Although the use of MG has never been licensed by the US Food and Drug Administration (FDA), its use in food products was initially permitted under an 'investigational new animal drug' status (Alderman, 1985). This status was revoked in 1983 and MG was listed as a priority chemical for toxicity and carcinogenicity testing (Culp and Beland, 1996; Culp, 2004). Similarly, in Canada the use of MG and the presence of its derivatives in food animals are not permitted and its continued use was advised against in 1992 when MG was classified as a class II health hazard (Canadian Food Inspection Agency 2010). Its use within the European Union has been subsequently banned in 2000 under EC directive 90/676/EEC; article 14, regulation 2377/90/EEC.

As a consequence of the widespread ban, enforced restrictions imposed on the use of MG and the concerns regarding the presence of derivatives in food-products (Herber, 2009), there has been extensive research in the last few decades focusing on the provision of alternative, effective and environmentally friendly products and management techniques for controlling *I. multifiliis* infections. Despite the global effort, no clear alternative management strategies have yet emerged. There is a strong commercial and scientific need for providing a critical summary of tested candidate and applied drugs but also an assessment of the potential of other management strategies to prove efficacious against *I. multifiliis* infections. It has been nearly 30 years since the last major reviews were published examining the use of drugs for the control of *I. multifiliis* (Cross, 1972; Hoffman and Meyer, 1974; Herwig,

1979) so that this review might be considered to be somewhat overdue.

This paper provides an overview and assessment of the current state of knowledge concerning drugs (compound, dose, duration and efficacy) and physical interventions employed or tested against *I. multifiliis* since the 3 earlier reviews were published. This review seeks to summarize the original research findings and to help identify the most suitable therapy against *I. multifiliis* while highlighting the most promising treatments for further research and application in farm systems.

#### ASSESSMENT OF CURRENTLY APPLIED CHEMOTHERAPIES

A large number of compounds have been tested for efficacy against *I. multifiliis* although relatively few of them have been widely deployed to provide effective control under field conditions. Table 1 provides a detailed list of 116 compounds used to control *I. multifiliis* under laboratory or field conditions from 1980 onwards. Of the compounds that are listed, all except quinine and some malachite green-based formulations have been tested against food fish species. These latter treatments, however, that have been evaluated for the ornamental trade, are included to provide a comprehensive overview of all compounds tested for the treatment of *I. multifiliis*. Of those given in Table 1, 18 entries listed by their commercial product name are cross-referenced, and details of their activity given, under their specific compound formulation. Sixteen of the compounds have been assessed by *in vitro* trials only, while of the remaining 81 compounds tested *in vivo*, 43 have been tested in-bath challenges and 51 by in-feed presentation. Of those used under field conditions, the most commonly used treatments are: formaldehyde, sodium chloride, copper sulphate, potassium permanganate, chloramine-T, hydrogen peroxide, metronidazole and toltrazuril (Dickerson, 2006; Noga, 2010). Whilst malachite green was previously the most extensively employed treatment, eliminating the protomont, theront and trophont stages, its use has been largely discontinued for food fish, particularly in the EU and the United States.

Some caution, however, should be taken with regard to the treatment efficacies provided in Table 1, in that these may be the result of how the study was conducted (i.e. natural, multi-age class infections compared to a standard, single age class infection) and/or evaluated (i.e. parasite numbers determined from skin scrapes as opposed to total parasite counts) and therefore the results may have been affected by the differential level of parasitaemia at the time of the treatment on the test and control fish. For efficacious compounds of interest, therefore, details on the treatment conditions used in the original work should be consulted. If the physiological trauma created by

exiting trophonts is considered as the primary cause of mortality, then a compound that successfully kills trophonts *in situ*, thereby preventing exit, could be considered efficacious (i.e. a statistically lower number of parasites and host mortality when compared to an appropriate control group).

### Formaldehyde

Formaldehyde has been proven to be very effective at eliminating the free-living stages of the parasite (i.e. protomonts, tomocysts and theronts) (Wahli *et al.* 1993; Shinn *et al.* 2005, Lahnsteiner and Weismann, 2007; Heinecke and Buchmann, 2009), however, when used for *in vivo* baths, fish survival can be compromised (Wahli *et al.* 1993; Tieman and Goodwin, 2001). Formaldehyde remains one of the most commonly used treatments to control *I. multifiliis* infections in aquaculture systems (Noga, 2010). However, efficiency is achieved only at high concentrations, which are serially repeatedly applied (i.e. 100 mg l<sup>-1</sup> for 30 min to 1 h over 10 consecutive days in salmonid farms), such that in flow-through systems with rapid water turn-over, as used for e.g. the intensive production of salmonids, high volumes are required. In addition, the use of formaldehyde has many reported side effects such as reducing the oxygen available in the water by 1 ppm for each 5 ppm of formaldehyde that is used (Cross, 1972; Pillay and Kutty, 2005). This can be particularly problematical in summer when increasing water temperatures both accelerate the life cycle of *I. multifiliis* and act to cause a concomitant reduction in the oxygen holding capacity of the water. Buchmann *et al.* (2004) also demonstrated that *O. mykiss* exposed to formaldehyde at concentrations of 200–300 ppm for 1 h had a reduced mucus production and were thus more susceptible to secondary infections by water moulds and bacteria. Accordingly, when formaldehyde is applied *in vivo* in the form of baths, fish survival can be compromised (e.g. for *O. mykiss* exposed to 2 treatments of 25 and 100 mg l<sup>-1</sup> of formaldehyde for 1 h on days 9 and 12 post-infection) (Wahli *et al.* 1993). Importantly, the effect of water quality parameters on the toxicity of formaldehyde to fish and to *I. multifiliis* remains poorly characterized (Meinelt *et al.* 2005). Although formaldehyde is an approved aquacultural therapeutic within the EU (Schlotfeld, 1993, 1998), in 2004 it was re-classified by the WHO International Agency for Research on Cancer as ‘carcinogenic to humans’ (WHO, 2006). Even though it is quickly metabolized by aquatic organisms and holds a low potential for bio-accumulation (Hohreiter and Rigg, 2001; Duffort *et al.* 2010), it might be envisaged that formaldehyde could soon be banned due to the hazard it poses to workers handling large volumes of the chemical (Wooster *et al.* 2005). Given the high volumes of formaldehyde required in a typical farm

treatment and the potential toxic risks this chemical poses to both fish stock and the farm workers handling it, the future of formaldehyde as a long-term acceptable and sustainable drug seems unlikely.

### Sodium chloride

Sodium chloride (salt) is the second most commonly used product for the treatment of *I. multifiliis* infections. The application of a minimum of 2.5 g l<sup>-1</sup> has been proven to reduce protomont and theront survival (Aihua and Buchmann, 2001; Shinn *et al.* 2005; Lahnsteiner and Weismann, 2007). A treatment regime of 1–5 g l<sup>-1</sup> salt applied continuously for a minimum period of 7 to 32 days, for example, was able to reduce the number of trophonts establishing on fish (Selosse and Rowland, 1990; Miron *et al.* 2003; Lahnsteiner and Weismann, 2007; Balta *et al.* 2008; Mifsud and Rowland, 2008). The use of higher concentrations of salt (e.g. 15–20 g l<sup>-1</sup>) over short periods of exposure (e.g. 20–60 min), however, was not able to reduce the level of infection (Lahnsteiner and Weismann, 2007; Balta *et al.* 2008). Additionally, the bath application of salt may be beneficial, in helping the host recover the osmotic imbalance and loss of salts created by exiting trophonts. The incorporation of salt in fish feed has also been explored with contradictory results. Rahkonen and Koski (2002) reported a reduction in infection levels in medicated fish when salt was incorporated at a level of 0.3–1.0% and fed for 3 to 11 days. Garcia *et al.* (2007), however, did not observe any significant reduction in parasite burdens when fish were fed a diet containing 1.2–6.0% salt for a period of 30 days. While the use of salt appears to represent an economically viable and safe treatment option for many farm and ornamental fish species, it should be used with caution in certain infected stenohaline freshwater fish species such as channel catfish (Noga, 2010).

### Copper sulphate

Copper sulphate has been shown to be effective at eliminating *I. multifiliis* in a range of fish species when used at low concentrations (Ling *et al.* 1993; Schlenk *et al.* 1998; Goodwin and Straus, 2006; Straus, 2008; Rowland *et al.* 2009). However, long periods of exposure can lead to toxicity, gill damage and growth suppression (Cardeilhac and Whitaker, 1988; Moore, 2005; Rábago-Castro *et al.* 2006). Copper has a very low therapeutic index (Boyd, 2005) and its toxicity to both fish host and *I. multifiliis* is known to vary widely with water chemistry parameters, particularly water alkalinity and hardness (Deilhac and Whitaker, 1988; Straus, 2008; Straus and Meinelt, 2009). Copper sulphate is a recognized algacide and is known to be toxic to a

wide range of invertebrate organisms (Boyd, 1990). When added to pond systems, there is a risk of phytoplankton mortality which consequentially might result in lower oxygen levels at night, which in turn compromises the trophic chain on which the fish stock might rely (Noga, 2010). It is vital therefore that its use on a small subsample of the fish stock in the local water is determined before it is applied on a large-scale basis. Particular care should be taken when using this compound in green water pond systems. Future research should be aimed at identifying the range of water quality parameters and concentrations within which this compound is effective against *I. multifiliis* infections and can be safely administered without risk to fish.

#### *Potassium permanganate*

Potassium permanganate (KMnO<sub>4</sub>) is also commonly used against *I. multifiliis*, mainly in farm pond systems (Brown and Gratzek, 1980; Noga, 2010). Low concentrations (e.g. 0.8–1.0 mg l<sup>-1</sup>) over short periods of exposure (30 min to 4 h) were able to eliminate the theront stage in the water column (Straus and Griffin, 2001). When tested *in vivo*, low concentrations (e.g. 0.25–2 mg l<sup>-1</sup>) require longer periods of exposure (continuously from 6 to 20 days) to significantly decrease the number of trophonts per fish (Tieman and Goodwin, 2001; Straus and Griffin, 2001, 2002). The application of higher concentrations (e.g. 10–20 mg l<sup>-1</sup>) for 30 min was found to be toxic to treated fish (Balta *et al.* 2008). Potassium permanganate is an algacide which oxidizes organic matter, reducing dissolved oxygen levels; its effects are notable when used in ponds. This compound has a low therapeutic index and can be very toxic when used in waters of a high pH when it can precipitate on gills leading to high mortalities (Tucker, 1987; Dolezelova *et al.* 2009; Noga, 2010). Potassium permanganate treatment against *I. multifiliis* shows very low efficacy at concentrations that are not toxic to fish, if the organic loading of the aquatic system is not taken into account. Large quantities of this compound and its continuous application, therefore, are often required to manage infections.

#### *Chloramine-T*

Chloramine-T is an organic chlorine compound, specifically a sodium salt that when mixed with water is a very strong disinfectant (Treves-Brown, 2000; Noga, 2010). When used to treat *I. multifiliis* stages, chloramine-T has been found to be very effective *in vitro* for the treatment of both the protomont and theront stages (Shinn *et al.* 2001). *In vivo*, however, chloramine-T was effective only when administered at high concentrations (e.g. 100 mg l<sup>-1</sup> for 30 min given over a period of 10 days) (Shinn *et al.* 2001; Tieman and Goodwin, 2001; Rahkonen and Koski,

2002; Shinn *et al.* 2003a; Rintamäki-Kinnunen *et al.* 2005a; Balta *et al.* 2008). The administration of high doses of chloramine-T can inflict damage to the gill epithelia and has been reported to affect the development of the swim bladder in young fry (Sanabria *et al.* 2009). The average lethal time (LT<sub>50</sub>) for a dose of 50 mg l<sup>-1</sup> chloramine-T was determined to be 166.8 min (Powell and Harris, 2004). Although these latter authors suggested that freshwater stages of Atlantic salmon, *Salmo salar* L., were as sensitive to chloramine-T toxicity as *O. mykiss*, and more sensitive than *I. punctatus*, the latter showed histopathological changes when exposed daily to 80 mg l<sup>-1</sup> in a static immersion bath for 3 h (Gaikowski *et al.* 2009). Future work, therefore, should explore the efficacy of using 30 min baths of chloramine-T ranging between 30 and 80 mg l<sup>-1</sup> over a period of 10 days (e.g. treatments on days: 1, 4, 7 and 10) (or the full duration of the parasite life cycle as dictated by the ambient water temperature).

#### *Hydrogen peroxide*

Hydrogen peroxide is a powerful oxidizer that has been used under field conditions to control *I. multifiliis*. Results for its use in *in vitro* tests against free-living stages of *I. multifiliis*, however, were disappointing (Shinn *et al.* 2005; Lahnsteiner and Weismann, 2007), with a 100 mg l<sup>-1</sup> treatment for 1 h effecting only a 15% mortality of theronts (Shinn *et al.* unpublished observations). It is not surprising, therefore, that a 20-day regime of 25 mg l<sup>-1</sup> hydrogen peroxide failed to bring about a reduction in the number of trophonts on stock, which consequentially resulted in high mortalities (Tieman and Goodwin, 2001). High doses, however, can cause gill damage leading to fish mortality (especially at high temperatures) (Schmidt *et al.* 2006; Noga, 2010).

#### *Metronidazole*

Metronidazole has been shown to be very successful at reducing the number of trophonts on infected fish when incorporated into diets (Tojo-Rodriguez and Santamarina-Fernandez, 2001; Tokşen and Nemli, 2010). This compound, which has been shown to be effective in the ornamental fish industry, is currently listed as being 'possibly carcinogenic to humans' by the World Health Organization and has been banned within the EU and USA for use in animal feed; in the US specifically for animals destined for human consumption. Its future use as a potential treatment in the fish food industry, therefore, is no longer considered.

#### *Toltrazuril*

The triazinetrione derivative coccidiostat toltrazuril has been shown to be effective against the protomont

stage in *in vitro* trials (Schmahl *et al.* 1989; Tojo-Rodriguez *et al.* 1994). However, when administered *in vivo* it is either ineffective (Schmahl *et al.* 1989; Tojo-Rodriguez *et al.* 1994) or toxic to the fish (From *et al.* 1992).

#### THE POTENTIAL OF ALTERNATIVE CHEMICAL COMPOUNDS

Despite recent extensive research to explore the utility of alternative, environmentally friendly chemical compounds, only a handful of compounds have been shown to display efficacy at reducing *I. multifiliis* infections *in vivo* (see Table 1).

#### *In-bath treatments*

Of the bath compounds that have been identified, acetic acid (4%), bronopol, peracetic acid-based products, combinations of peracetic acid and formaldehyde, humic acid (10%) and potassium ferrate (VI) displayed a good level of efficacy. Acetic/peracetic acid represents the cheapest treatment option, followed by, in rank order, formaldehyde, potassium ferrate (VI), and then significantly more expensive bronopol and humic acid, notably the latter. Of these compounds, acetic acid (4%) is widely used in Turkey to control protozoan infections (Kayis *et al.* 2009). When tested *in vivo* against *I. multifiliis*, a single short dip bath of 10 ml l<sup>-1</sup> for 3 min was able to reduce the trophont burden on treated fish (Balta *et al.* 2008).

Bronopol, the active compound of a product already licensed for use as an aquacultural drug, when applied at low concentrations (e.g. 2 and 5 mg l<sup>-1</sup>) over a long period of exposure (e.g. 27 days) was demonstrated to be highly effective against the free-swimming stages of *I. multifiliis*, as well as reducing the number of trophonts subsequently establishing in successive waves of infection (Shinn *et al.* 2011; Picón-Camacho *et al.* 2011a). Bronopol does not accumulate in fish tissues or in the environment and therefore no withdrawal period is required after its administration (Novartis, 2002). Bronopol presents no serious toxicological hazard to humans (Bryce *et al.* 1978) or to fish (Pottinger and Day, 1999), and, it degrades very quickly, especially when exposed to high intensity UV light (Noga, 2010). Bronopol-based products therefore show strong potential for the management of *I. multifiliis* infections in farm systems; however, timing of deployment with respect to parasite population dynamics and optimal treatment concentrations remain to be optimized for this product.

Formulations of peracetic acid (PAA), hydrogen peroxide and acetic acid have proven able to kill the protomont stage within 48 h of exposure at concentrations of 0.8–0.9 mg l<sup>-1</sup>. Importantly, tomocysts

recently attached to the substrate were also killed following a 12 h exposure to 1–3 mg l<sup>-1</sup> to PAA solutions (Meinelt *et al.* 2009). When used *in vivo*, formulations containing a high proportion of PAA were also able to reduce the number of trophonts on infected fish (Rintamäki-Kinnunen *et al.* 2005a; Sudová *et al.* 2010). Adding peroctanoic acid to a PAA formulation, further improved the anti-protozoal activity of the solution, such that tomocyst stages were killed after 60 min exposure (Bruzio and Buchmann, 2010; Picón-Camacho *et al.* 2011b). PAA's stability, however, has been shown to be closely linked to a range of water quality parameters such as temperature, organic matter content and pH (Pedersen *et al.* 2009) and therefore the degradation of PAA must be assessed over time and taken into account in establishing the most effective treatment regime to use on site. The efficacy of PAA, notably against the tomocyst and trophont stages, however, highlights the potential of this compound as a treatment against *I. multifiliis*.

