THE USE OF ANTIBIOTICS IN AQUACULTURE: HEALTH AND ENVIRONMENTAL ISSUES, CONTROL AND MITIGATION MEASURES

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Abstract: In Malaysia, antibiotics are commonly used in aquaculture for disease treatment. With the increasing awareness of Malaysians over environmental and health issues, there are growing concerns on their use, abuse and associated impacts on the environment, food safety and human health. Although the presence of antibiotics in food is controlled by the Food Act enforced by the Ministry of Health, there exist only the Codes of Practice to ensure judicious use in aquaculture. Presently, the Ministry of Health has limited capacities to monitor for antibiotics in all fresh meat and meat products, and concentrates mainly on the detection of nitrofurans in poultry. Health and environmental issues include the emergence and spread of antibiotic-resistant bacteria, the tainting of cultured and non-targeted aquatic species, the inhibition of microbiological activity in sediments and changes in benthos diversity. More thorough evaluation of antibiotics before their approval, more stringent controls over their sale, and more awareness programmes to educate farmers may help to reduce improper usage. Research programmes directed at waste treatment to reduce the amount of antibiotics going into the environment could be given priority. Research efforts directed at the production of vaccines and high-health fry should also be emphasised since this will reduce the need for antibiotic use. Aquaculture should also move towards the same direction taken by the manufacturing sector, and should adopt a more proactive stand in addressing environmental and health issues. The bigger farms should actively seek ISO 14000 accreditation to ensure that their activities are not detrimental to the sustainability of the aquatic environment, and Hazard Analysis and Critical Control Point (HACCP) accreditation for farm management and production to ensure food safety.

Keywords: antibiotics, aquaculture, health and environmental issues, control and mitigation measures

INTRODUCTION

Antibiotics are commonly defined as chemical compounds that are produced by microorganisms and possess the ability to control or destroy bacteria and/or other microorganisms. Antimicrobials, which are groups of compounds with similar functions are not produced by bacteria but are chemically synthesised and are often considered separate from antibiotics. Regulation 40 of The Food Act 1983 and Food Regulations 1985, Malaysia, merges these two groups of compounds together and refer to them as antibiotics. In compliance with this definition, "antibiotics" in this report refers also to antimicrobials.

In Malaysia, antibiotics are commonly used in aquaculture for disease treatment, but are less frequently used as a prophylactic or growth promoter. However, there are no statistics to substantiate this statement since official records on the amount of antibiotics used and the purpose for their use are not available. Owing to its widespread application, and the possibility of abuse in its use, there are growing concerns regarding the contamination of the aquatic environment, as well presence of residues in the cultured as well as the non-targeted animal groups.

Although the presence of antibiotics in food is controlled by the Food Act, there exist only the Codes of Practice to ensure the judicious use in aquaculture practices. The Codes formulated by the Department of Fisheries for marine finfish farming in floating cages and for shrimp farming recommended that only approved antibiotics be used for culture. The list of approved drugs, however, is currently not listed in the Codes. Since the Codes act only as guidelines, antibiotic use in farms are therefore not regulated.

This paper attempts to review the use of antibiotics in aquaculture in Malaysia because of the heightened concerns over its use and abuse and its impacts on human health and the environment. Health and environmental issues relating to antibiotic use and measures that can reduce or control the impacts are also discussed.

Use of Antibiotics in Aquaculture

Before the 1980s, there was little concern over the use of antibiotics in aquaculture. Culture systems for prawns and fish then were mainly extensive, and cultured organisms were not subjected to conditions that are as stressful as those under semi-intensive and intensive cultures practised nowadays. Aquatic pollution problems were also less common and water was of better quality, and hence disease problems related to poor water quality were less frequently encountered.

