

Pharmacology of Fish: Basic Principles

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Act 101 of 1965 Medicines and Related Substances Control Act

- Governs use of antibiotics and hormones. Available on prescription from the consulting veterinarian only. Animals for which he prescribes an Act 101 drug must be under his direct care.
- The Act is administered by the medicines Control Council which have an inspectorate.

Act 36 of 1947 Fertilizers, Farm Feeds, Agricultural and Stock Remedies Act

- Act 36 – Over the counter (OTC) medicines
- no registered fish medicines currently available
- Chemicals and disinfectants used to treat fish need to be registered under Act 36 if intention is to use them for disease control. Failing this they fall under legislation governed by Act 101 and become off label prescription drugs

Act 54 of 1972 Foodstuffs Cosmetics and Disinfectants Act

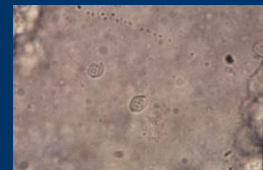
- Controls any residues in foodstuffs
- Administered by the SABS
- Disinfectants not used for disease control are registered under this Act
- The Act is reactive where traces are identified in food. Involves the Department of Health
- If a farmer uses a chemical that is not registered or contrary to label instructions he can be prosecuted

Points to consider

- Fish are poikilothermic – systemic drugs are usually metabolised more slowly than in terrestrial animals.
- Chemical therapeutants used for external treatment may alter dissolved oxygen availability to the fish
- Many chemical therapeutants are potentially toxic to fish and function within a narrow therapeutic range.
- Many chemical therapeutants will interfere with biological filters used in recirculated systems
- Fish should always be starved for 24 hours before treatments are given

Anti-parasitic drugs

- Various chemicals used in food fish production
- Majority of medicines from pet shops are aimed at parasite treatment
- Currently no OTC registered medicines for fish available in South Africa
- Some hazardous chemicals in common use
- Many are harmful to biological filters



Drugs against external protozoan infections - FORMALIN

- Good all-purpose parasiticide and disinfectant
- Deoxygenating effect. Use with care in fish with gill disease and anaemia
- Avoid white deposit that forms as formalin ages. This is PARAFORMALDEHYDE and is extremely toxic to fish



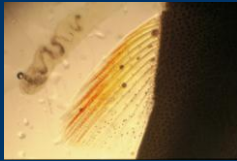
Acriflavine

- Effective against external protozoa
- Therapeutic dose lies close to toxic level
- Use neutral acriflavine
- Produces temporary sterility in both egg laying and livebearing fish
- Toxic to some plants
- Can be used in sea water



Potassium permanganate

- Good disinfecting properties
- Rapidly destroyed by organic material
- Can be used for emergency oxygenation
- Treatment of external protozoal and monogenean parasites and bacterial gill disease
- Avoid use with scaleless fish



Methylene blue

- Effective against external fungal and protozoal infection
- Increases respiratory capacity of fish
- At high doses useful in sea water
- Use only pure grades
- Toxic to scaleless fish



Drugs against external monogenean flukes

- Formalin – gill flukes
- Potassium permanganate
- Organophosphates, dichlorophos and trichlorphon
- Benzimidazoles, particularly
- Mebendazole
- Praziquantel



Drugs against external copepods

Lernaea cyprini – anchor worm

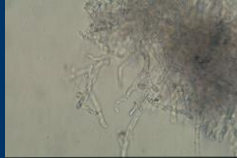
- Traditionally dichlorophos and trichlorphon have been used, particularly by the salmon industry against *Lepeophtheirus* and *Caligus* sea lice
- Dimilin (diflubenzaron) very effective and safe in freshwater



Argulus – fish louse

Malachite green

- Used only in non-food producing fish
- Banned for use in food fish in western countries
- Teratogenic
- Traditionally used to prevent fungal overgrowth of salmonid eggs
- Useful against external protozoa in combination with formalin.

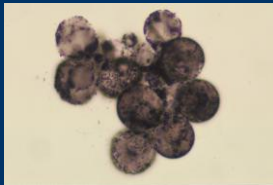


Malachite green

- Only the zinc free form is safe for use in fish
- Respiratory poison in fish – mitochondrial enzyme inhibitor
- Affinity for organic matter, then oxidised in presence of air and light
- In water MG gradually changes to the colourless carbinol form
- Penetrates tissues more deeply than previously anticipated

Antibiotics

- Parenteral
- In feed
- No registered antibiotics for use in food fish in South Africa
- Correct dispensing procedure
- Off-label use, Act 101
- Limitation – sick fish stop feeding!



Antibiotics

- Establish that infection is caused by a bacterial pathogen
- Identify the pathogen involved and determine the antibacterial sensitivity
- Start treatment as soon as possible
- Reduce stocking density and improve pond hygiene
- Avoid prophylactic use of antibiotics

Antibiotics

- For environmental and food safety reasons veterinarians should encourage farmers to follow protocols that minimize reliance on antibiotics for production of food fish species.
- Drug elimination times vary with water temperature. A minimum of 4 weeks withdrawal should be maintained in the absence of specific elimination data.
- Oxytetracycline and amoxycillin most commonly used in South Africa.