Low concentrations of humic acid (10%) (100–150 µl l<sup>-1</sup>) were found to disrupt the development of protomonts; however, when the same concentrations were used *in vivo*, the results were inconsistent and appeared to be highly dependent on water temperature and the treatment regime used (Lahnsteiner and Weismann, 2007).

Ling *et al.* (2010) demonstrated that 4.8 mg l<sup>-1</sup> potassium ferrate (VI) for 2 h was very effective *in vitro*, in killing theronts. When the same dose was used as an *in vivo* continuous bath treatment for 3 days, it resulted in an 80% reduction in the number of trophonts on the test fish. An increase in concentration to 19.2 mg l<sup>-1</sup> applied for 3 days managed to completely eradicate the infection from the fish stock suggesting that potassium ferrate (VI) is very successful at disrupting trophont development. Potassium ferrate (VI) is an environmentally friendly, strong oxidizing agent (Ma and Liu, 2002), that is less toxic to fish and humans than closely related potassium salts such as potassium permanganate (Ling *et al.* 2010). The effectiveness and degradation rate of potassium ferrate (VI) in the aquatic environment, however, is strongly linked to pH and water temperature (Johnson and Sharma, 1999) and these must be considered when establishing a treatment regime based on its use.

Of the bath chemicals that have investigated in recent years, potassium ferrate (VI), bronopol and the peracetic acid-based products all possess potential as promising alternatives to current chemotherapies for the control of *I. multifiliis* infections.

#### *In-feed treatments*

Of the in-feed treatments described in Table 1, the compounds with the highest apparent efficacy *in vivo* in controlling *I. multifiliis* infections are amprolium

hydrochloride, vitamin C, quinine, SalarBec, salinomycin sodium and secnidazole. Shinn *et al.* (2003b) demonstrated that the two anti-coccidiostats compounds, amprolium hydrochloride and salinomycin sodium, when incorporated into a commercial feed, were able to significantly reduce the number of trophonts establishing on fish. Treatment with 100 mg l<sup>-1</sup> of amprolium hydrochloride (a thiamine, vitamin B1, analogue) for 1 h compromised the survival of the tomocyst stage *in vitro*, ultimately killing 85–90% of the tomocysts (Shinn *et al.* 2001). Incorporation of 1 g kg<sup>-1</sup> of feed given over 8 days post-infection did not manage to reduce the trophont burden on fish (Tojo-Rodriguez *et al.* 1994). A dose 63 mg kg<sup>-1</sup> of feed of amprolium hydrochloride given 10 days prior the infection, however, reduced the number of trophonts subsequently establishing on fish by up to 78% when compared to the control groups (Shinn *et al.* 2003b). Salinomycin sodium has only been tested *in vivo*, with promising results. Infected fish fed a diet containing 47–63 mg kg<sup>-1</sup> of feed of salinomycin sodium for a period of 10 days were found to show a significant reduction (80–93%) in number of trophonts when compared to the control groups (Shinn *et al.* 2003b). The same authors also tested SalarBec, a blend of Vitamin C, E and B group. When SalarBec was incorporated at a rate of 3.2 g kg<sup>-1</sup> feed and given to fish for a period of 10 days prior to infection with *I. multifiliis*, a 65% reduction in the number of trophonts surviving on challenged fish was found (Shinn *et al.* 2005).

Vitamin C on its own or in combination with Vitamin E has also been tested with success *in vivo* (Wahli *et al.* 1985, 1995, 1998). Quinine when incorporated into feed at a rate of 5 g kg<sup>-1</sup> feed and given over a period of 7 to 10 days effected the complete elimination of *I. multifiliis* on medicated fish (Schmahl *et al.* 1996). Medicated fish using vitamin C and quinine, however, showed growth suppression as a result of decreased food intake.

Finally, secnidazole is an antibiotic which has been shown to reduce *I. multifiliis* infections when incorporated into feed and presented at 24–36 mg kg<sup>-1</sup> of body weight (Tokşen and Nemli, 2010) or 40 g kg<sup>-1</sup> of feed for 10 days (Tojo-Rodriguez and Santamarina-Fernandez, 2001). While secnidazole appeared to be effective, the cost of using it on a large commercial scale would be prohibitive (Noga, 2010).

Although the use of in-feed treatments appears to be an efficient, targeted strategy for reducing trophont burdens, the general inappetence displayed by heavily infected fish means that getting the target dose into infected fish in the later stages of an infection can be a challenge. This can, in part, be circumvented by top dressing unpalatable medicated diets (e.g. salinomycin sodium, see Shinn *et al.* 2003b) with bait flavouring to mask bitter ingredients

and/or by incorporating feed stimulants (e.g. garlic) into the diet (Shinn unpublished data).

#### NATURAL EXTRACTS

Some new treatments involve the use of plant extracts such as those from garlic, *Allium sativum* L., which showed promising results when tested *in vitro* (Buchmann *et al.* 2003). However, when incorporated in-feed and tested *in vivo* this extract did not manage to significantly reduce infection levels when compared to control groups (Shinn *et al.* unpublished observations). Other natural products such as those from papaya *Carica papaya* L. and the velvet bean *Mucuna pruriens* L. were successful when tested *in vitro* and *in vivo* against protomonts and trophonts (Ekamen *et al.* 2004). Concentrations of 200 and 250 mg l<sup>-1</sup> of *C. papaya* reduced the infection levels on treated fish by 89–92%. *M. pruriens* administered at 100, 150 and 200 mg l<sup>-1</sup> also reduced the parasite burden on the treated fish by 59–92%. Recent research by Yao *et al.* (2010) using the extract from *Macleaya cordata* Willd has shown high efficacy in *in vitro* trials against protomonts and an important trophont reduction (e.g. 75–97%) when administered *in vivo* at low concentrations (e.g. 0.6–0.9 mg l<sup>-1</sup>) for 48 h. The use of probiotics as an in-feed treatment (e.g. 10<sup>8</sup> cells of *Aeromonas sobria* g<sup>-1</sup> feed for 14 days) has also proven to be very effective at reducing infections in medicated fish (Pieters *et al.* 2008).

There may therefore be considerable potential for the use of such natural products to control *I. multifiliis* infections; however, *in vivo* trials carried out under field conditions are a critical requirement prior to wider deployment of such treatments.

#### NON-DRUG INTERVENTIONS

In the last few years, a wide range of non-drug interventions (see Table 2) have been tested against *I. multifiliis*.

Farley and Heckmann (1980) used 'electrotherapy' as a possible treatment to control whitespot infections. Whilst there was some protomont mortality following exposure to short pulses of electricity (5 sec), it seems that this was probably due to water hydrolysis rather than lysis of the parasite. It was concluded that the amperage necessary to disrupt trophonts within the fish epidermis would be too high and lethal to the fish.

The utilization of a single UV lamp (91900 µW s<sup>-1</sup> cm<sup>-2</sup>) has, in contrast, successfully managed to reduce the mortality of fish infected with *I. multifiliis* in a closed re-circulation system by controlling the spread of *I. multifiliis* stages between tanks (Gratzek *et al.* 1983).

The mechanical filtration of inlet water, considering that the size of theronts ranges from

57.4 × 28.6 μm (at 5 °C) and 28.6 × 20.0 μm (at 30 °C), is not a feasible method to prevent the entry of the parasite to farm systems (Aihua and Buchmann, 2001). Nonetheless, a combination of an 80 μm mesh followed by a treatment of sodium percarbonate prevented protomonts from entering the system and killed theronts (Heinecke and Buchmann, 2009).

Bodensteiner *et al.* (2000) demonstrated that increasing the flow rate and water turnover in fish farms above 85 cm min<sup>-1</sup> and 2.1 l h<sup>-1</sup> managed to reduce infection levels by flushing the free-swimming stages of the parasite out of the system. However, since water availability in farms can fluctuate greatly over the year, often reducing significantly over the summer months at the same time as water temperature increases exacerbate *I. multifiliis* infections, this cannot always provide a viable control solution.

Shinn *et al.* (2009) recently demonstrated that the combination of regular cleaning with a vacuum cleaning head and the use of a low adhesion polymer to line rainbow trout raceways is able to remove tomocysts and reduce infection levels by up to 99.55% when compared to control groups. Notwithstanding their apparent efficacy, none of the management strategies described above have been adopted so far in a commercial fish farm context.

Despite these non-drug interventions, fish that are exposed to a certain level of *I. multifiliis* infection are able to acquire a protective immunity which can last from several months to a year (Hines and Spira, 1974; Burkart *et al.* 1990; Matthews, 1994). This acquired immunity has stimulated efforts towards the development of a vaccine against *I. multifiliis* which is in progress (Matthews, 2005; Sommerset *et al.* 2005; Dickerson, 2006).

## CONCLUSION

Currently, the most frequent method employed to control *I. multifiliis* infections in farm systems is the use of in-bath chemical treatments. Because of its asynchronous life cycle and continuous release into the water column of different stages (Lom and Dyková, 1992; Matthews, 2005), multiple applications are often required over long periods of time, notably during the summer months when water temperatures can rise rapidly. In addition, outbreaks can occur in the spring and autumn seasons during which sharp changes in water temperature can induce physiological stress, as seen in channel catfish pond culture (Noga, 2010). Such treatment regimes involve the use of large quantities of chemicals when the infections levels are high (e.g. formaldehyde and sodium chloride), leading to high costs and potentially high environmental impacts. Repeated or prolonged use of a single drug without rotation of treatment types is also likely to increase the probability of development of drug resistance in the targeted pathogen, as documented for bacterial and

copepod fish pathogens (Fallang *et al.* 2004; Lees *et al.* 2008; Heuer *et al.* 2009). While development of resistance by *I. multifiliis* has yet to be investigated, it is clear that drug resistance would act to increase the quantities of drug used and the environmental impacts of treatment.

In the present overview we have assessed the efficacy and practicality of a wide range of drug and non-drug strategies that are potentially available to be used in farm systems. However, there remain considerable difficulties in comparing efficacies between products, since no standardized methods are employed across the stakeholder community for culturing the parasite, assessing viability of the theront stage and infecting fish. The greatest current discrepancy in determining the efficacy of a treatment follows from the counting method employed for enumerating the trophont stage in *in vivo* studies. Some researchers only consider the trophonts present on skin scrapes or gills while others take into account direct observations of the number of visible trophonts present in skin, fins and gills. In addition to these methodological variations, there is the fact that different strains/genotypes of *I. multifiliis* can behave very differently in terms of infectivity (Elsayed *et al.* 2006; Swennes *et al.* 2007; Ling *et al.* 2009), host specificity and susceptibility to treatment (Straus and Meinelt, 2009; Straus *et al.* 2009). Hence, a chemical treatment demonstrated to successfully eliminate one strain might not exhibit the same efficacy when applied to treat a different one.

From this review, chemical treatments remain the principal method for controlling *I. multifiliis* infections in aquaculture, despite numerous attempts to develop and implement physical and farm management-based alternatives. With the introduction of a ban on the use of malachite green in food-fish and a likely future ban on the use of formaldehyde, options for effective drug treatment remain severely depleted. For these reasons, considerable research has been conducted to develop new drugs or screen existing compounds, both natural and synthesized, for efficaciousness against one or more stages of this parasite. New products, where deployed, will need to be derived from sustainable sources and of themselves be more environmentally friendly and more suitable for use in food-fish than previous compounds. As part of the attempt to reduce the use of drugs, new deployment strategies (e.g. extended low-dose treatments), management strategies helping to reduce initial infection levels (e.g. flow control), breeding fish for resistance and the development of DNA vaccines need to be considered.

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Table 1. Chemical treatments tested against infections of *Ichthyophthirius multifiliis* Fouquet, 1876(A compound is regarded as being partially effective if it kills 50–80%, and effective if it kills  $\geq 80\%$  of the stages under test. Mortality refers to the parasite stages unless otherwise stated.)

Compound	Dose	Host/parasite stage	Efficacy	Reference	
Acaprin (1, 3-di-6-quinolylurea)	<i>In vitro</i>	200 mg l <sup>-1</sup> for 2 h	Protomonts	Partially effective – 62.5% mortality after 1–2 h	Tojo-Rodriguez <i>et al.</i> (1994)
	<i>In vivo</i> – bath	200 mg l <sup>-1</sup> for 3 h	<i>Oncorhynchus</i>	60% of surviving protomonts develop normally Not effective – all trophonts developed normally †	Tojo-Rodriguez <i>et al.</i> (1994)
	In-feed	500 mg kg <sup>-1</sup> for 8 d	<i>mykiss</i>	Not effective – all trophonts developed normally †	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Acetic acid (4%)		40 g kg <sup>-1</sup> for 10 d		Not effective – no details	
	<i>In vivo</i> – bath	10 ml l <sup>-1</sup> for 3 min	<i>O. mykiss</i> <i>Salvelinus fontinalis</i> <i>Salmo trutta</i>	Partially effective – reduction of the number of trophonts on treated fish but no details given	Balta <i>et al.</i> (2008)
<i>Allium sativum</i> (garlic extract)	<i>In vitro</i>	0.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h	Theronts	Not effective – < 50% mortality	Buchmann <i>et al.</i> (2003)
		2.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h		Not effective – < 50% mortality	
		12.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h		Not effective – < 50% mortality	
		62.5 mg l <sup>-1</sup> for 1.5 and 3 h		Not effective – < 50% mortality	
		62.5 mg l <sup>-1</sup> for 15 h		Partially effective – > 50% mortality	
		312.5 mg l <sup>-1</sup> for 1.5 h		Not effective – < 50% mortality	
		312.5 mg l <sup>-1</sup> for 3 and 15 h		Partially effective – > 50% mortality	
1562.5 mg l <sup>-1</sup> for 3 and 15 h	Partially effective – > 50% mortality				
Amphotericin B (dissolved in Na-desoxycholate)	<i>In vitro</i>	30 mg l <sup>-1</sup> for 24 h	Tomocysts	Not effective – 13% mortality	Buchmann <i>et al.</i> (2003)
		117 mg l <sup>-1</sup> for 24 h		Partially effective – 53% mortality	
		570 mg l <sup>-1</sup> for 24 h		Effective – 100% mortality	
Amphotericin B (dissolved in Na-desoxycholate)	<i>In vitro</i>	0.25 mg l <sup>-1</sup> for 24 h	Adults**	Effective – 100% mortality after 24 h	Wahli <i>et al.</i> (1993)
		2.5 mg l <sup>-1</sup> for 24 h		Effective – 100% mortality after 1 h	
		0.25 mg l <sup>-1</sup> for 24 h	Tomocysts	Effective – 100% mortality after 24 h	
		2.5 mg l <sup>-1</sup> for 24 h		Effective – 100% mortality after 24 h	
		0.25 mg l <sup>-1</sup> for 3 h	Theronts	Effective – 100% mortality after 1 h	
		2.5 mg l <sup>-1</sup> for 3 h		Effective – 100% mortality after 5 min	
<i>In vivo</i> – bath	0.25 mg l <sup>-1</sup> – 2 × for 1 h 1st: day 9 p.i., 2nd: day 12 p.i.	<i>O. mykiss</i>	Not effective – no details	Wahli <i>et al.</i> (1993)	
Amprolium hydrochloride (1-[(4-amino-2-propyl-5-pyrimidinyl) methyl]-2-picolinium chloride hydrochloride) commercialised as Amprolmix	<i>In vitro</i>	20 mg l <sup>-1</sup> for 1 h	Protomonts	Not effective – 10% mortality	Shinn <i>et al.</i> (unpublished)
		50 mg l <sup>-1</sup> for 1 h		Not effective – 10% mortality	