Mollusc culture, represented mainly by cockle culture, is the mainstay of the aquaculture production in Malaysia. Molluscs (cockle, oyster and mussel) contribute as much as over 90% of the total aquaculture production, and their cultures, which utilise natural spat that are transplanted from spatfall areas to other suitable areas for grow-out, do not require the use of antibiotics. Disease problems are insignificant in mollusc culture compared to the culture of other aquatic species. Bacterial or viral disease has not been reported so far. However, infestations attributed to predators that include the oyster drill (*Thais* sp.) which predates on oysters and cockles, and the flatworm, belonging to the genus Turbellaria which may be an opportunistic predator in the mussel, *Perna viridis*, have been documented (Choo 1983; Choo 1992).

The semi-intensive and intensive culture of prawns and fish, however, may require the use of antibiotics especially when disease problems are encountered. Commonly used antibiotics include furanex, furazolidone (both banned in 1996), chloramphenicol, tetracycline, oxytetracycline, erythromycin, neomycin, norfloxacin, flumequine, oxolinic acid and daimeton sodium. The Food Regulations (Amendment) 1998 listed nitrofurans and chloramphenicol as the two antibiotics that are not allowed in food or foodstuff. Chloramphenicol, however, is still permissible for animal treatment if prescribed by a veterinarian.

Apart from antibiotics brought in through the official channels by pharmacists holding a license A, they are also brought in, sometimes without proper labels, by farmers or traders through neighbouring countries. Traders may also repack antibiotics for resale without proper labels, especially in the aquarium trade. In the United States of America, agriculture use account for more than 40% of all antibiotics manufactured in that country (Lieberman & Wooten 1998). In Norway, 37 tonnes of antibiotics and chemotherapeutants were used to produce 160,000 tonnes of salmon in 1990 (Hansen *et al.* 1993). No statistics are available on the amount of antibiotics used by the aquaculture industry in Malaysia.

Local brands of prawn and fish feed generally do not contain antibiotics. Antibiotics can either be given through a bath or incorporated into the feeds. They are added into feeds by utilising one of two commonly used methods. The antibiotic is mixed into some squid oil that is poured or sprayed on the pellet feeds (for shrimp) or on the moist dough of trash fish used for feeding fish. The other method is to dissolve the antibiotics in water that is mixed into pellet feeds or wet dough. The dough is then extruded through a meat mincer and cut into pellets. Feed millers in Malaysia do not normally accept orders for medicated feeds unless for consignments of four tonnes or more (Che Utama Che Musa, *pers. com.*). A total of 77 types of antibiotics approved for incorporation into animal feeds by the Ministry of Health Malaysia are listed under the License for type B poisons.

Prawn Culture

The two species of prawns commonly cultured are the Malaysian freshwater giant prawn, *Macrobrachium rosenbergii*, and the penaeid prawns. The tiger prawn, *Penaeus monodon*, comprises more than 99% of the penaeid prawn cultured, with less than 1% comprising the banana prawn, *P. merguiensis*. In 1996, 114.27 tonnes of the freshwater giant prawn, 88.67 tonnes of banana prawn and 7659.57 tonnes of tiger prawn were produced (Annual Fisheries Statistics 1996).

For the larviculture and grow-out production of the Malaysian freshwater prawn, antibiotics are generally not used unless there are serious disease problems. Antibiotics, however, were commonly used as a prophylactic for penaeid prawn larviculture, especially with the adoption of the intensive culture method popularised by the Aquaculture Team of the *Centre Oceanologique du Pacifique* (Aquacop).

Antibiotics used include furazolidone, chloramphenicol and oxytetracycline, applied at a concentration ranging from 2 ppm on day three of culture to 10 ppm on day fifteen (Aquacop 1983), with the antibiotic selection made through antibiograms and tests on larvae. With prolonged application, higher and higher doses of antibiotics were needed for them to be effective in the hatchery and to sustain the targeted postlarvae production of around 45 PL4 (four-day old postlarvae) per litre of water. In the 1990s, however, the use of antibiotics as a prophylactic is discouraged, although they are still used when disease problems are encountered. Penaeid prawn hatcheries are not only able to meet the local demand for fry but are able to export fertilised eggs, nauplii and postlarvae to overseas markets.