Antibiotics

Oxytetracycline

- 75 mg/kg daily for 10 days
- Withdrawal period 350 degree days for rainbow trout

Amoxycillin

- 40-80 mg/kg daily for 10 days
- Withdrawal period 150 degree days in atlantic salmon

Other antibiotics

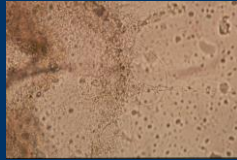
- Florfenicol (Nuflor) – very effective in fish. Registered for use in fish in countries other than South Africa
- Erythromycin – not readily available for fish in South Africa. Used elsewhere
- Nifurpirinol (Furanace) – banned from use in fish
- Chloramphenicol – banned from use in fish

Antibiotics

- Antibiotic medicated feed is given daily for 10 days.
- Daily feed is reduced by 50 %
- Vegetable oil is used at 10 % of daily feed to mix the daily dose of medication
- Oil and antibiotic mixture is top dressed onto feed
- Fish are treated daily for 10 days

Drugs against bacterial infections

- Benzalkonium chloride
- cationic surface-active agent and germicide
- Causes shedding of mucus layer from skin and gills
- Chemicals effective against external protozoal infections all have some disinfectant properties



Drugs used against external fungal (oomycete) infections

- Malachite green
- Methylene blue
- Bromopol (Pyces) registered in UK, alternative to MG
- Formalin
- Hydrogen peroxide



Drugs used to manipulate breeding

- Pituitary gland extract
- Gonadotropin releasing hormones – synthetic analogue, Aquaspawn (has restricted registration under Act 36 – use only under direction of veterinarian or fish scientist)
- HCG

Drugs used to manipulate sex of off-spring

- Methyl testosterone used in minute quantities in feed of first feeding trout fry
- 3 mg hormone per kg of food
- Swim-up fry are fed hormone medicated feed for 750 degree days
- Results in genotypic females expressing male phenotype and producing ductless seminiferous tissue in place of ovaria

Production of all female stock

- Sex reversed male fish produce only 'X' chromosome carrying sperm
- When used to fertilize ova all offspring are 'XX' – female
- Sterile triploid fish can be produced if the fertilized ova are exposed to high pressure
- Common practice in a few trout hatcheries in South Africa
- Potential for use in tilapia hatcheries.

Anaesthetics and tranquilizers

primarily used to minimize stress during handling procedures

Stages

- I loss of equilibrium
- II loss of gross body movements but with regular opercular movements
- III as in stage II with cessation of opercular movement

Anaesthetics

Physiological changes

- Reflect hypoxia
- Fall in PO_2
- Increase in PCO_2
- Decline in blood pH
- Cortisol concentrations decline
- Adrenalin increases but declines during recovery
- Transient increase in haematocrit

Anaesthetics

- Benzocaine
- Tricaine methane sulphonate (MS222)
- Quinaldine
- 2 phenoxyethanol
- Propoxate
- Eugenol 30 mg/L
- Metomidate

Disinfectants

- Potentially lethal to fish
- Hatchery equipment – chlorine, formalin
- Nets – benzalkonium chloride
- Footbaths – iodine
- Earthen ponds – quicklime or slaked lime
- Concrete ponds – sodium hydroxide plus teepol

Fish medicines

- Must be demonstrably effective
- Safe to the
 - target animal
 - consumer
 - environment

Registration of medicines

- Scientific assessment of data supplied by applicant
- Statutory criteria for safety, quality and efficacy
- Positive risk:benefit ratio

Verner-Jeffreys, D., Algoet, M. (2005) Trout News 39

Medicinal product definition

- Any substance or combination of substances presenting as having properties for treating or preventing disease; or any substance or combination of substances which may be used in, or administered to, animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medicinal diagnosis (EEC Directive 2001/82/EC)

Illegal use of fish medicinal products

- Available in pet shops and through the Internet
- Available OTC's for non aquatic animals under Act 36 of 1947

Absence of registered fish products

- Prescribing cascade for the veterinarian
- Veterinarian must have responsibility for the care of the aquatic animals concerned
- Where no medicine is registered for a particular condition administer in accordance to off-label provision under Act 101 of 1965

“Off-label use” cascade

- A medicine registered for use in another species or for a different use in the same species
- A medicine registered for human use
- A medicine made up by the veterinarian on a one-off basis or by a properly authorized person to the veterinarians specifications

Verner-Jeffreys, D., Algoet, M. (2005) Trout News 39

Food-producing animals

- Off-label medicines used may only contain substances found in medicine registered for a food-producing species
- When a non registered medicine is used a withdrawal period of 500 degree days must be applied
- The veterinarian must keep specified records

Verner-Jeffreys, D., Algoet, M. (2005) Trout News 39

Commercial chemicals

- Widely available (eg. formalin, malachite green, methylene blue)
- Not marketed as medicines
- Unregulated medicinal use
- Concerns over safety to the user, the animal, the environment and the consumer
- Use of commercial chemicals for medicinal purpose is illegal

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Feed additives (EC1831/2003)

- Substances that are microorganisms or preparations of microorganisms, other than feed material and premixes, that are intentionally added to feed or water in order to perform one or more of the following:

Feed additive (EC1831/2003)

- Favourably affect the characteristics of: feed, animal products, the colour of ornamental fish and birds, the environmental consequences of animal production, animal production, performance or welfare, particularly by affecting gastrointestinal flora or digestibility of feeding stuffs
- Satisfy the nutritional needs of animals
- Have a coccidiostatic or histomonostatic effect

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Feed additives

- Regarded as medicines if certain product claims are made
- Prebiotics and probiotics
- Immunostimulants and stress relievers

Prebiotics and probiotics

- Prebiotics – nutrients added to feed to selectively stimulate populations of bacteria in the gut that are already present and established
- Probiotics – in aquaculture are live microbial cultures added to rearing systems through feed or water, which improve the performance of the cultured animals

Immunostimulants

- If sold with health promoting claims then need to be registered as medicines