	100 mg l <sup>-1</sup> for 1 h		Not effective – 90% mortality	
	200 mg l <sup>-1</sup> for 2 h	Protomonts	Not effective – 0% mortality after 2 h; protomonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
	1000 mg l <sup>-1</sup> for 48 h		Not effective – survival not affected	Farley and Heckmann (1980)
	100 mg l <sup>-1</sup> for 15 h	Tomocysts	Effective – 85% mortality	Shinn <i>et al.</i> (2001)
	100 mg l <sup>-1</sup> for 41 h		Effective – 90% mortality	
	20 mg l <sup>-1</sup> for 1 h	Theronts	Not effective – 22.4% mortality	Shinn <i>et al.</i> (unpublished)
<i>In vivo</i> – bath	50 mg l <sup>-1</sup> for 1 h		Not effective – 20.4% mortality	
	100 mg l <sup>-1</sup> for 1 h		Not effective – 22.3% mortality	Shinn <i>et al.</i> (2001)
	200 mg l <sup>-1</sup> for 3 h day 6 p.i.	<i>O. mykiss</i>	Not effective – all trophonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
In-feed	63 mg kg <sup>-1</sup> feed for 10 d prior inf.	<i>O. mykiss</i>	Partially effective – 77.6% reduction in trophont numbers	Shinn <i>et al.</i> (2003b)
	75 mg kg <sup>-1</sup> feed for 10 d p.i.		Not effective – 32.2% reduction in trophont numbers	
	75 mg kg <sup>-1</sup> feed for 10 d prior inf.		Partially effective – 63% reduction in trophont numbers	Shinn <i>et al.</i> (2001)
	104 mg kg <sup>-1</sup> feed for 10 d p.i.		Partially effective – 62% reduction in trophont numbers	Shinn <i>et al.</i> (2003b)
	1000 mg kg <sup>-1</sup> feed for 8 d p.i.	<i>O. mykiss</i>	Not effective – all trophonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
Amprol mix				
See entry for amprolium hydrochloride				
<i>Aeromonas sobria</i>				
<i>In vivo</i> – In-feed	10 <sup>8</sup> cells g <sup>-1</sup> feed for 14 d	<i>O. mykiss</i>	Effective – there was no mortality of treated fish	Pieters <i>et al.</i> (2008)
Aquahumin				
See entry for humic acid (10% solution)				
Ascorbate-2-phosphate (vitamin C)				
<i>In vivo</i> – In-feed	5000 mg kg <sup>-1</sup> feed for 9 d	<i>O. mykiss</i>	Partially effective but 2–16% of medicated fish died	Wahli <i>et al.</i> (1985)
	50 mg 200 kg <sup>-1</sup> feed	<i>O. mykiss</i>	Partially effective – reduction in trophont numbers but no details	Wahli <i>et al.</i> (1995)
	50 mg 2000 kg <sup>-1</sup> feed		Partially effective – reduction in trophont numbers but no details	
	1–3 g kg <sup>-1</sup> feed for 1 week–1 month	Not specified	Effective – no detail	Rahkonen and Koski (2002)
Ascorbate-2-phosphate (Vitamin C) + d-1-alpha-tocopheryl acetate (Vitamin E) complex diet				
<i>In vivo</i> – In-feed for 7 weeks	0 + 1.8 mg kg <sup>-1</sup> feed	<i>O. mykiss</i>	Not effective – 44% of medicated fish died	Walhi <i>et al.</i> (1998)
	4.3 + 771.0 mg kg <sup>-1</sup> feed		‘Effective’ but ~20% of medicated fish died	
	24.8 + 34.0 mg kg <sup>-1</sup> feed		Not effective – 62% of medicated fish died	
	27.5 + 776.0 mg kg <sup>-1</sup> feed		‘Effective’ but ~20% of medicated fish died	
	2065.0 + 2.5 mg kg <sup>-1</sup> feed		‘Effective’ but <20% of medicated fish died	
	2093.3 + 30.8 mg kg <sup>-1</sup> feed		‘Effective’ but ~20% of medicated fish died	
	2025.0 + 754.3 mg kg <sup>-1</sup> feed		‘Effective’ but <20% of medicated fish died	

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
Ascorbyl phosphate				
<i>In vivo</i> – In-feed	50 mg 2000 kg <sup>-1</sup> feed	<i>O. mykiss</i>	Partially effective – reduction in trophont numbers but no details	Wahli <i>et al.</i> (1995)
Baycox				
	See entry for toltrazuril			
Bithionol				
<i>In vivo</i> – In feed	40 g kg <sup>-1</sup> of feed for 10 d	<i>O. mykiss</i>	Not effective – 68% fish with high number of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Bronopol (2-bromo-2-nitropropane-1, 3-diol)				
<i>In vitro</i>	20 mg l <sup>-1</sup> for 30 min	Protomonts	Partially effective – 76·2% mortality	Shinn <i>et al.</i> (in press)
	50 mg l <sup>-1</sup> for 30 min		Effective – 97·2% mortality	
	100 mg l <sup>-1</sup> for 30 min		Effective – 100% mortality	
	20 mg l <sup>-1</sup> for 30 min	Tomocysts	Not effective – 3·3% mortality; tomocyst development delayed	Shinn <i>et al.</i> (in press)
	50 mg l <sup>-1</sup> for 30 min		Not effective – 10% mortality; tomocyst development delayed	
	0·1 mg l <sup>-1</sup> for 12 h	Theronts	Not effective – 7·15% mortality	Shinn <i>et al.</i> (in press)
	0·1 mg l <sup>-1</sup> for 24 h		Not effective – 31·55% mortality	
	0·1 mg l <sup>-1</sup> for 36 h		Not effective – 31·66% mortality	
	0·1 mg l <sup>-1</sup> for 48 h		Not effective – 18% mortality	
	0·25 mg l <sup>-1</sup> for 12 h		Not effective – 14·03% mortality	
	0·25 mg l <sup>-1</sup> for 24 h		Not effective – 30·95% mortality	
	0·25 mg l <sup>-1</sup> for 36 h		Not effective – 40·0% mortality	
	0·25 mg l <sup>-1</sup> for 48 h		Not effective – 34·84% mortality	
	0·5 mg l <sup>-1</sup> for 12 h		Not effective – 22·38% mortality	
	0·5 mg l <sup>-1</sup> for 24 h		Not effective – 38·77% mortality	
	0·5 mg l <sup>-1</sup> for 36 h		Not effective – 26·51% mortality	
	0·5 mg l <sup>-1</sup> for 48 h		Partially effective – 59·21% mortality	
	0·75 mg l <sup>-1</sup> for 12 h		Not effective – 8·88% mortality	
	0·75 mg l <sup>-1</sup> for 24 h		Not effective – 40·0% mortality	
	0·75 mg l <sup>-1</sup> for 36 h		Not effective – 26·51% mortality	
	0·75 mg l <sup>-1</sup> for 48 h		Partially effective – 68·57% mortality	
	1 mg l <sup>-1</sup> for 12 h		Not effective – 13·88% mortality	
	1 mg l <sup>-1</sup> for 24 h		Not effective – 37·93% mortality	
	1 mg l <sup>-1</sup> for 36 h		Not effective – 44·44% mortality	
	1 mg l <sup>-1</sup> for 48 h		Partially effective – 75·0% mortality	
	1 mg l <sup>-1</sup> for 12 h		Partially effective – 70·84% mortality	
	1 mg l <sup>-1</sup> for 24 h		Effective – 100% mortality	
	20 mg l <sup>-1</sup> for 30 min		Not effective – 18·5% mortality	Shinn <i>et al.</i> (in press)

	0 mg l <sup>-1</sup> for 30 min		Not effective – 31·3% mortality	
	100 mg l <sup>-1</sup> for 30 min		Partially effective – 51·7% mortality	
	100 mg l <sup>-1</sup> for 30 min		Effective – 50% mortality; all dead after 43 h	Shinn <i>et al.</i> (in press)
<i>In vivo</i> – bath	1 mg l <sup>-1</sup> for 36 d p.i.	<i>O. mykiss</i>	Not effective – number of trophonts increased on treated groups	Picón-Camacho <i>et al.</i> (in press a)
	2 mg l <sup>-1</sup> for 36 d p.i.		Effective – 46% reduction in trophont numbers on the 2nd wave of infection; 83% reduction in trophont numbers on 3rd wave	
	2 mg l <sup>-1</sup> 24 h prior inf. and 72 h p.i.		Partially effective – 35–48% trophont reduction on treated groups of infection; 97% reduction in trophont numbers on 3rd wave	
	5 mg l <sup>-1</sup> for 36 d p.i.		Effective – 83% reduction in trophont numbers on the 2nd wave	
	50 mg l <sup>-1</sup> daily for 1 h for 10 d	<i>O. mykiss</i>	Not effective – no reduction in trophont numbers on treated fish	Shinn <i>et al.</i> (2003a)
	50 mg l <sup>-1</sup> for 30 min for 10 d (alternate days)	<i>O. mykiss</i>	Not effective – no significant reduction in trophont numbers	Shinn <i>et al.</i> (unpublished)
	100 mg l <sup>-1</sup> daily for 30 min for 10 d		Not effective – 33·3% reduction in trophont numbers	Shinn <i>et al.</i> (2003a)
	100 mg l <sup>-1</sup> daily for 30 min for 10 d		Effective – 81·1% reduction in trophont numbers	
	100 mg l <sup>-1</sup> for 1 h on day 7		Not effective – no reduction in trophont numbers on treated fish	
<i>Brochothrix thermosphacta</i>				
<i>In vivo</i> – In-feed	10 <sup>10</sup> cells g <sup>-1</sup> feed for 14 d	<i>O. mykiss</i>	Not effective – 98% mortality on treated fish	Pieters <i>et al.</i> (2008)
Cadmium chloride				
<i>In vitro</i>	0·005 ppm for 18–22 h	Theronts	Not effective – 0% mortality	Bisharyan <i>et al.</i> (2003)
	0·05 ppm for 10 min, 1 and 5 h		Not effective – 0% mortality	
	0·05 ppm for 18–22 h		Effective – 50–90% mortality	
	0·5 ppm for 10 min and 1 h		Not effective – 0% mortality	
	0·5 ppm for 5 h		Effective – 50–90% mortality	
	0·5 ppm for 18–22 h		Effective – 100% mortality	
	5 ppm for 10 min		Not effective – reduction in swimming velocity	
	5 ppm for 1 h		Effective – 50–90% mortality	
	5 ppm for 5 h		Effective – 100% mortality	
	50 ppm for 10 min		Not effective – reduction in swimming velocity	
	50 ppm for 1 h		Effective – 100% mortality	
	500 ppm for 10 min		Effective – 100% mortality	
<i>Carica papaya</i> (papaya)				
<i>In vitro</i>	100 mg l <sup>-1</sup> for 3 h	Trophonts*	Not effective – 0% mortality	Ekamen <i>et al.</i> (2004)
	100 mg l <sup>-1</sup> for 6 h		Not effective – 10% mortality	
	150 mg l <sup>-1</sup> for 3 h		Not effective – 5% mortality	
	150 mg l <sup>-1</sup> for 6 h		Partially effective – 55% mortality	
	200 mg l <sup>-1</sup> for 3 h		Not effective – 25% mortality	
	200 mg l <sup>-1</sup> for 6 h		Effective – 100% mortality	
	250 mg l <sup>-1</sup> for 3 h		Effective – 90% mortality	

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
<i>In vivo</i> – bath	250 mg l <sup>-1</sup> for 6 h	<i>Carassius a. auratus</i>	Effective – 100% mortality	Ekamen <i>et al.</i> (2004)
	200 mg l <sup>-1</sup> for 92 h		Effective – 89% reduction in trophont number on the skin and fins	
	250 mg l <sup>-1</sup> for 92 h		Effective – 92% reduction in trophont number on the skin and fins	
Chloramine-T (sodium p-toluenesulfonchloramide)				
<i>In vitro</i>	5 mg l <sup>-1</sup> for 1 h	Protomonts	Effective – 100% mortality	Shinn <i>et al.</i> (2001)
	50 mg l <sup>-1</sup> for 15 min	Theronts	Effective – 100% mortality	
<i>In vivo</i> – bath	1 mg l <sup>-1</sup> daily for 11 d	<i>I. punctatus</i>	Not effective – 100% mortality on treated fish	Tieman and Goodwin (2001)
	2 mg l <sup>-1</sup> daily for 11 d	<i>O. mykiss</i> <i>S. fontinalis</i> <i>S. trutta</i>	Not effective – 100% mortality on treated fish	
	5 mg l <sup>-1</sup> daily for 11 d		Not effective – 100% mortality on treated fish	
	5, 10 and 15 mg l <sup>-1</sup> for 1 h		Not effective – no details	Balta <i>et al.</i> (2008)
	10 mg l <sup>-1</sup> for 6 h	<i>O. mykiss</i>	Not effective – no reduction in trophont numbers	
	14 mg l <sup>-1</sup> 3 times a week for 3 weeks	<i>Salmo salar</i>	Not effective – parasite numbers increased over infection period	Shinn <i>et al.</i> (unpublished)
	16 mg l <sup>-1</sup> 3 times a week for 2 weeks	<i>O. mykiss</i>	Trial inconclusive – low parasite numbers across all groups	Rintamäki-Kinnunen <i>et al.</i> (2005a)
	100 mg l <sup>-1</sup> for 30 min daily over 10 d period		Effective – 93% reduction in trophont numbers	Rintamäki-Kinnunen <i>et al.</i> (2005a)
	100 mg l <sup>-1</sup> for 1 h on day 7 p.i.		Not effective – 14% reduction in trophont numbers	Shinn <i>et al.</i> (2003a)
	100 mg l <sup>-1</sup> for 6 h on day 7 p.i.	<i>O. mykiss</i>	Not effective – no reduction in trophont numbers	Rahkonen and Koski (2002)
100 mg l <sup>-1</sup> daily for 30 min for 10 d	Effective – 90.5% reduction in trophont numbers			
100 mg l <sup>-1</sup> daily for 30 min for 10 d	Effective – 97.3% reduction in trophont numbers			
100 mg l <sup>-1</sup> for 30 min 4 times over 10 d	Partially effective – significant reduction in 50% of the tanks			
Chloramine-T (sodium p-toluenesulfonchloramide) + formaldehyde				
<i>In vivo</i> – bath	10 + 100 mg l <sup>-1</sup> 3 times a week for 4 weeks	<i>S. salar</i>	Not effective – no details	Rintamäki-Kinnunen <i>et al.</i> (2005a)
	8 + 125 mg l <sup>-1</sup> 3 times a week for 5 weeks		Effective – no details	
Chloramphenicol (D (-) threo-2,2-dichloro-N-[hydroxy- $\alpha$ (hydroxymethyl)-p-nitrophenethyl] acetamide)				
<i>In vitro</i>	100 mg l <sup>-1</sup> for 3 h	Theronts	Not effective – no details	Wahli <i>et al.</i> (1993)
	100 mg l <sup>-1</sup> for 24 h	Adults**	Not effective – no details	
	100 mg l <sup>-1</sup> for 24 h	Tomocysts	Not effective – no details	

Chloroquine <i>In vitro</i>	200 mg l <sup>-1</sup> for 2 h	Protomonts	Partially effective – 50% mortality after 2 h.	Tojo-Rodriguez <i>et al.</i> (1994)
<i>In vivo</i> – bath	200 mg l <sup>-1</sup> for 3 h	<i>O. mykiss</i>	Protomonts surviving develop normally Not effective – all trophonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
In-feed	1000 mg kg <sup>-1</sup> feed for 8 d 40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – all trophonts developed normally Not effective – high numbers of trophonts on all treated fish	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Chlortetracycline <i>In vitro</i>	100 mg l <sup>-1</sup> for 24 h 100 mg l <sup>-1</sup> for 3 h 100 mg l <sup>-1</sup> for 24 h	Adults** Theronts Tomocysts	Effective – 100% mortality after 1 h Effective – 100% mortality after 5 min Effective – 100% mortality after 24 h	Wahli <i>et al.</i> (1993)
<i>In vivo</i> – bath	100 mg l <sup>-1</sup> – 2 × for 1 h	<i>O. mykiss</i>	Not effective – no details	Wahli <i>et al.</i> (1993)
In-feed	1st: day 9 p.i, 2nd: day 12 p.i 75 mg kg <sup>-1</sup> fish for 10 d		Not effective – no details	
Citroicide <i>In vivo</i> – In-feed	10 mg kg <sup>-1</sup> feed for 7 d p.i.	<i>O. mykiss</i>	Not effective ~ 40% reduction in trophont numbers	Shinn <i>et al.</i> (2005)
Citrox BC <i>In vivo</i> – In-feed	10 mg kg <sup>-1</sup> feed for 7 d p.i.	<i>O. mykiss</i>	Not effective – 25% reduction in trophont numbers	Shinn <i>et al.</i> (2005)
Clopidol (3,5-dichloro-2,6-dimethyl-4-pyridinol) commercialised as Coyden <i>In vivo</i> – In-feed	65 mg kg <sup>-1</sup> feed for 10 d prior inf. 92 mg kg <sup>-1</sup> feed for 10 d prior inf. 72 mg kg <sup>-1</sup> feed for 10 d prior inf.	<i>O. mykiss</i>	Not effective – 35.2% reduction in trophont numbers Not effective – 20.1% reduction in trophont numbers Not effective – 35.6% reduction in trophont numbers	Shinn <i>et al.</i> (2003a) Shinn <i>et al.</i> (unpublished)
Copper sulphate (CuSO <sub>4</sub> ) <i>In vitro</i>	55 µg l <sup>-1</sup> for 24 h 110 µg l <sup>-1</sup> for 24 h 160 µg l <sup>-1</sup> for 24 h	Tomites	Not effective – 100% manage to infect <i>C. auratus</i> Not effective – 90% manage to infect <i>C. auratus</i> Effective – tomites inactive but 20% manage to infect <i>C. auratus</i> Effective – 100% mortality Effective – 100% mortality	Ling <i>et al.</i> (1993)
	255 µg l <sup>-1</sup> for 24 h 220 µg l <sup>-1</sup> for 24 h			
	0.027 mg Cu l <sup>-1</sup> as CuSO <sub>4</sub> for 3 h (alkalinity 48 mg l <sup>-1</sup> ) 0.028 mg nonchelated liquid CuSO <sub>4</sub> l <sup>-1</sup> for 3 h (alkalinity 48 mg l <sup>-1</sup> ) 0.027 mg Cu l <sup>-1</sup> as CuSO <sub>4</sub> for 3 h (alkalinity 48 mg l <sup>-1</sup> ) 0.05 mg Cu l <sup>-1</sup> as CuSO <sub>4</sub> for 3 h (alkalinity 48 mg l <sup>-1</sup> ) 0.05 mg nonchelated liquid CuSO <sub>4</sub> l <sup>-1</sup> for 2 h (alkalinity 48 mg l <sup>-1</sup> )	Theronts	Partially effective – 50% mortality Partially effective – 50% mortality Partially effective – 50% mortality Effective – 95% mortality Effective – 95% mortality	Goodwin and Straus (2006)