The penaeid prawn grow-out industry encountered serious disease problems, mainly viral in origin, in the mid-1990s, resulting in mass mortality in culture areas in Merbok, Kedah, and to a lesser extent, in Manjung, Perak. Till today, many of the farmers in Merbok have yet to recover from the losses, and only a few of them returned to this industry after the widespread disease epidemic. Some farmers, out of desperation, resorted to all sorts of "cures" and medication including the use of garlic that is mixed into the prawn feed. This kind of desperation is not uncommon amongst farmers who are faced with devastating losses and are gamed to try all sorts of "cures" to recover their losses.

Fish Culture

In fish culture, freshwater fish constitutes 75% of the total fish production. In 1996, out of a total fish production of 27,313.9 tonnes, 21872.89 tonnes were from freshwater with 5441.01 tonnes from brackishwater (Annual Fisheries Statistics 1996). Freshwater species cultured include common carp *(Cyprinus carpio)*, javanese carp *(Puntius gonionotus)*, grass carp *(Ctenopharyngodon idellus)*, big head carp *(Aristichthys nobilis)*, black and red tilapia *(Oreochromis* sp.), marbled goby *(Oxyleotris marmoratus)* and catfishes *(Pangasius micronemus* and *P. pangasius)*. Brackishwater species cultured include the seabass *(Lates calcarifer)*, grouper *(Epinephelus* sp., *Chromoleptis altivelis)*, mangrove snapper *(Lutanius argentimaculatus)* and red tilapia.

Most of the freshwater fish fry are produced locally, although some species where demand exceeds supply or when the demand and supply are not synchronised, are imported. Species imported include the big head carp and the grass carp which are imported mainly from Hong Kong or Taiwan, the marbled goby and the catfish which are imported from Thailand. The hatchery and grow-out production of tilapia fry are normally free of disease, but that of the catfish and carps are more problematic, and diseases due to protozoans and bacteria are more frequently encountered. Antibiotics commonly used include teramycin, sulfonomides and tetracyclines. Before nitrofurans were banned, they were commonly used in the cultures too. Chloramphenicol is also used in freshwater fish culture. Feeding offal of poultry to fish for grow-out, example in catfish culture, may also cause antibiotic tainting as they are commonly incorporated into poultry feeds as a growth promoter or prophylactic, and if the use of antibiotics in poultry farming is not well controlled.

More than 90% of the brackishwater fish production are derived from floating net cages, with only around 6–7% of the production coming from brackishwater ponds. The marine fish fry production industry is very small, and in Malaysia, there are only 11 hatcheries and they are not able to meet the local demand for fry. Hence, more than 80% of the fry requirement are sourced from overseas, mainly from Thailand. Bacterial diseases such as vibriosis and scale drop disease are the main cause of mortality, and severe infections may cause mortality to be as high as 95%. It is not usual for prophylactics to be used when the fry arrive at the farm and diseased fish may suffer heavy mortality. Leong (1997) reported that sodium nifurstyrenate is effective as a prophylactic for groupers, and furanex for snappers. Both these compunds are nitrofurans, and therefore should not be used in the farms. Feeding with trash fish may be one of the major causes of disease problems. In many instances, these fish which are not properly refrigerated are in a state of decay and may harbour bacteria. Feeding them without vitamin and mineral supplements to cultured fish may cause some nutritional deficiencies since the trash fish may be lacking in some essential nutrients. The carrying capacity of the culture sites is very often not given due consideration, and cages are constructed close to each other, often with too many cages in one location, hence giving rise to poor water circulation and self-pollution. Depending on the size of fish, which may vary from 2–6 cm, during stocking, the survival rate till marketable size ranges from 10–30%.