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
	0.056 Cu l <sup>-1</sup> as CuSO <sub>4</sub> for 3 h (alkalinity 243 mg l <sup>-1</sup> )		Partially effective – 50% mortality	
	0.053 mg nonchelated liquid CuSO <sub>4</sub> l <sup>-1</sup> for 3 h (alkalinity 243 mg l <sup>-1</sup> )		Partially effective – 50% mortality	
	0.075 mg Cu l <sup>-1</sup> as CuSO <sub>4</sub> for 3 h (alkalinity 243 mg l <sup>-1</sup> )		Effective – ~ 95% mortality	
	0.075 mg nonchelated liquid CuSO <sub>4</sub> l <sup>-1</sup> for 3 h (alkalinity 243 mg l <sup>-1</sup> )		Effective – ~ 95% mortality	
	<0.25 mg l <sup>-1</sup> Cu l <sup>-1</sup> as CuSO <sub>4</sub> or nonchelated liquid CuSO <sub>4</sub> l <sup>-1</sup> up to 1 h (alkalinity 48 and 243 mg l <sup>-1</sup> )		Not effective – no reduction in theront survival	
<i>In vivo</i> – bath	0.05 mg l <sup>-1</sup> for 10 d	<i>I. punctatus</i>	Not effective – 100% of infected fish died on day 10	Schlenk <i>et al.</i> (1998)
	0.05 mg l <sup>-1</sup> daily for 17 d	<i>B. bidyanus</i>	Not effective – treated fish remained infected	Rowland <i>et al.</i> (2009)
	0.1 mg l <sup>-1</sup> for 10 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish	Schlenk <i>et al.</i> (1998)
	0.1 mg l <sup>-1</sup> for 8 d		Not effective – all treated fish died on day 13	
	0.1 mg l <sup>-1</sup> daily for 17 d	<i>B. bidyanus</i>	Effective – treated fish free of trophonts	Rowland <i>et al.</i> (2009)
	0.20 mg l <sup>-1</sup> daily for 14 d		Effective – treated fish free of trophonts	
	0.25 mg l <sup>-1</sup> daily for 14 d		Effective – treated fish free of trophonts	
	255 µg Cu <sup>+2</sup> l <sup>-1</sup> for 1 week	<i>C. auratus</i>	‘Effective’ but 11.1% of infected fish died	Ling <i>et al.</i> (1993)
	255 µg Cu <sup>+2</sup> l <sup>-1</sup> for 2 weeks		‘Effective’ but 33.3% of infected fish died	
	255 µg Cu <sup>+2</sup> l <sup>-1</sup> for 3 weeks		Not effective – 44.4% of infected fish died	
	288 µg Cu <sup>+2</sup> l <sup>-1</sup> for 15 min		Not effective – 100% of infected fish died	
	288 µg Cu <sup>+2</sup> l <sup>-1</sup> for 30 min		Not effective – 66.70% of infected fish died	
	288 µg Cu <sup>+2</sup> l <sup>-1</sup> for 60 min		Not effective – 44.4% of infected fish died	
	288 µg Cu <sup>+2</sup> l <sup>-1</sup> for 2 h		‘Effective’ but 11.1% of infected fish died	
(static tanks)	0.4 mg l <sup>-1</sup> for 8 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish	Schlenk <i>et al.</i> (1998)
	0.5 mg l <sup>-1</sup> for 10 d		Effective – no trophonts found on treated fish	
	0.5 mg l <sup>-1</sup> daily for 17 d	<i>B. bidyanus</i>	Not effective – 100% of infected fish died†	Rowland <i>et al.</i> (2009)
	0.8 mg l <sup>-1</sup> for 8 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish	Schlenk <i>et al.</i> (1998)
	1 mg l <sup>-1</sup> for 10 d		Effective – no trophonts found on treated fish	
	1 mg l <sup>-1</sup> daily for 17 d	<i>B. bidyanus</i>	Not effective – 100% of infected fish died†	Rowland <i>et al.</i> (2009)
	1 mg l <sup>-1</sup> daily for 11 d (alkalinity 68 mg l <sup>-1</sup> )	<i>I. punctatus</i>	Not effective – 80–100% of the treated infected fish died	Tieman and Goodwin (2001)
	1 mg l <sup>-1</sup> daily for 11 d (alkalinity 180 and 250 mg l <sup>-1</sup> )		Not effective – 80% of the treated infected fish died	
	1 mg l <sup>-1</sup> alternate day for 11 d (alkalinity 150 mg l <sup>-1</sup> )		Not effective – all the treated infected fish died	
	1.1 mg l <sup>-1</sup> (8 d trial) Treatment: d1, 3, 5 and 7	<i>I. punctatus</i>	‘Effective’ – 15% of the treated infected fish died	Straus (2008)
	1.2 mg l <sup>-1</sup> for 8 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish	Schlenk <i>et al.</i> (1998)
1.5 mg l <sup>-1</sup> for 10 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish		

(static tanks)	1.5 mg l <sup>-1</sup> daily for 11 d (alkalinity 68 mg l <sup>-1</sup> )	<i>I. punctatus</i>	Not effective – 40% of the treated infected fish died (treated fish remain infected)	Tieman and Goodwin (2001)
	1.5 mg l <sup>-1</sup> daily for 11 d (alkalinity 180 and 250 mg l <sup>-1</sup> )		Not effective – all the treated infected fish died	
	1.5 mg l <sup>-1</sup> alternate day for 11 d (alkalinity 50 mg l <sup>-1</sup> )		Not effective – all the treated infected fish died	
	1.6 mg l <sup>-1</sup> for 8 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish	Schlenk <i>et al.</i> (1998)
	2.0 mg l <sup>-1</sup> for 10 d	<i>I. punctatus</i>	Effective – no trophonts found on treated fish	Schlenk <i>et al.</i> (1998)
	2.2 mg l <sup>-1</sup> (8 d trial)	<i>I. punctatus</i>	Not effective – 81.7% of the treated infected fish died	Straus (2008)
	Treatment: d1, 3, 5 and 7			
	3.3 mg l <sup>-1</sup> (8 d trial)		Not effective – 98.3% of the treated infected fish died	
	Treatment: d1, 3, 5 and 7			
	4.4 mg l <sup>-1</sup> (8 d trial)		Not effective – 96.7% of the treated infected fish died	
	Treatment: d1, 3, 5 and 7			
Coyden				
	See entry clopidol (3, 5-dichloro-2, 6-dimethyl-4-pyridinol)			
Decoquinat				
<i>In vivo</i> – In-feed	100 mg kg <sup>-1</sup> feed 10 d prior to infection	<i>O. mykiss</i>	Not effective – no reduction in trophont numbers on treated fish	Shinn <i>et al.</i> (2003a)
Desirox				
	See entry for peracetic acid + acetic acid + hydrogen peroxide based formulations (13% PAA + 20% AA + 20% H <sub>2</sub> O <sub>2</sub> )			
Detarox				
	See entry for peracetic acid + acetic acid + hydrogen peroxide based formulations			
Diethylcarbamazine				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Partially effective – lower trophont counts observed in skin scrapes (60% of treated fish free of infection)	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Dimetridazole (DMZ)				
<i>In vitro</i>	5 mg l <sup>-1</sup> for 3 h	Theronts	Not effective – no details	Wahli <i>et al.</i> (1993)
	5 mg l <sup>-1</sup> for 24 h	Adults**	Not effective – no details	
	5 mg l <sup>-1</sup> for 24 h	Tomocysts	Not effective – no details	
<i>In vivo</i> – bath	28 mg/feed mixed with lactate (Emetryl®) for 10 d	<i>O. mykiss</i>	Effective – no visible signs of infection by day 7 p.i.	Rapp (1995)
In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – 85% of treated fish have high numbers of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Diminazine aceturate				
<i>In vitro</i>	100 mg l <sup>-1</sup> for 2 h	Protomonts	Partially effective – 75% mortality after 2 h	Tojo-Rodriguez <i>et al.</i> (1994)
	200 mg l <sup>-1</sup> for 2 h		Effective – 100% mortality after 45 min	
<i>In vivo</i> – bath	100 mg l <sup>-1</sup> for 3 h	<i>O. mykiss</i>	Not effective – all protomonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
In-feed	1000 mg kg <sup>-1</sup> feed for 8 d		Not effective – all protomonts developed normally	
Elancoban	See entry for monensin sodium			
Emetryl ®	See entry for dimetrazole			
Enheptin (2-amino-5-nitrothiazole) diluted in ethyl alcohol and acetone				
<i>In vitro</i>	100 mg l <sup>-1</sup> for 2 min	Trophozoites*	Effective – 100% mortality after 2 h post exposure	Post and Vesley (1983)
Formaldehyde				
<i>In vitro</i>	10 µl l <sup>-1</sup> for 10 h	Trophonts*	Not effective – 7% mortality	Lahnsteiner and Weismann (2007)
	45 µl l <sup>-1</sup> for 10 h		Effective – 7% mortality, no viable theronts produced	
	55 µl l <sup>-1</sup> for 10 h		Effective – 100% mortality	
	25 mg l <sup>-1</sup> for 24 h	Adults**	Effective – 100% mortality after 24 h	Wahli <i>et al.</i> (1993)
	32 mg l <sup>-1</sup> for <2 h 30 min	Protomonts	Effective – 100% mortality	Heinecke and Buchmann (2009)
	64 mg l <sup>-1</sup> for <1 h		Effective – 100% mortality	
	100 mg l <sup>-1</sup> for 24 h	Adults**	Effective – 100% mortality after 1 h	Wahli <i>et al.</i> (1993)
	128 mg l <sup>-1</sup> for <15 min	Protomonts	Effective – 100% mortality	Heinecke and Buchmann (2009)
	25 mg l <sup>-1</sup> for 24 h	Tomocysts	Effective – 100% mortality after 24 h	Wahli <i>et al.</i> (1993)
	100 mg l <sup>-1</sup> for 24 h		Effective – 100% mortality after 24 h	
	8 mg l <sup>-1</sup> for 2 h 30 min (21–22 °C)	Theronts	Effective – 100% mortality	Heinecke and Buchmann (2009)
	8 mg l <sup>-1</sup> for 5 h (11–12 °C)		Effective – 100% mortality	
	10 mg l <sup>-1</sup> for 1 h		Not effective – ~ 5% mortality	Shinn <i>et al.</i> (2005)
	16 mg l <sup>-1</sup> for ~ 2 h (11–12 °C)		Effective – 100% mortality	Heinecke and Buchmann (2009)
	16 mg l <sup>-1</sup> for ~ 1 h 5 min (21–22 °C)		Effective – 100% mortality	
	25 mg l <sup>-1</sup> for 3 h		Effective – 100% mortality after 30 min	Wahli <i>et al.</i> (1993)
	32 mg l <sup>-1</sup> for ~ 1 h 5 min (11–12 °C)		Effective – 100% mortality	Heinecke and Buchmann (2009)
	32 mg l <sup>-1</sup> for ~ <50 min (21–22 °C)		Effective – 100% mortality	
	50 mg l <sup>-1</sup> for 1 h		Not effective – ~ 10% mortality	Shinn <i>et al.</i> (2005)
	64 mg l <sup>-1</sup> for <50 min (11–12 °C)		Effective – 100% mortality	Heinecke and Buchmann (2009)
	64 mg l <sup>-1</sup> for 15 min (21–22 °C)		Effective – 100% mortality	
	100 mg l <sup>-1</sup> for 1 h		Not effective – ~ 3% mortality	Shinn <i>et al.</i> (2005)
	100 mg l <sup>-1</sup> for 3 h		Effective – 100% mortality after 30 min	Wahli <i>et al.</i> (1993)

<i>In vivo</i> – bath	200 mg l <sup>-1</sup> for 1 h	<i>O. mykiss</i>	Not effective – ~ 40% mortality	Shinn <i>et al.</i> (2005)
	10 µl l <sup>-1</sup> for 6 h for 5 d (18 °C, 24 h intervals)		Not effective – 0% survival of treated fish on d1 and 3	Lahnsteiner and Weismann (2007)
	40 µl l <sup>-1</sup> for 4 h for 5 d (18 °C, 24 h intervals)	<i>C. carpio</i>	Not effective – 30% survival of treated fish on d1; 0% survival on d 3	Lahnsteiner and Weismann (2007)
	80 µl l <sup>-1</sup> for 1 h for 5 d (18 °C, 24 h intervals)		Effective – 50% survival on treated fish on d1 and 3; no trophonts seen on fish on d1 and 3	
	80 µl l <sup>-1</sup> for 2 h for 5 d	<i>O. mykiss</i>	Effective – all treated fish survived; low number of trophonts on d1 and 3	Lahnsteiner and Weismann (2007)
	110 µl l <sup>-1</sup> for 2 h for 5 d		Effective – all treated fish survived; no trophonts on d1 and 3	
	110 µl l <sup>-1</sup> for 1 h for 5 d (18 °C, 24 h intervals)	<i>O. mykiss</i>	Effective – 90% survival of treated fish on d1 and 3; no trophonts on d1 and 3	Lahnsteiner and Weismann (2007)
	110 µl l <sup>-1</sup> for 1 h for 5 d (10 °C, 48 h intervals)		Effective – 100% survival of treated fish on d1 and 3; no trophonts on d1 and 3	
	110 µl l <sup>-1</sup> for 1 h for 5 d (18 °C, 24 h intervals)	<i>O. mykiss</i>	Effective – 100% survival of treated fish on d1 and 3; no trophonts on d1 and 3	Lahnsteiner and Weismann (2007)
	110 µl l <sup>-1</sup> for 1 h for 5 d (18 °C, 48 h intervals)		Not effective – 50% and 10% survival of treated fish on d1 and 3; heavy infections on d1 and 3	
	110 µl l <sup>-1</sup> for 1 h for 5 d (25 °C, 24 h intervals)	<i>O. mykiss</i>	Not effective – 0% survival of treated fish on d1 and 3; heavy infections on d1 and 3	Lahnsteiner and Weismann (2007)
	110 µl l <sup>-1</sup> for 12 h (25 °C)		Not effective – 100% and 10% survival of treated fish on d1 and 3; moderate and heavy infections on d1 and 3	
	110 µl l <sup>-1</sup> for 3 × 1 h for 5 d (25 °C, 24 h intervals)	<i>O. mykiss</i>	Not effective – 70% and 0% survival of treated fish on d1 and 3; Moderate infection on d1	Lahnsteiner and Weismann (2007)
	110 µl l <sup>-1</sup> for 5 × 1 h for 5 d (25 °C, 24 h intervals)		Not effective – 30% and 0% survival of treated fish on d1 and 3; moderate infection on d1	
	110 µl l <sup>-1</sup> for 7 × 1 h for 5 d (25 °C, 24 h intervals)	<i>O. mykiss</i>	Not effective – 0% and 0% survival of treated fish on d1 and 3; heavy infection on d1	Lahnsteiner and Weismann (2007)
	110 µl l <sup>-1</sup> for 12 h (18 °C)		Not effective – 100% and 10% survival of treated fish on d1 and 3 medium and very heavy infections on d1 and 3	
	110 µl l <sup>-1</sup> for 3 × 1 h for 5 d (18 °C, 24 h intervals)	<i>O. mykiss</i>	Not effective – 100% and 40% survival of treated fish on d1 and 3; low and heavy infections on d1 and 3	Lahnsteiner and Weismann (2007)
110 µl l <sup>-1</sup> for 5 × 1 h for 5 d (18 °C, 24 h intervals)	Effective – 100% survival of treated fish on d1 and 3; no infection on d1 and 3			
110 µl l <sup>-1</sup> for 7 × 1 h for 5 d (18 °C, 24 h intervals)	<i>O. mykiss</i>	Effective – 100% survival of treated fish on d1 and 3; no infection on d1 and 3	Lahnsteiner and Weismann (2007)	
0.1, 0.15 and 0.2 ml l <sup>-1</sup> for 1 h		Effective – reduction in the number of trophonts on treated fish		
	<i>S. fontinalis</i>			
	<i>S. trutta</i>			

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
	10 mg l <sup>-1</sup> for 17 d	<i>B. bidyanus</i>	Not effective – all treated infected fish died	Rowland <i>et al.</i> (2009)
	20 mg l <sup>-1</sup> for 17 d		Not effective – all treated fish still infected	
	25 mg l <sup>-1</sup> – 2 × for 1 h	<i>O. mykiss</i>	Not effective – not specified but fish survival compromised	Wahli <i>et al.</i> (1993)
(static tanks)	1st: day 9 p.i, 2nd: day 12 p.i 25 mg l <sup>-1</sup> for 4 h for 4 d week <sup>-1</sup>	<i>I. punctatus</i>	Not effective – 40–70% of treated infected fish died	Bodensteiner <i>et al.</i> (2000)
	25 mg l <sup>-1</sup> alternate days for 20 d	<i>I. punctatus</i>	Not effective – all treated infected fish died	Tieman and Goodwin (2001)
	25 mg l <sup>-1</sup> daily for 20 d		Partially effective – 20–60% of treated infected fish died	
	25 mg l <sup>-1</sup> 3–4 times a week for 6 weeks	<i>S. salar</i>	Not effective – parasite load increased on treated fish	Rintamäki-Kinnunen <i>et al.</i> (2005b)
	25 mg l <sup>-1</sup> 3–4 times a week for 6 weeks	<i>S. trutta</i>	Not effective – parasite load increased on treated fish	Rintamäki-Kinnunen <i>et al.</i> (2005b)
	30 mg l <sup>-1</sup> for 17 d	<i>B. bidyanus</i>	Effective – no trophonts found on treated fish	Rowland <i>et al.</i> (2009)
	50 mg l <sup>-1</sup> alternate day for 20 d	<i>I. punctatus</i>	Not effective – all treated infected fish died	Tieman and Goodwin (2001)
	50 mg l <sup>-1</sup> daily for 20 d		Partially effective – 20–60% of treated infected fish died	
	50 mg l <sup>-1</sup> 3–4 times a week for 6 weeks	<i>S. salar</i>	Not effective – parasite load increased on treated fish	Rintamäki-Kinnunen <i>et al.</i> (2005b)
	50 mg l <sup>-1</sup> 3–4 times a week	<i>S. trutta</i>	Not effective – parasite load increased on treated fish	
	100 mg l <sup>-1</sup> – 2 × for 1 h	<i>O. mykiss</i>	Not effective – not specified but fish survival compromised	Wahli <i>et al.</i> (1993)
(static tanks)	1st: day 9 p.i, 2nd: day 12 p.i 100 mg l <sup>-1</sup> daily for 20 d	<i>I. punctatus</i>	Not effective – all treated infected fish died	Tieman and Goodwin (2001)
(flow through)	100 mg l <sup>-1</sup> alternate day for 20 d 60 – 250 mg l <sup>-1</sup> for 20 min- 1 h	Not specified	Not effective – all treated infected fish died † 'Effective' – efficacy though not specified	Rahkonen and Koski (2002)
Formaldehyde + Desirox (13% peracetic acid, 20% acetic acid and 20% hydrogen peroxide)				
<i>In vivo</i> – bath	25 + 10 mg l <sup>-1</sup> 3–4 times a for 4 weeks week	<i>S. salar</i>	'Effective' – parasite load reduced on treated fish	Rintamäki-Kinnunen <i>et al.</i> (2005b)
	50 + 10 mg l <sup>-1</sup> 3–4 times a week for 4 weeks		'Effective' – parasite load reduced on treated fish	
	100 + 10 mg l <sup>-1</sup> 3 times a week for 4 weeks	<i>S. salar</i>	Trial inconclusive – details missing	Rintamäki-Kinnunen <i>et al.</i> (2005a)
	123 + 8 mg l <sup>-1</sup> 4 times a week for 5 weeks		Not effective – parasite load increased on treated fish	Rintamäki-Kinnunen <i>et al.</i> (2005a)

Formaldehyde + hydrogen peroxide <i>In vivo</i> – bath	100 + 100 mg l <sup>-1</sup> 3 times a week for 3 weeks		Trial inconclusive – details missing	Rintamäki-Kinnunen <i>et al.</i> (2005a)
Formaldehyde + malachite green <i>In vitro</i>	25 + 0.1 mg l <sup>-1</sup> for 24 h 100 + 0.4 mg l <sup>-1</sup> for 24 h 25 + 0.1 mg l <sup>-1</sup> for 24 h 100 + 0.4 mg l <sup>-1</sup> for 24 h 25 + 0.1 mg l <sup>-1</sup> for 3 h 100 + 0.4 mg l <sup>-1</sup> for 3 h	Adults**  Tomocysts  Theronts	Effective – 100% mortality after 24 h Effective – 100% mortality after 30 min Effective – 100% mortality after 5 min	Wahli <i>et al.</i> (1993)
<i>In vivo</i> – bath	25 + 0.05 mg l <sup>-1</sup> 25 + 0.1 mg l <sup>-1</sup> – 2 × for 1 h  1st: day 9 p.i, 2nd: day 12 p.i 100 + 0.4 mg l <sup>-1</sup> – 2 × for 1 h  1st: day 9 p.i, 2nd: day 12 p.i 225 + 0.83 mg l <sup>-1</sup> for 3 times a week <i>S. salar</i> for 3 weeks 225 + 0.83 mg l <sup>-1</sup> for 3 times a week for 2 weeks	<i>Cichla ocellaris</i> <i>O. mykiss</i>	'Effective' – efficacy not specified Partially effective against the parasites – efficacy not specified  Partially effective against the parasites – efficacy not specified	Guest (1983) Wahli <i>et al.</i> (1993)
Furacin ([5-nitrofuranyl methylideneamino] urea) <i>In vitro</i>	100 mg l <sup>-1</sup> for 2 min	Trophozoites*	Effective – 30% mortality after 12 h, 80% after 24 h post exposure	Post and Vesley (1983)
Furazolidone (mixed with ethanol) <i>In vitro</i>	100 mg l <sup>-1</sup> for 24 h 100 mg l <sup>-1</sup> for 24 h 100 mg l <sup>-1</sup> for 3 h	Adults** Tomocysts Theronts	Not effective – no details Effective – 100% mortality after 24 h Not effective – no details	Wahli <i>et al.</i> (1993)
<i>In vivo</i> – bath	25 mg l <sup>-1</sup> – 2 × for 1 h 1st: day 9 p.i, 2nd: day 12 p.i	<i>O. mykiss</i>	Not effective – no details	Wahli <i>et al.</i> (1993)
In-feed	50 mg kg <sup>-1</sup> fish for 10 d		Not effective – no details	
Furoxone (3-[(5-nitrofuranyl methylideneamino)-1,3-oxazolidin-2-one] diluted in ethyl alcohol and acetone) <i>In vitro</i>	100 mg l <sup>-1</sup> for 2 min	Trophozoites*	Not effective – 0% mortality after 24 h post exposure	Post and Vesley (1983)
β-Glucan (from <i>Saccharomyces cerevisiae</i> ) <i>In vivo</i> – In-feed	0.2% for 14 d prior inf.  0.2% for 35 d prior inf.	<i>O. mykiss</i>	Not effective – 14% trophont reduction  Not effective – 18% trophont reduction	Lauridsen and Buchmann (2010)
HbβP-1 (peptide from the β-haemoglobin peptide family) <i>In vitro</i>	12.5 μg ml <sup>-1</sup> for 5 min 21 s 12.5 μg ml <sup>-1</sup> for 1 min 35 s 12.5 μg ml <sup>-1</sup> for 2 min 50 s 25 μg ml <sup>-1</sup> for 6 min 36 s 25 μg ml <sup>-1</sup> for 1 min 54 s 25 μg ml <sup>-1</sup> for 4 min 14 s	Trophonts*(323 μm) (222 μm) (500 μm) (323 μm) (231 μm) (519 μm)	Effective – 100% mortality Effective – 100% mortality	Ullal and Noga (2010)

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
Humic acid (10% solution) commercially sold as Aquahumin	50 $\mu\text{g ml}^{-1}$ for 4 min 3 s	(323 $\mu\text{m}$ )	Effective – 100% mortality	Lahnsteiner and Weismann (2007)
	100 $\mu\text{g ml}^{-1}$ for 3 min 18 s	(323 $\mu\text{m}$ )	Effective – 100% mortality	
	200 $\mu\text{g ml}^{-1}$ for 3 min 15 s	(323 $\mu\text{m}$ )	Effective – 100% mortality	
<i>In vitro</i>	50 $\mu\text{l l}^{-1}$ for 10 h	Trophonts*	Not effective – 10% mortality	Lahnsteiner and Weismann (2007)
	100 $\mu\text{l l}^{-1}$ for 10 h		Partially effective – 77% mortality	
	150 $\mu\text{l l}^{-1}$ for 10 h		Effective – 90% mortality, no theronts produced by surviving trophonts	Lahnsteiner and Weismann (2007)
<i>In vivo</i> – bath	200 $\mu\text{l l}^{-1}$ for 10 h		Effective – 100% mortality	
	100 $\mu\text{l l}^{-1}$ for 2 h for 5 d	<i>O. mykiss</i>	Effective – 90% survival of treated fish; no infections d1 and 3	Lahnsteiner and Weismann (2007)
(daily for 5 d)	100 $\mu\text{l l}^{-1}$ for 4 h for 5 d	<i>C. carpio</i>	Not effective – 100% and 60% survival of treated fish on d1 and 3; moderate and heavy infections on d1 and 3	
	150 $\mu\text{l l}^{-1}$ for 2 h for 5 d	<i>O. mykiss</i>	Effective – 100% survival of treated fish; no infections d1 and 3	Lahnsteiner and Weismann (2007)
	150 $\mu\text{l l}^{-1}$ for 4 h for 5 d	<i>C. carpio</i>	Not effective – 100% and 70% survival of treated fish on d1 and 3; moderate and heavy infections on d1 and 3 on treated fish	
	150 $\mu\text{l l}^{-1}$ for 2 h for 5 d (10 °C, 48 h interval)	<i>O. mykiss</i>	Effective – 100% survival of treated fish; no infections d1 and 3	Lahnsteiner and Weismann (2007)
	150 $\mu\text{l l}^{-1}$ for 2 h for 5 d (18 °C, 24 h interval)		Partially effective – 70% survival of treated fish; no infections d1 and 3	
	150 $\mu\text{l l}^{-1}$ for 2 h for 5 d (18 °C, 48 h interval)		Not effective – 0% survival on treated fish	Shinn <i>et al.</i> (2005)
	150 $\mu\text{l l}^{-1}$ for 2 h for 5 d (25 °C, 24 h interval)		Not effective – 0% survival of treated fish; heavy infections on d1 and 3 on treated fish	
	200 $\mu\text{l l}^{-1}$ for 4 h for 5 d	<i>C. carpio</i>	Not effective – 100% and 60% survival of treated fish on d1 and 3; moderate and heavy infections on d1 and 3 on treated fish	Shinn <i>et al.</i> (unpublished)
Hydrogen peroxide (H <sub>2</sub> O <sub>2</sub> )	< 50 mg l <sup>-1</sup> for 10 h	Trophonts*	Not effective – trophonts developed normally	
<i>In vitro</i>	10 mg l <sup>-1</sup> for 1 h	Theronts	Not effective – ~ 10% mortality	Shinn <i>et al.</i> (unpublished)
	50 mg l <sup>-1</sup> for 1 h		Not effective – ~ 5% mortality	
	100 mg l <sup>-1</sup> for 1 h		Not effective – ~ 5% mortality	
	200 mg l <sup>-1</sup> for 1 h		Not effective – ~ 15% mortality; 20% mortality	

<i>In vivo</i> – bath	25 mg l <sup>-1</sup> daily for 20 d (flow through)	<i>I. punctatus</i>	Not effective – 80% of treated infected fish died	Tieman and Goodwin (2001)
	25 mg l <sup>-1</sup> daily for 20 d (static tanks)		Not effective – all treated infected fish died	
Hydrogen peroxide + acetic acid based formulation commercialized as Perotan				
<i>In vitro</i>	50 µl l <sup>-1</sup> for 10 h	Trophonts*	Not effective – 7% mortality	Lahnsteiner and Weismann (2007)
	100 µl l <sup>-1</sup> for 10 h		Effective – 100% mortality	
Incimaxx Aquatic				
See entry for peracetic acid + acetic acid + hydrogen peroxide + peroctanoic acid based formulation				
Iodine				
<i>In vivo</i> – bath	0.25 mg l <sup>-1</sup> daily for 11 d	<i>I. punctatus</i>	Not effective – all treated infected fish died	Tieman and Goodwin (2001)
(static tanks)	0.50 mg l <sup>-1</sup> daily for 11 d		Not effective – all treated infected fish died	
	1.00 mg l <sup>-1</sup> daily for 11 d		Not effective – all treated infected fish died	
	1.00 mg l <sup>-1</sup> for 11 d (alternate days)		Not effective – all treated infected fish died	
Ivermectin commercialised as Ivomec				
<i>In vitro</i>	< 50 mg l <sup>-1</sup> for 10 h	Trophonts*	Not effective – trophonts developed normally	Lahnsteiner and Weismann (2007)
Ivomec				
See entry for Ivermectin				
Ketoconazole				
<i>In vitro</i>	200 mg l <sup>-1</sup> for 2 h		Effective – 0% mortality after 2 h but protomonts do not develop	Tojo-Rodriguez <i>et al.</i> (1994)
<i>In vivo</i> – bath	200 mg l <sup>-1</sup> for 3 h	<i>O. mykiss</i>	Not effective – all trophonts develop normally	Tojo-Rodriguez <i>et al.</i> (1994)
In-feed	1000 mg kg <sup>-1</sup> feed for 8 d		Not effective – toxic to the fish; all trophonts develop normally	
	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Partially effective – 50% of medicated fish with low numbers of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Levamisole				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – 40% of medicated fish with low numbers of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Macleaya cordata (active compound sanguinarine)				
<i>In vitro</i>	60 mg l <sup>-1</sup> for 4 h	Trophonts*	Not effective – 32.5% mortality	Yao <i>et al.</i> (2010)
(Butanol extract)	80 mg l <sup>-1</sup> for 4 h		Not effective – 47.5% mortality	
	100 mg l <sup>-1</sup> for 4 h		Partially effective – 65% mortality	
	120 mg l <sup>-1</sup> for 4 h		Partially effective – 70% mortality	
(Chloroform extract)				
	30 mg l <sup>-1</sup> for 4 h		Partially effective – 67.5% mortality	
	50 mg l <sup>-1</sup> for 4 h		Effective – 82.5% mortality	

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference	
	70 mg l <sup>-1</sup> for 4 h	Trophonts*	Effective – 100% mortality	Yao <i>et al.</i> (2010)	
	90 mg l <sup>-1</sup> for 4 h		Effective – 100% mortality		
(Ethyl acetate extract)	60 mg l <sup>-1</sup> for 4 h		Not effective – 37.5% mortality		
	80 mg l <sup>-1</sup> for 4 h		Partially effective – 52.5% mortality		
	100 mg l <sup>-1</sup> for 4 h		Effective – 80% mortality		
	120 mg l <sup>-1</sup> for 4 h		Effective – 80% mortality		
(Petroleum ether extract)	60 mg l <sup>-1</sup> for 4 h		Not effective – 27.5% mortality		
	80 mg l <sup>-1</sup> for 4 h		Not effective – 30% mortality		
	100 mg l <sup>-1</sup> for 4 h		Not effective – 30% mortality		
	120 mg l <sup>-1</sup> for 4 h		Not effective – 40% mortality		
(Water extract)	60 mg l <sup>-1</sup> for 4 h		Not effective – 7.5% mortality		
	80 mg l <sup>-1</sup> for 4 h		Not effective – 17.5% mortality		
	100 mg l <sup>-1</sup> for 4 h		Not effective – 25% mortality		
	120 mg l <sup>-1</sup> for 4 h		Not effective – 27.5% mortality		
(Fractions from the chloroform extract)					
(Fraction A)	10 mg l <sup>-1</sup> for 4 h				Not effective – 12.5% mortality
	20 mg l <sup>-1</sup> for 4 h				Not effective – 15% mortality
	30 mg l <sup>-1</sup> for 4 h				Not effective – 22.5% mortality
(Fraction B)	10 mg l <sup>-1</sup> for 4 h				Not effective – 12.5% mortality
	20 mg l <sup>-1</sup> for 4 h				Not effective – 20% mortality
	30 mg l <sup>-1</sup> for 4 h		Not effective – 25% mortality		
(Fraction C)	10 mg l <sup>-1</sup> for 4 h		Not effective – 42.5% mortality		
	20 mg l <sup>-1</sup> for 4 h		Not effective – 67.5% mortality		
	30 mg l <sup>-1</sup> for 4 h		Not effective – 87.5% mortality		
(Fraction D)	5 mg l <sup>-1</sup> for 4 h		Effective – 90% mortality		
	9 mg l <sup>-1</sup> for 4 h		Effective – 100% mortality		
	11 mg l <sup>-1</sup> for 4 h		Effective – 100% mortality		
(Fraction E)	10 mg l <sup>-1</sup> for 4 h		Partially effective – 55% mortality		
	20 mg l <sup>-1</sup> for 4 h		Partially effective – 77.5% mortality		
	30 mg l <sup>-1</sup> for 4 h		Effective – 92.5% mortality		
(Fraction F)	10 mg l <sup>-1</sup> for 4 h		Not effective – 7.5% mortality		
	20 mg l <sup>-1</sup> for 4 h		Not effective – 20% mortality		
	30 mg l <sup>-1</sup> for 4 h		Not effective – 25% mortality		
(Fraction G)	10 mg l <sup>-1</sup> for 4 h		Not effective – 5% mortality		
	20 mg l <sup>-1</sup> for 4 h		Not effective – 7.5% mortality		
	30 mg l <sup>-1</sup> for 4 h		Not effective – 15% mortality		