Monitoring for Antibiotics and Food Safety

The Ministry of Health is the agency authorised by the Malaysian Government to ensure the safety of food for human consumption. The Ministry routinely monitors for the presence of nitrofurans in poultry, and presently has not built up its capabilities both in terms of manpower and expertise to monitor for other antibiotics as well as checking for their presence in other food groups. Seafood, example shrimps, meant for export are generally not checked for antibiotics, but the onus is on the exporting agencies which have been advised to ensure that they are aware of the requirements from importing countries. Some exporters have requested the Ministry of Health to test for the presence of antibiotics in their consignments designated for export. Presently most laboratories belonging to the Ministry of Health have limited capabilities and are able to analyse only a few types of antibiotics, mainly nitrofurans and chloramphenicol. Checks so far indicated that no shrimp or fish exports have been rejected by the importing countries because of contamination with antibiotics. A consignment of shrimps from Sarawak to France this year, however, was first suspected to contain antibiotic residues but was later cleared by the importing country (David Lau, Ministry of Health, Sarawak, *pers. com.*).

Apart from the Ministry of Health, the Department of Fisheries (DOF) is also committed to ensuring food safety at the point source or farm level. The latter is in the process of implementing the guidelines and regulations for sustainable aquaculture practices (Choy 1999). It is also developing its capability to ensure fish quality and safety through its Fish Inspection and Quality Control Programmes, and is at the initial stage in formulating a Hazard Analysis Control Point (HACCP) system for aquaculture farm management and production.

Health and Environmental Issues

One of the greatest health concerns over the use of antibiotics in human medicine and animal husbandry is the emergence and spread of antibiotic resistant bacteria. Bacteria are known to have the ability of evolving defense mechanisms against antibiotics and in the process become resistant to their effects. When such resistance develops, the bacteria will not succumb to the treatment and thus the antibiotic is no longer capable of treating or curing the disease. The more often an antibiotic is used, the greater the likelihood for the bacteria to become resistant to that drug. The resistant bacteria can reproduce and multiply freely and pass on the antibiotic-resistant genes to the next generation. The bacteria can also transfer that resistance to other bacteria species, thus causing cross-resistance. This happens when bacteria come into contact with each other and exchange plasmids that contain the anti-resistant genes. One of the greatest impacts of antibiotic resistance on health care is the increase cost of treating diseases. Antibiotic resistance also increases the seriousness of diseases. Development of new antibiotics has not kept pace with the emergence of antibiotic resistance, and there may come a time when there will be no effective antibiotics to treat certain diseases.

While medical use of antibiotics is probably the major contributor to the emergence of antibiotic resistance, use in animal husbandry and agriculture also pose a problem (Lieberman & Wootan 1998). Sub-therapeutic use of antibiotics such as oxytetracycline, tetracycline and chloramphenicol that are also used in human medicine may pose a hazard to human health, and also contribute to cross-resistance to antibiotics in human medicine. In 1969, the Swann Committee in the United Kingdom recommended that antibiotics that are used for human chemotherapy or those that cause cross-resistance against antibiotics used in humans should not be used as growth promoters (Witte 1998).

Smith *et al.* (1994a) reported that data obtained from developed countries in the temperate zone showed that although the frequency of resistant plasmids is elevated in the fish farm environment, such plasmids make only a very small and transient contribution to the numbers of resistant plasmids in human pathogens. However, data are lacking in developing countries in the tropics and studies have to be carried out before potential risks can be assessed.

Choo (1999) reported that the impacts of antibiotic use on the aquatic environment will be greater when antibiotics with long half-life are used. Studies on oxytetracycline, one of the antibiotics frequently used in aquaculture, showed that it has a short half-life in water in both tropical and temperate conditions but a long half-life in sediments (Jacobsen & Berglind 1988; Samuelsen 1989; Björklund *et al.* 1990; 1991; Lunestad 1991; Choo 1994). Under temperate conditions, initial disappearance of oxytetracycline was rapid in sediments, but residues persisted up to 18 months (Samuelsen *et al.* 1992). It was also found in concentrations capable of causing antimicrobial effects for up to 12 weeks in bottom sediments after its use in fish farms (Jacobsen & Berglind 1988). Furazolidone has a short half-life in water (Choo 1998) as well as in sediments (Samuelsen *et al.* 1991). Despite that, furazolidone is banned in many countries because of its mutagenic characteristics. Studies showed that oxolinic acid has a long half-life in water under both temperate and tropical conditions (Lunestad 1991; Choo 1999), but does not persist in sediments (Björklund *et al.* 1991).