(Compounds from Fraction D)				
(Compound I)	5 mg l <sup>-1</sup> for 4 h	Trophonts*	Not effective – 17.5% mortality	
	7 mg l <sup>-1</sup> for 4 h		Not effective – 22.5% mortality	
	9 mg l <sup>-1</sup> for 4 h		Not effective – 22.5% mortality	
(Compound II)	5 mg l <sup>-1</sup> for 4 h		Not effective – 22.5% mortality	
	7 mg l <sup>-1</sup> for 4 h		Not effective – 30% mortality	
	9 mg l <sup>-1</sup> for 4 h		Not effective – 37.5% mortality	
(Compound III)	0.5 mg l <sup>-1</sup> for 4 h		Effective – 87.5% mortality	
	0.9 mg l <sup>-1</sup> for 4 h		Effective – 100% mortality	
	1.3 mg l <sup>-1</sup> for 4 h		Effective – 100% mortality	
(Compound IV)	5 mg l <sup>-1</sup> for 4 h		Not effective – 5% mortality	
	7 mg l <sup>-1</sup> for 4 h		Not effective – 7.5% mortality	
	9 mg l <sup>-1</sup> for 4 h		Not effective – 22.5% mortality	
<i>In vivo</i> – bath				
(Compound I)	0.2 mg l <sup>-1</sup> for 48 h	<i>Ctenopharyngodon idella</i>	Not effective – 16.1% trophont reduction on treated fish	
	0.3 mg l <sup>-1</sup> for 48 h		Not effective – 17.3% trophont reduction on treated fish	
	0.4 mg l <sup>-1</sup> for 48 h		Not effective – 32.9% trophont reduction on treated fish	
	0.5 mg l <sup>-1</sup> for 48 h		Partially effective – 53.9% trophont reduction on treated fish	
	0.6 mg l <sup>-1</sup> for 48 h		Partially effective – 75.3% trophont reduction on treated fish	
	0.7 mg l <sup>-1</sup> for 48 h		Effective – 82.3% trophont reduction on treated fish	
	0.8 mg l <sup>-1</sup> for 48 h		Effective – 89.4% trophont reduction on treated fish	
	0.9 mg l <sup>-1</sup> for 48 h		Effective – 96.8% trophont reduction on treated fish	
Malachite green				
<i>In vitro</i>	1 mg l <sup>-1</sup> for 24 h	Adults**	Effective – 100% mortality after 1 h	Wahli <i>et al.</i> (1993)
	0.15 mg l <sup>-1</sup> for 24 h	Tomocysts	Effective – 100% mortality	Buchman <i>et al.</i> (2003)
	1 mg l <sup>-1</sup> for 24 h	Tomocysts	Effective – 100% mortality after 24 h	Wahli <i>et al.</i> (1993)
	0.004 mg l <sup>-1</sup> for 1.5, 3 and 15 h	Theronts	Not effective – < 50% mortality	Buchman <i>et al.</i> (2003)
	0.02 mg l <sup>-1</sup> for 1.5, 3 and 15 h		Not effective – < 50% mortality	
	0.10 mg l <sup>-1</sup> for 1.5 and 3 h		Not effective – < 50% mortality	
	0.10 mg l <sup>-1</sup> for 15 h		Partially effective – > 50% mortality	
	1 mg l <sup>-1</sup> for 3 h		Effective – 100% mortality after 1 h	Wahli <i>et al.</i> (1993)
	50 mg l <sup>-1</sup> for 15 h		Partially effective – > 50% mortality	Buchman <i>et al.</i> (2003)
	50 mg l <sup>-1</sup> for 1.5, 3 and 15 h		Partially effective – > 50% mortality	
<i>In vivo</i> – bath	25 mg l <sup>-1</sup> – 2 × for 1 h	<i>O. mykiss</i>	'Effective' – no details	Wahli <i>et al.</i> (1993)
	1st: day 9 p.i, 2nd: day 12 p.i			
	0.1 mg l <sup>-1</sup> daily for 20 d (static tanks)	<i>I. punctatus</i>	'Effective' – no trophonts on treated fish but toxic to fish experiment stopped on d9	Tieman and Goodwin (2001)

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
	0.1 mg l <sup>-1</sup> daily for 20 d (flow through)		Effective – no trophonts on treated fish; 0% fish mortality	Tieman and Goodwin (2001)
Malachite green (coloured salt)				
<i>In vivo</i> – In-feed	1.2 g kg <sup>-1</sup> feed for 10 d (fish species with stomach)	<i>Paracheirodon axelrodi</i> <i>Hyphessobrycon herbertaxelrodi</i> <i>Hyphessobrycon flammeu</i> <i>Hasemanina nana</i> <i>Aequidens pulcher</i>	Effective – medicated fish free of trophonts by d 5–8	Ruider <i>et al.</i> (1997)
	1.2 g kg <sup>-1</sup> feed for 10 d (fish species without stomach)	<i>Xiphophorus helleri</i> <i>Barbus tetrazona tetrazona</i> <i>Xiphophorus maculatus</i>	Effective – medicated fish free of trophonts by d 7–8	Ruider <i>et al.</i> (1997)
Malachite green (carbinolbase)				
<i>In vivo</i> – In-feed	1.2 g kg <sup>-1</sup> feed for 10 d (fish species with stomach)	<i>P. axelrodi</i>  <i>H. herbertaxelrodi</i> <i>H. flammeus</i> <i>H. nana</i> <i>A. pulcher</i> <i>X. helleri</i>	Effective – medicated fish free of trophonts by d 6–8	Ruider <i>et al.</i> (1997)
	1.2 g kg <sup>-1</sup> feed for 10 d (fish species without stomach)	<i>X. maculatus</i>	Effective – medicated fish free of trophonts by d 6–7	Ruider <i>et al.</i> (1997) <i>B. tetrazona tetrazona</i>
Malachite green (leucoform)				
<i>In vivo</i> – In-feed	1.2 g kg <sup>-1</sup> feed for 10 d (fish species with stomach)	<i>P. axelrodi</i> <i>H. herbertaxelrodi</i> <i>H. flammeus</i> <i>H. nana</i> <i>A. pulcher</i> <i>X. helleri</i>	Not effective – all medicated fish died across d 4–10	Ruider <i>et al.</i> (1997)
	1.2 g kg <sup>-1</sup> feed for 10 d (fish species without stomach)	<i>B. tetrazona tetrazona</i> <i>X. maculatus</i>	Not effective – all medicated fish died across d 4–10	Ruider <i>et al.</i> (1997)
Malachite green (p-dimethylaminobenzophenone)				
<i>In vivo</i> – In-feed	1177 mg kg <sup>-1</sup> feed for 6 d	<i>H. flammeus</i> <i>B. tetrazona tetrazona</i> <i>X. helleri</i>	Not effective – no reduction in trophont numbers on treated fish	Ruider <i>et al.</i> (1997)

Malachite green (N,N-dimethylaniline) <i>In vivo</i> – In-feed	316 mg kg <sup>-1</sup> feed for 4 d	<i>H. nana</i> <i>X. heller</i> <i>X. maculatus</i>	Not effective – no reduction in trophont numbers on treated fish	Ruider <i>et al.</i> (1997)
Methylene blue <i>In vitro</i>	100 mg l <sup>-1</sup> for 2 min	Protomonts	Effective – 100% mortality after 12 h	Post and Vesely (1983)
<i>In vivo</i> – bath (static tanks)	2 mg l <sup>-1</sup> daily for 20 d	<i>I. punctatus</i>	'Effective' – no trophonts on treated fish but 20% fish mortality†	Tieman and Goodwin (2001)
	Alternate days for 20 d: 2 mg l <sup>-1</sup> and 100 mg l <sup>-1</sup> formaldehyde (static tanks)		Not effective – no trophonts on treated fish but 40–70% fish mortality†	Tieman and Goodwin (2001)
Metronidazole <i>In vitro</i>	25 mg l <sup>-1</sup> for 3 h 25 mg l <sup>-1</sup> for 24 h 25 mg l <sup>-1</sup> for 24 h	Theronts Adults** Tomocysts	Not effective – no details Not effective – no details Not effective – no details	Wahli <i>et al.</i> (1993)
<i>In vivo</i> – In-feed	7.5 mg kg <sup>-1</sup> b.w for 7 d 24 mg kg <sup>-1</sup> b.w for 10 d 36 mg kg <sup>-1</sup> b.w for 10 d 40 g kg <sup>-1</sup> feed for 10 d	Salmonids not specified <i>C. auratus</i> <i>O. mykiss</i>	'Effective' – no details Effective – no trophonts on treated fish Effective – no trophonts on treated fish Not effective – 35% of medicated fish were free of infection	Rahkonen and Koski (2002) Tokşen and Nemli (2010) Tojo-Rodriguez and Santamarina-Fernandez (2001)
N-methylglucamine <i>In vitro</i>	200 mg l <sup>-1</sup> for 2 h	Protomonts	Not effective – 12.5% mortality after 2 h; surviving protomonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
<i>In vivo</i> – bath	200 mg l <sup>-1</sup> for 6 d	<i>O. mykiss</i>	Not effective – all trophonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
In-feed	1000 mg kg <sup>-1</sup> feed for 8 d 40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – all trophonts developed normally Not effective – all medicated fish had high numbers of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
MinnFinn™	See entry for peracetic Acid (PAA) + acetic acid + hydrogen peroxide based formulation (4.5% PAA + 9% AA + 22% H <sub>2</sub> O <sub>2</sub> )			
Monensin sodium based formulation sold as commercial product as Elancoban <i>In vitro</i>	20 mg l <sup>-1</sup> for 1 h	Trophonts*	Effective – 100% mortality after 14.5 h of exposure	Shinn <i>et al.</i> (unpublished)
	50 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality after 14.5 h of exposure	
	100 mg l <sup>-1</sup> for 1 h	Trophonts*	Effective – 100% mortality	Shinn <i>et al.</i> (2001)
	20 mg l <sup>-1</sup> for 1 h	Theronts	Not effective – 27.4% mortality	Shinn <i>et al.</i> (unpublished)
	50 mg l <sup>-1</sup> for 1 h		Not effective – 36.8% mortality	
	100 mg l <sup>-1</sup> for 1 h		Partially effective – 48.2% mortality	Shinn <i>et al.</i> (2001)
<i>In vivo</i> – In-feed	2 mg kg <sup>-1</sup> feed for 10 d		Not effective – no significant reduction in trophont numbers	Shinn <i>et al.</i> (unpublished)
	5 mg kg <sup>-1</sup> feed for 10 d		Not effective – no significant reduction in trophont numbers	

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
	10 mg kg <sup>-1</sup> feed for 10 d		Not effective – no significant reduction in trophont numbers	
	100 mg kg <sup>-1</sup> feed for 10 d prior to inf.	<i>O. mykiss</i>	Not effective – no reduction in trophont numbers	Shinn <i>et al.</i> (2003a)
<i>Mucuna pruriens</i> (velvet bean)				
<i>In vitro</i>	100 mg l <sup>-1</sup> for 3 h	Trophonts*	Not effective – 0% mortality	Ekamen <i>et al.</i> (2004)
	100 mg l <sup>-1</sup> for 6 h		Partially effective – 65% mortality	
	150 mg l <sup>-1</sup> for 3 h		Not effective – 25% mortality	
	150 mg l <sup>-1</sup> for 6 h		Effective – 100% mortality	
	200 mg l <sup>-1</sup> for 3 h		Not effective – 35% mortality	
	200 mg l <sup>-1</sup> for 6 h		Effective – 100% mortality	
<i>In vivo</i> – bath	100 mg l <sup>-1</sup> for 72 h	<i>C. a. auratus</i>	Partially effective – 59% reduction on the skin/60% on the gills	Ekamen <i>et al.</i> (2004)
	150 mg l <sup>-1</sup> for 72 h		Effective – 79% reduction in trophonts on the skin/83% on the gills	
	200 mg l <sup>-1</sup> for 72 h		Effective – 92% reduction in trophonts on the skin/91% on the gills	
Na-desoxycholate				
<i>In vitro</i>	25 mg l <sup>-1</sup> for 3 h	Theronts	Not effective – no details	Wahli <i>et al.</i> (1993)
	25 mg l <sup>-1</sup> for 24 h	Adults**	Not effective – no details	
	25 mg l <sup>-1</sup> for 24 h	Tomoysts	Not effective – no details	
Netobimin				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Partially effective – 75% of medicated fish with moderate number of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Nicarbazin				
<i>In vivo</i> – In-feed	100 mg kg <sup>-1</sup> feed for 10 d prior inf.	<i>O. mykiss</i>	Not effective – no reduction in trophont numbers on treated fish	Shinn <i>et al.</i> (2003a)
Niridazole				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Effective – 90% of medicated fish with low numbers of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Nitroscanate				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Partially effective – 50% of medicated fish had no trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
N-methylglucamine				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – all medicated fish had high numbers of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)



Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference	
	0.24 mg l <sup>-1</sup> for 1–4 h		Not effective – 30% mortality (trial 1); 60% mortality (trial 2)		
	0.28 mg l <sup>-1</sup> for 1–4 h		Partially effective – 50% mortality (trial 1); 70–80% mortality (trial 2)		
	0.32 mg l <sup>-1</sup> for 1–4 h		Effective – 60% mortality (trial 1); 80–90% mortality (trial 2)		
	0.36 mg l <sup>-1</sup> for 1–4 h		Effective – 70% mortality (trial 1); 80–95% mortality (trial 2)		
	0.40 mg l <sup>-1</sup> for 1–4 h		Effective – 80% mortality (trial 1); 90–95% mortality (trial 2)		
<i>In vivo</i> – bath (40% PAA solution)	1 mg l <sup>-1</sup> for 4 d	<i>C. carpio</i>	Effective – significant reduction on the number of trophonts on treated fish	Sudová <i>et al.</i> (2010)	
Peracetic Acid (PAA) + hydrogen peroxide + based formulation (4.5% PAA + 22% H <sub>2</sub> O <sub>2</sub> + 9% AA) sold as the commercial product as MinnFinn™					
<i>In vitro</i>					
(theronts from <i>Notemigonus crysoleucas</i> )					
	0.0225 mg l <sup>-1</sup> for 1–4 h		Not effective – 0% mortality	Straus and Meinelt (2009)	
	0.0450 mg l <sup>-1</sup> for 1–4 h		Not effective – 0% mortality		
	0.0675 mg l <sup>-1</sup> for 1–4 h		Not effective – 5% mortality		
	0.0900 mg l <sup>-1</sup> for 1–4 h		Not effective – 5–20% mortality		
	0.1125 mg l <sup>-1</sup> for 1–4 h		Not effective – 20–40% mortality		
	0.1350 mg l <sup>-1</sup> for 1 h		Not effective – 30% mortality		
	0.1350 mg l <sup>-1</sup> for 2–4 h		Partially effective – 50% mortality		
	0.1575 mg l <sup>-1</sup> for 1 h		Not effective – 40% mortality		
	0.1575 mg l <sup>-1</sup> for 2–4 h		Partially effective – 60% mortality		
	0.1800 mg l <sup>-1</sup> for 1 h		Not effective – 40% mortality		
	0.1800 mg l <sup>-1</sup> for 2–4 h		Partially effective – 60% mortality		
	0.2025 mg l <sup>-1</sup> for 1 h		Not effective – 40% mortality		
	0.2025 mg l <sup>-1</sup> for 2–4 h		Partially effective – 70% mortality		
	0.2250 mg l <sup>-1</sup> for 1–4 h		Partially effective – 50–70% mortality		
(theronts from <i>Xiphophorus hellerii</i> )					
	0.0225 mg l <sup>-1</sup> for 1–4 h		Not effective – 0–10% mortality		
	0.0450 mg l <sup>-1</sup> for 1–4 h		Not effective – 10% mortality		
	0.0675 mg l <sup>-1</sup> for 1–4 h		Not effective – 10–20% mortality		
	0.0900 mg l <sup>-1</sup> for 1–4 h		Not effective – 10–30% mortality		
	0.1125 mg l <sup>-1</sup> for 1–3 h		Not effective – 20–40% mortality		
	0.1125 mg l <sup>-1</sup> for 4 h		Partially effective – 50% mortality		
	0.1350 mg l <sup>-1</sup> for 1 h		Not effective – 40% mortality		
	0.1350 mg l <sup>-1</sup> for 2–4 h		Partially effective – 50% mortality		
	0.1575 mg l <sup>-1</sup> for 1–4 h		Partially effective – 50–60% mortality		
	0.1800 mg l <sup>-1</sup> for 1–4 h		Effective – 60–80% mortality		

	0.2025 mg l <sup>-1</sup> for 1–4 h		Effective – 60–90% mortality	
	0.2250 mg l <sup>-1</sup> for 1–4 h		Effective – 70–95% mortality	
Peracetic acid + acetic acid + hydrogen peroxide based formulation sold as the commercial product Detarox				
<i>In vivo</i> – bath	10 mg l <sup>-1</sup> for 25–45 min 2nd treatment after 4–7 d	Salmonids – not specified	‘Effective’ – no details	Rhakonen and Koski (2002)
Peracetic acid + acetic acid + hydrogen peroxide based formulation (13% PAA + 20% AA + 20% H <sub>2</sub> O <sub>2</sub> ) sold as commercial product Per Aqua				
<i>In vitro</i>	0.08 mg l <sup>-1</sup> for 30 min up to 60 min	Protomonts	Not effective – 0–20% mortality	Bruzio and Buchmann (2010)
	0.08 mg l <sup>-1</sup> for 1.5 h up to 4.5 h		Not effective – 30–40% mortality	
	0.8 mg l <sup>-1</sup> for 15 min		Not effective – 20% mortality	
	0.8 mg l <sup>-1</sup> for 30 min		Effective – ~ 90% mortality	
	0.8 mg l <sup>-1</sup> for 45 min		Effective – ~ 100% mortality	
	0.8 mg l <sup>-1</sup> for 15 min	Theronts	Effective – 100% mortality	
	8 mg l <sup>-1</sup> for 15 min		Effective – 100% mortality	
<i>In vivo</i> – bath	40 mg l <sup>-1</sup> 3 times a week for 3 weeks	<i>S. salar</i>	Not effective – infections rose throughout the infection period	Rintamäki-Kinnunen <i>et al.</i> (2005a)
Peracetic acid + acetic acid + hydrogen peroxide based formulation (13% PAA + 20% AA + 20% H <sub>2</sub> O <sub>2</sub> ) sold as commercial product Desirox + formaldehyde				
<i>In vivo</i> – bath	10 + 100 mg l <sup>-1</sup> 3 times a week for 4 weeks	<i>S. salar</i>	Trial inconclusive – details missing	Rintamäki-Kinnunen <i>et al.</i> (2005a)
Peracetic acid + acetic acid + hydrogen peroxide + peroctanoic acid based formulation sold as commercial product Incimaxx Aquatic				
<i>In vitro</i>	0.08 mg l <sup>-1</sup> for 30 min up to 4.5 h	Protomonts	Not effective – ~ 15–20% mortality	
	0.8 mg l <sup>-1</sup> for 15 min		Not effective – 40% mortality	Bruzio and Buchmann (2010)
	0.8 mg l <sup>-1</sup> for 30 min		Effective – 80% mortality	
	0.8 mg l <sup>-1</sup> for 45 min		Effective – 100% mortality	
	8 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	Picón-Camacho <i>et al.</i> (in press <i>b</i> )
	12 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	
	15 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	
	8 mg l <sup>-1</sup> for 1 h	Tomocysts	Effective – 100% mortality	Picón-Camacho <i>et al.</i> (in press <i>b</i> )
	12 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	
	15 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	
	0.8 mg l <sup>-1</sup> for 15 min	Theronts	Effective – 100% mortality	Bruzio and Buchmann (2010)
	8 mg l <sup>-1</sup> for 15 min		Effective – 100% mortality	
	8 mg l <sup>-1</sup> for 1 h		Effective – 98.3% mortality	Picón-Camacho <i>et al.</i> (in press <i>b</i> )
	12 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	
	15 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	

## Per Aqua

See entry for peracetic acid + acetic acid + hydrogen peroxide based formulations (13% PAA + 20%AA + 20%H<sub>2</sub>O<sub>2</sub>)

## Perotan

See entry for hydrogen peroxide + acetic acid based formulations

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
Piscidin 2 (antimicrobial polypeptide)				
<i>In vitro</i>	12.5 µg ml <sup>-1</sup> for 9 min 46 s	Trophonts*	Effective – 100% mortality	Ullal <i>et al.</i> (2008)
	25 µg ml <sup>-1</sup> for 7 min 33 s		Effective – 100% mortality	
	50 µg ml <sup>-1</sup> for 6 min		Effective – 100% mortality	Colorni <i>et al.</i> (2008)
	100 µg ml <sup>-1</sup> for 6 min 15 s		Effective – 100% mortality	
	200 µg ml <sup>-1</sup> for 6 min 25 s		Effective – 100% mortality	
	3.1 µg ml <sup>-1</sup> for 4 h	Theronts	Not effective – 0% killed, but less active than those in the controls	
	6.3 µg ml <sup>-1</sup> for 10 min		Effective – 100% mortality	
	12.5 µg ml <sup>-1</sup> for 10 min		Effective – 100% mortality	
	100 µg ml <sup>-1</sup> for 5 min		Effective – 100% mortality	
Piperazine				
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Partially effective – 55% of the medicated fish had a low number of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Potassium ferrate (VI)				
<i>In vitro</i>	0.096 for 30 min up to 4 h	Theronts	Not effective – 0% mortality	Ling <i>et al.</i> (2010)
	0.96 mg l <sup>-1</sup> for 30 min and 1 h		Not effective – 0% mortality	
	0.96 mg l <sup>-1</sup> for 2 h		Not effective – 14% mortality	
	0.96 mg l <sup>-1</sup> for 4 h		Not effective – 25% mortality	
	1.92 mg l <sup>-1</sup> for 30 min		Not effective – 0% mortality	
	1.92 mg l <sup>-1</sup> for 1 h		Not effective – 20% mortality	
	1.92 mg l <sup>-1</sup> for 2 h		Not effective – 24% mortality	
	1.92 mg l <sup>-1</sup> for 4 h		Partially effective – 56% mortality	
	4.80 mg l <sup>-1</sup> for 30 min		Not effective – 38% mortality	
	4.80 mg l <sup>-1</sup> for 1 h		Partially effective – 58% mortality	
	4.80 mg l <sup>-1</sup> for 2 h		Effective – 100% mortality	
	9.60 mg l <sup>-1</sup> for 30 min		Partially effective – 50% mortality	
	9.60 mg l <sup>-1</sup> for 1 h		Partially effective – 64% mortality	
	9.60 mg l <sup>-1</sup> for 2 h		Effective – 100% mortality	
	14.40 mg l <sup>-1</sup> for 30 min		Partially effective – 59% mortality	
	14.40 mg l <sup>-1</sup> for 1 h		Effective – 100% mortality	
	19.20 mg l <sup>-1</sup> for 30 min		Partially effective – 69% mortality	
	19.20 mg l <sup>-1</sup> for 1 h	Effective – 100% mortality		
	24.00 mg l <sup>-1</sup> for 30 min	Effective – 100% mortality		
	48.00 mg l <sup>-1</sup> for 30 min	Effective – 100% mortality		
<i>In vivo</i> – bath	1.92 mg l <sup>-1</sup> for 3 d	<i>C. auratus</i>	Partially effective – 71.94% trophont reduction	Ling <i>et al.</i> (2010)
	4.80 mg l <sup>-1</sup> for 3 d		Effective – 80.30% trophont reduction	
	9.60 mg l <sup>-1</sup> for 3 d		Effective – 83.39% trophont reduction	
	19.20 mg l <sup>-1</sup> for 3 d		Effective – 100% trophont reduction	

Potassium permanganate (KMnO <sub>4</sub> )				
<i>In vitro</i>	0.1 – 0.5 mg l <sup>-1</sup> for 15 up to 45 min	Theronts	Not effective – no details	Straus and Griffin (2001)
	0.6 mg l <sup>-1</sup> for 15 min up to 4 h		Not effective – 0–1% mortality	
	0.7 mg l <sup>-1</sup> for 15 min up to 4 h		Not effective – 5–10% mortality	
	0.8 mg l <sup>-1</sup> for 15 min		Not effective – 0% mortality	
	0.8 mg l <sup>-1</sup> for 30 min up to 4 h		Partially effective – 70% mortality	
	0.9 mg l <sup>-1</sup> for 15 min		Not effective – 0% mortality	
	0.9 mg l <sup>-1</sup> for 30 min up to 4 h		Effective – 90–95% mortality	
	1.0 mg l <sup>-1</sup> for 15 min		Not effective – 0% mortality	
	1.0 mg l <sup>-1</sup> for 30 min up to 4 h		Effective – 95 – >99% mortality	
<i>In vivo</i> – bath	0.25 mg l <sup>-1</sup> for 6 d	<i>I. punctatus</i>	Partially effective – low number of trophonts on treated fish	Straus and Griffin (2001)
	0.50 mg l <sup>-1</sup> for 6 d		Partially effective – low number of trophonts on treated fish	
	0.75 mg l <sup>-1</sup> for 6 d		Partially effective – low number of trophonts on treated fish	
	1.0 mg l <sup>-1</sup> for 6 d		Effective – No trophonts on treated fish	
	2 mg l <sup>-1</sup> daily for 20 d (static tanks and flow through)	<i>I. punctatus</i>	Not effective – all treated infected fish died; trophonts present	Tieman and Goodwin (2001)
	0.25 mg l <sup>-1</sup> for 8 d	<i>Tilapia aurea</i>	Effective – No trophonts on treated fish	Straus and Griffin (2001)
	0.50 mg l <sup>-1</sup> for 8 d		Effective – No trophonts on treated fish	
	0.5 mg l <sup>-1</sup> daily for 10 d	<i>I. punctatus</i>	Not effective – high number of trophonts on treated fish	Straus and Griffin (2002)
	0.75 mg l <sup>-1</sup> daily for 10 d		Not effective – high number of trophonts on treated fish	
	1.0 mg l <sup>-1</sup> daily for 10 d		Effective – no trophonts on treated fish	
	1.25 mg l <sup>-1</sup> daily for 10 d		Effective – no trophonts on treated fish	
	1.25 mg l <sup>-1</sup> daily for 10 d		Not effective – toxic to treated fish	
	4 mg l <sup>-1</sup> 3 times a week for 2 weeks	<i>S. salar</i>	Trial inconclusive – low parasite numbers across all groups	Rintamäki-Kinnunen <i>et al.</i> (2005a)
	10–20 mg l <sup>-1</sup> for 30 min	<i>O. mykiss</i> <i>S. fontinalis</i> <i>S. trutta</i>	'Effective' – there was a reduction in trophont number on treated fish but was toxic to all three fish species	Balta <i>et al.</i> (2008)
Potassium permanganate (KMnO <sub>4</sub> ) + dimetrazole				
<i>In vivo</i> – bath	3 mg l <sup>-1</sup> every 2nd d,	<i>O. mykiss</i>	Effective – no signs of infection by d 7	Rapp (1995)
+ in-feed	5 times + dimetrazole in feed 28 mg/fish for 10 d			
Potassium persulfate + sodium dodecylbenzosulfonate + malic acid + sulfamic acid based formulation commercialised as Virkon S				
<i>In vitro</i>	1 mg l <sup>-1</sup> for 1 h	Theronts	Not effective – ~ 8% mortality	Shinn <i>et al.</i> (2005)
	10 mg l <sup>-1</sup> for 1 h		Partially effective – ~ 55% mortality	
	100 mg l <sup>-1</sup> for 1 h		Not effective – 60% mortality†	
	< 50 µl l <sup>-1</sup> for 10 h	Trophonts*	Not effective – trophonts develop normally	Lahnsteiner and Weismann (2007)

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference	
<i>In vivo</i> – bath	10 $\mu\text{l l}^{-1}$ for 2 h for 5 d	<i>O. mykiss</i>	Not effective – none of the treated fish survived	Lahnsteiner and Weismann (2007)	
	10 $\mu\text{l l}^{-1}$ for 4 h for 5 d	<i>C. carpio</i>	Not effective – 90% of the treated fish had survived on d 1; 50% were still alive by d3 but had a high number of trophonts		
Pyceze™ See entry for bronopol					
Quinacrine					
<i>In vitro</i>	200 mg $\text{l}^{-1}$ for 2 h	Protomonts	Partially effective – 50% mortality after 2 h; 50% of protomonts develop normally	Tojo-Rodriguez <i>et al.</i> (1994)	
<i>In vivo</i> – bath	100 mg $\text{l}^{-1}$ for 3 h, d 6 p.i.	<i>O. mykiss</i>	Not effective – 50% fish mortality; all trophonts developed normally		
In-feed	500 mg $\text{kg}^{-1}$ for 8 d		Not effective – all trophonts developed normally; signs of feed rejection from d 4		
Quinine					
<i>In vivo</i> – In-feed	5 g $\text{kg}^{-1}$ feed for 7 d	<i>Poecilia sphenops</i>	Effective – 100% elimination of trophonts	Schmahl <i>et al.</i> (1996)	
	5 g $\text{kg}^{-1}$ feed for 8 d	<i>X. heller</i>	Effective – 100% elimination of trophonts		
	5 g $\text{kg}^{-1}$ feed for 10 d	<i>Hyphessobrycon herbertaxelrodi</i>	Effective – 100% elimination of trophonts		
1,3-di-6-quinolyurea					
<i>In vivo</i> – In-feed	40 g $\text{kg}^{-1}$ feed for 10 d	<i>O. mykiss</i>	Not effective – all treated fish had a high number of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)	
Ronidazole (1-methyl-2-carboxymethyl-5-nitroimidazole)					
<i>In vitro</i>	250 mg $\text{l}^{-1}$ for 1 h – 48 h	Trophozites*	Not effective – 0% mortality	Farley and Heckmann (1980)	
	500 mg $\text{l}^{-1}$ for 1 h – 4 h		Not effective – 0% mortality		
	500 mg $\text{l}^{-1}$ for 8 h		Not effective – 25% mortality		
	500 mg $\text{l}^{-1}$ for 24 h		Partially effective – 65.5% mortality (3 repeat trials)		
	500 mg $\text{l}^{-1}$ for 48 h		Partially effective – 65.5% mortality		
	750 mg $\text{l}^{-1}$ for 1 h		Not effective – 0% mortality		
	750 mg $\text{l}^{-1}$ for 2 h		Not effective – 2.5% mortality		
	750 mg $\text{l}^{-1}$ for 4 h		Not effective – 47.5% mortality		
	750 mg $\text{l}^{-1}$ for 8 h		Effective – 82.5% mortality		
	750 mg $\text{l}^{-1}$ for 24 h		Effective – 87.5% mortality (trial 1); 100% mortality (trial 2)		
	500 mg $\text{l}^{-1}$ for 1 h	Tomites	Not effective – 10% mortality		Farley and Heckmann (1980)
	500 mg $\text{l}^{-1}$ for 2 h		Not effective – 23% mortality		
	500 mg $\text{l}^{-1}$ for 4, 8 and 24 h		Effective – 55%, 90% and 96% mortality respectively		

	750 mg l <sup>-1</sup> for 1 h 750 mg l <sup>-1</sup> for 2, 4, 8 and 24 h		Not effective – 19% mortality Effective – 51.5%, 77.5%, 79% and 96.5% mortality respectively	
<i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – 100% medicated fish high number of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
SalarBec <i>In vivo</i> – In-feed	0.32 mg kg <sup>-1</sup> feed for 10 d prior infection	<i>O. mykiss</i>	Partially effective – 65% trophont reduction	Shinn <i>et al.</i> (2005)
Salinomycin sodium <i>In vivo</i> – In-feed	38 mg kg <sup>-1</sup> feed for 10 d p.i. 43 mg kg <sup>-1</sup> feed for 10 d p.i. 47 mg kg <sup>-1</sup> feed for 10 d p.i.	<i>O. mykiss</i>	Effective – 80.2% trophonts reduction Partially effective – 71.9% trophonts reduction Effective – 93.3% trophonts reduction	Shinn <i>et al.</i> (2003b)
Secnidazole <i>In vivo</i> – In-feed	24 mg kg <sup>-1</sup> b.w for 10 d 36 mg kg <sup>-1</sup> b.w for 10 d 40 g kg <sup>-1</sup> feed for 10 d	<i>C. auratus</i> <i>O. mykiss</i>	Effective – no trophonts on treated fish Effective – no trophonts on treated fish Partially effective – 75% medicated fish free of infection	Tokşen and Nemli (2010) Tojo-Rodriguez and Santamarina-Fernandez (2001)
Silver nitrate <i>In vitro</i>	0.67 mg l <sup>-1</sup>	Tomites	Effective – 100% mortality in less than 15 sec	Farley and Heckmann (1980)
Sodium carbonate peroxyhydrate <i>In vivo</i> – bath	60–90 mg l <sup>-1</sup> daily for 30–1 h for 4–6 d	Not specified	Not effective – no details	Rahkonen and Koski (2002)
Sodium chloride (NaCl) <i>In vitro</i>	2.5 g l <sup>-1</sup> for 24 h 5 g l <sup>-1</sup> for 24 h 10 g l <sup>-1</sup> for 24 h 15 g l <sup>-1</sup> for 10 h	Theronts Trophonts*	Partially effective – ~ 50% mortality Effective – ~ 95% mortality Effective – ~ 98% mortality Not effective – 0% mortality	Shinn <i>et al.</i> (2005) Lahnsteiner and Weismann (2007)
<i>In vivo</i> – bath	20 g l <sup>-1</sup> for 10 h 1 g l <sup>-1</sup> for 12 d  1 g l <sup>-1</sup> for 16 d  2 g l <sup>-1</sup> for 12 d  2 g l <sup>-1</sup> for 16 d	<i>B. bidyanus</i>	Effective – 100% mortality 100% theronts killed; trophonts 57% lower than controls* (8.7 ± 15.1% fish survive vs 0% of control fish) Theronts 74.9% and trophonts 89.8% lower than controls* (96.7 ± 4.7% fish survive vs 66.7 ± 47.1% of control fish) 100% theronts and protomonts mortality* (96.7 ± 4.7% fish survive vs 0% of control fish) 100% theronts and protomonts mortality* (96.7 ± 4.7% fish survive vs 66.7 ± 47.1% of control fish)	Mifsud and Rowland (2008)