Build-up of antibiotics at the sea floor can also cause inhibition of microbiological activity in the bottom sediments below the fish cages (Hansen *et al.* 1992). This would then affect the rate of degradation of accumulating organic matter under the cages. Changes in benthos community as a result of the accumulation of excess medicated feed and faecal pellets have also been reported (Brown *et al.* 1987; Weston 1990).

Antibiotics used in aquaculture reaching non-target groups in the coastal areas have given rise to concern over seafood safety. Moster (1986) found detectable concentrations of oxytetracycline in blue mussels 80 m from a farm using this antibiotic. Björklund *et al.* (1990) reported the presence of oxytetracycline in wild fish caught in the vicinity of two farms where medication was used. Lunestad (1991) found residues of oxolinic acid in wild fish from cages where fish were medicated with this antibiotic. On the day when medication was terminated, the average concentration of oxolinic acid in the muscle of wild fish was 3800 ppb. However, no residues were detected in wild fish 12 days after medication.

Control and Mitigation Measures

In order to ensure the proper use of antibiotics in aquaculture, some control over its use is required. Lack of data on the aquatic chemistry and biological effects of many of these substances, has tended to fuel environmental concerns. This has prompted a call for a more thorough evaluation of these chemicals before they are approved for use in aquaculture (ICES 1989; HMSO 1992; Spencer 1993 – cited from Redshaw 1995). Redshaw (1995) recommended that ecotoxicological testing and risk assessment be carried out before a drug is approved for use in aquaculture. A list of approved drugs should then be compiled with instructions on its use, together with the required withdrawal time. To have better control, drugs should be prescribed by a veterinarian or a qualified person, and to be purchased only through licensed pharmacists. There should be a central agency to keep track of the amount of antibiotics used for aquaculture purposes, and farmers should be made aware of the importance of the proper use of antibiotics.

Presently, little work is carried out on the genetic selection of cultured species to produce high-health fry. There is also a need to produce more vaccines and to research on the nutritional requirements of the tropical species cultured so that their immunity towards diseases can be enhanced. Better understanding of the aquatic environment and the carrying capacity of the culture site should also be emphasised.

Studies to reduce antibiotic residues in farm effluents aim to minimise contamination of the aquatic environment should be conducted. Smith *et al.* (1994b) reported that correct design of effluent treatment systems could significantly reduce the environmental impact of antibiotics from land-based fish farms. It was found that a filter of nominal porosity of 50 µm was capable of at least a 500–650 fold concentration of the oxytetracycline into the filter, thus reducing the oxytetracycline concentration in the effluents.

Understanding the kinetics of antibiotics in the aquatic environment is also important. Half-lifes of antibiotics in the aquatic environment are dependent on the roles played by sediments and the cultured organisms. Pouliquen *et al.* (1993) reported that the disappearance of oxytetracycline from seawater was faster in fish farms where fish were cultured in raceways than in shellfish farms. This observation was attributed to the persistence of oxytetracycline in the bottom sediments of the shellfish farm and their slow escape into the water by absorption diffusion. The shellfish, which are filter feeders may have helped also to accumulate the oxytetracycline.

Initially, the fastest way to ensure proper use of antibiotics in the farms may be through the regulatory and enforcement approach. However, for the "control and command" approach to be effective, considerable amount of cost and manpower are required. In future, aquaculture farms should also become more proactive like industries in the manufacturing sector. They should voluntarily seek accreditation through the implementation of environmental programmes like the ISO 14000 series to ensure the sustainability of the aquatic environment, as well as the HACCP system in farm management and production to ensure food safety.

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