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
	3 g l <sup>-1</sup> for 16 d		100% theronts and protomonts mortality*	
	3 g l <sup>-1</sup> daily for 20 d (static tanks)	<i>I. punctatus</i>	(100% fish survive vs 66.7 ± 47.1% of control fish) Not effective – all treated fish died	Tieman and Goodwin (2001)
	4 g l <sup>-1</sup> for 45 d	<i>Rhamdia quelen</i>	24.7% of the treated fish survived versus 8.1% of the control fish	Miron <i>et al.</i> (2003)
	4 g l <sup>-1</sup> daily for 30 d	<i>R. quelen</i>	'Effective' – reduction in the number of trophonts on treated fish	Garcia <i>et al.</i> (2007)
	5 g l <sup>-1</sup> for 14 d at 11–18 °C	<i>B. bidyanus</i>	Effective – no trophonts visible on treated fish	Selosse and Rowland (1990)
	5 g l <sup>-1</sup> for 8 d at 24 °C	<i>B. bidyanus</i>	Effective – no trophonts visible on treated fish	
	5 g l <sup>-1</sup> for 7 d at 19–22 °C	<i>Maccullochella peeli</i>	Effective – no trophonts visible on treated fish	
	5 g l <sup>-1</sup> for 7 d at 23–26 °C	<i>Tandanus tandanus</i>	Effective – no trophonts visible on treated fish	
	10 and 15 g l <sup>-1</sup> for 20 min	<i>O. mykiss</i> <i>S. fontinalis</i> <i>S. trutta</i>	Not effective – no details	Balta <i>et al.</i> (2008)
	20 g l <sup>-1</sup> for 1 h for 5 d	<i>O. mykiss</i>	Partially effective – 60% of treated fish survived, no infections on d1 but a high infection on d 3	Lahnsteiner and Weismann (2007)
	20 g l <sup>-1</sup> for 1 h for 5 d	<i>C. carpio</i>	Not effective – 0% survival on treated fish†; no infections d 1 but high infection on d 3	
	20 g l <sup>-1</sup> for 20 min	<i>O. mykiss</i> <i>S. fontinalis</i> <i>S. trutta</i>	'Effective' – reduction in the number of trophonts on treated fish	Balta <i>et al.</i> (2008)
In-feed	0.3–1.0% feed for 3–11 d	<i>C. carpio</i>	'Effective' – no details	Rahkonen and Koski (2002)
	1.2% feed for 30 d	<i>R. quelen</i>	Not effective – high mortality within the treated groups	Garcia <i>et al.</i> (2007)
	2.5% feed for 30 d		Not effective – high mortality within the treated groups	
	5.0% feed for 30 d		Not effective – high mortality on treated groups	
	6.0% feed for 30 d		Not effective – high mortality on treated groups	
Sodium percarbonate				
<i>In vitro</i>	12.5 mg l <sup>-1</sup> for 3 h	Theronts/tcysts	Effective on theronts but not effective on tomocysts	Jensen <i>et al.</i> (2001)
	12.5 mg l <sup>-1</sup> for 24 h	Tomocysts	Not effective – 11% mortality	
	13 mg l <sup>-1</sup> for few hours (no details)		Effective on theronts but not effective on tomocysts	
	63 mg l <sup>-1</sup> for 1 h		Effective on theronts but not effective on tomocysts	Buchmann <i>et al.</i> (2003)
	512 mg l <sup>-1</sup> for <1 h	Protomonts	Effective – 100% mortality	Heinecke and Buchmann (2009)
	256 mg l <sup>-1</sup> for <1 h 30 min		Effective – 100% mortality	

	128 mg l <sup>-1</sup> for <4 h 15 min		Effective – 100% mortality	
	0.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h 2.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h 8 mg l <sup>-1</sup> for 30–60 min	Theronts	Not effective – < 50% mortality Not effective – < 50% mortality Not effective – ~ 0% mortality	Buchman <i>et al.</i> (2003) Bruzio and Buchmann (2010)
	8 mg l <sup>-1</sup> for 1.5 h 8 mg l <sup>-1</sup> for 2 h 8 mg l <sup>-1</sup> for 2.5 h 8 mg l <sup>-1</sup> for 3 h 8 mg l <sup>-1</sup> for ~ 5 h (11–12 °C)		Not effective – ~ 40% mortality Partially effective – ~ 70% mortality Partially effective – ~ 70% mortality Effective – ~ 100% mortality Effective – 100% mortality	Heinecke and Buchmann (2009)
	8 mg l <sup>-1</sup> for ~ 2 h 20 min (21–22 °C) 12.5 mg l <sup>-1</sup> for 1.5 h 12.5 mg l <sup>-1</sup> for 3 and 15 h 16 mg l <sup>-1</sup> for ~ 1 h 20 min (11–12 °C)		Effective – 100% mortality Not effective – < 50% mortality Partially effective – > 50% mortality Effective – 100% mortality	Buchman <i>et al.</i> (2003) Heinecke and Buchmann (2009)
	16 mg l <sup>-1</sup> for ~ 1 h 40 min (21–22 °C) 32 mg l <sup>-1</sup> for ~ 1 h 10 min (11–12 °C) 32 mg l <sup>-1</sup> for ~ 30 min (21–22 °C) 62.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h 64 mg l <sup>-1</sup> for ~ 30 min (11–12 °C)		Effective – 100% mortality Effective – 100% mortality Effective – 100% mortality Partially effective – > 50% mortality Effective – 100% mortality	Buchman <i>et al.</i> (2003) Heinecke and Buchmann (2009)
	64 mg l <sup>-1</sup> for ~ 10 min (21–22 °C) 312.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h 1562.5 mg l <sup>-1</sup> for 1.5, 3 and 15 h		Effective – 100% mortality Partially effective – > 50% mortality Partially effective – > 50% mortality	Buchman <i>et al.</i> (2003)
<i>In vivo</i> – bath	Concentration not specified for 20 min every 2nd and 3rd day	<i>O. mykiss</i>	Not effective – no details	Rahkonen and Koski (2002)
Sulfachlorpyrazine <i>In vitro</i>	100 mg l <sup>-1</sup> for 3 h 100 mg l <sup>-1</sup> for 24 h 100 mg l <sup>-1</sup> for 24 h	Theronts Adults** Tomocysts	Not effective – high survival rate after 3 h Not effective – high survival rate after 24 h Not effective – high survival rate after 24 h	Wahli <i>et al.</i> (1993)
Sulfaquinoxaline <i>In vitro</i>	200 mg l <sup>-1</sup> for 2 h	Protomonts	Not effective – 12.5% mortality after 2 h; protomonts surviving treatment developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
<i>In vivo</i> – bath	200 mg l <sup>-1</sup> for 3 h, day 6 p.i.	<i>O. mykiss</i>	Not effective – all protomonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
In-feed	1000 mg kg <sup>-1</sup> for 8 d		Not effective – all protomonts developed normally; 4% fish mortality on day 6 p.i.; no feed unpalatability	
Thiophanate <i>In vivo</i> – In-feed	40 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – 100% medicated fish high number of trophonts	Tojo-Rodriguez and Santamarina-Fernandez (2001)
Toltrazuril				

Table 1. (Cont.)

Compound	Dose	Host/parasite stage	Efficacy	Reference
<i>In vitro</i>	10 µg ml <sup>-1</sup> for 2 h 200 mg l <sup>-1</sup> for 2 h	Protomonts	Effective – 100% mortality Effective – 0% mortality but protomonts did not develop	Schmahl <i>et al.</i> (1989) Tojo-Rodriguez <i>et al.</i> (1994)
	< 50 mg l <sup>-1</sup> for 10 h	Trophonts*	Not effective – trophonts developed normally	Lahnsteiner and Weismann (2007)
<i>In vivo</i> – bath	10 µg ml <sup>-1</sup> for 2 h	Theronts	Not effective – 0% mortality	Schmahl <i>et al.</i> (1989)
	d1 10 mg l <sup>-1</sup> (2 h) d2 and d3 20 mg l <sup>-1</sup> (1 h)	Various spp.	Trophonts affected but not theronts	Mehlhorn <i>et al.</i> (1988)
	d1 10 mg/l (4 h) d3 and d5 10 mg/l (4 h)	Various spp.	100% trophonts killed but theronts not affected	Mehlhorn <i>et al.</i> (1988)
	1 µg ml <sup>-1</sup> for 4·5 h 5 µg ml <sup>-1</sup> for 4·5 h	<i>A. rostrata</i> <i>A. rostrata</i>	Not effective – no details Not effective – one third of the parasites dropped off the fish within 24 h. New infections established within 2 d	Schmahl <i>et al.</i> (1989)
	10 µg ml <sup>-1</sup> for 2 h		Effective – two thirds of the parasites dropped off the fish within 24 h, fish were free from new infections over the following 14 days	
	10 µg ml <sup>-1</sup> , 2 h (1st d) 20 µg ml <sup>-1</sup> , 1 h (2nd d) 20 µg ml <sup>-1</sup> , 2 h (3rd d)	<i>A. rostrata</i>	‘Effective’ – no details	Schmahl <i>et al.</i> (1989)
	5 mg l <sup>-1</sup> 10 mg l <sup>-1</sup> 20 mg l <sup>-1</sup> 50 mg l <sup>-1</sup> 200 mg l <sup>-1</sup> for 3 h, day 6 p.i.	<i>O. mykiss</i> <i>O. mykiss</i>	Not effective – toxic, after 5 h 100% fish mortality Not effective – toxic, after 3·5 h 100% fish mortality Not effective – toxic, after 2 h 100% fish mortality Not effective – toxic, after 2 h 100% fish mortality Not effective – all trophonts developed normally	From <i>et al.</i> (1992) Tojo-Rodriguez <i>et al.</i> (1994)
In-feed	1000 mg kg <sup>-1</sup> for 8 d	<i>O. mykiss</i>	Not effective – all trophonts developed normally	Tojo-Rodriguez <i>et al.</i> (1994)
Tramisol (6S)-6-phenyl-2,3,5,6-tetrahydroimidazo[2,1-b][1,3]thiazole)				
<i>In vitro</i>	100 mg l <sup>-1</sup> for 2 min	Trophozoites*	Effective – 50% mortality after 2 h; 100% mortality post exposure	Post and Vesley (1983)
Tricaine methanesulfonate (TM)				
<i>In vitro</i>	50 mg l <sup>-1</sup> buffered with Na CaCO <sub>3</sub> (time of exposure not specified)	Protomonts	Not effective – 4·9% mortality	Xu <i>et al.</i> (2008)
	50 mg l <sup>-1</sup> not buffered (time of exposure not specified)		Not effective – 1·1% mortality	
	150 mg l <sup>-1</sup> buffered with Na CaCO <sub>3</sub> for 2–3 min		Not effective – 1·8% mortality	
	150 mg l <sup>-1</sup> buffered with Na CaCO <sub>3</sub> (time of exposure not specified)		Not effective – 9·2% mortality	
	150 mg l <sup>-1</sup> not buffered for 2–3 min		Not effective – 6·1% mortality	

	150 mg l <sup>-1</sup> not buffered (time of exposure not specified)		Not effective – 9.9% mortality	
	300 mg l <sup>-1</sup> buffered with Na CaCO <sub>3</sub> (time of exposure not specified)		Not effective – 7.3% mortality	
	300 mg l <sup>-1</sup> not buffered (time of exposure not specified)		Effective – 100% mortality	
Triclabendazole (5-chloro-6-(2, 3-dichlorophenoxy)-2-methylthio-1H- benzimidazole)				
<i>In vivo</i> – In-feed	20 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Not effective – 100% medicated fish with >50 trophonts	Luzardo-Álvarez <i>et al.</i> (2003)
Triclabendazole + $\beta$ -cyclodextrin (ratio 1:2)				
<i>In vivo</i> – In-feed	10 g kg <sup>-1</sup> feed for 10 d	<i>O. mykiss</i>	Partially effective – 58% reduction in trophont number compared to control	Luzardo-Álvarez <i>et al.</i> (2003)
	20 g kg <sup>-1</sup> feed for 10 d		Partially effective – 42% reduction in trophont number compared to control	
Vitamin C				
	See entry for ascorbate-2-phosphate			
Vitamin E				
	See entry for d-1-alpha-tocopheryl acetate			
Violet C				
<i>In vivo</i> – bath	0.01 mg l <sup>-1</sup> for 2 d	<i>C. carpio</i>	Not effective – not specified	Kurovskaya (2005)
	0.02 mg l <sup>-1</sup> for 6 d		Effective – no trophonts on treated fish	
	50 mg l <sup>-1</sup> for 30 min		Effective – no trophonts on treated fish	
Virkon S				
	See the entry for potassium persulfate + sodium dodecylbenzenesulfonate + malic acid + sulfamic acid based formulation			
Wofasteril®				
	See entry peracetic Acid (PAA) + hydrogen peroxide + acetic acid (40% PAA + 15% H <sub>2</sub> O <sub>2</sub> + 25% AA)			

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Abbreviations: d: days; h: hours; inf.: infection; p.i.: post-infection; \*authors use the term ‘trophont/trophozoites’ for the free-swimming stage which exited the fish host; \*\* authors used the term ‘adults’ for the free-swimming stage which exited the fish host; †: toxic to fish; <sup>a</sup> carp/trout/eels/ornamental fish.

Table 2. Management strategies tested against infections of *Ichthyophthirius multifiliis* Fouquet, 1876(A strategy is regarded as being partially effective if it kills 50–80%, and effective if it kills  $\geq 80\%$  of the stages under test. Mortality refers to the parasite stages unless otherwise stated.)

Electrotherapy						
<i>In vitro</i> – Trophozoites*						
Electrode type	Volts per 2.5 cm separation	Current	Duration (s)	Efficacy	Reference	
Carbon	55–150	150–350	5	Not effective – 14.35% mortality after 24 h	Farley and Heckmann (1980)	
Carbon	104–150	200–350	5	Not effective – 7.09% mortality after 24 h		
Carbon	150		3	Effective – 100% mortality		
Carbon	150		3	Effective – 100% mortality		
Carbon	250		3	Effective – 100% mortality		
Carbon	350		3	Effective – 100% mortality		
Carbon	350		3	Effective – 100% mortality		
Copper	88–115	135–200	5	Effective – 100% mortality after 24 h		
Copper	115	135	5	Effective – 100% mortality after 24 h		
Steel hardware cloth 150–240		160–400	5	Not effective – 2.99% mortality after 24 h		
Steel hardware cloth 150		340	5	Not effective – 0.87% mortality after 24 h		
Mechanical filtration						
<i>In vitro</i> – protomonts						
Mesh size ( $\mu\text{m}$ )	Efficacy					
500	Not effective – 0% protomonts filtered out				Heinecke and Buchmann (2009)	
300	Not effective – 6% protomonts filtered out					
160	Not effective – 22% protomonts filtered out					
80	Effective – 100% protomonts filtered out					
Mechanical removal of the tomocysts						
<i>In vitro</i> – protomonts						
Lining surface	Efficacy					
Crystal polyesterin	Not effective – 9.8% mortality				Shinn <i>et al.</i> (2009)	
Polypropylene – based plastic	Effective – 90.2% mortality					
Polyethylene – based plastic	Partially effective – 76.5% mortality					
Chlovar chlorinated rubber	Not effective – 46.6% mortality					
<i>In vivo</i> – commercial raceways in <i>O. mykiss</i> hatchery (Suction head + lining of the bottom of the raceways)						
Visit number	Efficacy					
1 (after 2 weeks)	No infection in control and experimental raceways				Shinn <i>et al.</i> (2009)	
2 (after 4 weeks)	No infection in control and experimental raceways					
3 (after 6 weeks)	Low infection levels in both control and experimental raceways					
4 (after 8 weeks)	Effective – 92% reduction in trophont numbers compared to the control					
5 (after 10 weeks)	Effective – 99% reduction in trophont numbers compared to the control					

(Suction head stopped, only lining of the bottom of the raceways) 6 (after 12 weeks)					Partially effective – 54% reduction in trophont numbers compared to the control	
UV light						
<i>In vivo</i> - fish species not specified						
Number of UV bulbs used (UV light generated)					Efficacy	
0					Not effective – 82.81% fish mortality	Gratzek <i>et al.</i> (1983)
1 (91 900 $\mu\text{W s cm}^{-2}$ )					Effective – 1.33% fish mortality	
2 (183 800 $\mu\text{W s cm}^{-2}$ )					Effective – 0.7% fish mortality	
Water flow						
<i>In vivo</i> – experimental raceways of <i>I. punctatus</i> fingerlings						
Fish density (no. $\text{L}^{-1}$ )	Flow rate ( $\text{L min}^{-1}$ )	Velocity ( $\text{cm min}^{-1}$ )	Turn-over (no. $\text{h}^{-1}$ )	Efficacy		
0.33	5		4.1	0.5	Not effective – 100% mortality of infected fish	Bodensteiner <i>et al.</i> (2000)
0.25	15		12.2	1.5	Not effective – 52% mortality of infected fish	
0.25	25		20.3	2.5	Effective – 14% mortality of infected fish	
0.33–0.66	5		4.1	0.5	Not effective – 100% mortality of infected fish	
0.33–0.66	25		20.3	2.5	Effective – 9% mortality of treated fish	
0.33–0.66	45		36.5	4.5	Effective – 7% mortality of treated fish	
<i>In vivo</i> – production raceways of <i>I. punctatus</i> fingerlings						
0.89–1.29	> 2800		> 85	> 2.1	Effective – no trophonts observed	
0.71–1.40	> 2800		> 85	> 2.1	Effective – no trophonts observed	

Abbreviations: s: seconds, \*authors use the term ‘trophozites’ for the free-swimming stage which exited the fish host.

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