Pollution of Water Bodies by Drugs in the Aquaculture Industry in China

LWS 548 Major Project

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Executive summary

Previously, people relied on agriculture and fishing for wild fish to obtain food for protein. However, with modernization, global climate change caused by human activities has seriously threatened agricultural production, resulting in lower yields or lower quality of crops. At the same time, the establishment of more and more factories has led to the flow of wastewater into rivers and oceans, and has poisoned aquatic animals. The consumption of contaminated aquatic products can have a negative impact on people's health. As a result, aquaculture is becoming an important source of fish protein.

In aquaculture, it is common for drugs including antibiotics to be used to improve the yield of aquaculture products as well as to prevent infectious diseases in animals. China is one of the world's largest producers of aquaculture products. This report analyzes the Chinese aquaculture industry as a case study, focusing on the species cultured in the Chinese marine aquaculture industry and some of the main antibiotics used. In addition, since antibiotics cannot be fully absorbed and utilized by animals, the analysis of the effects caused by their residues reveals that these antibiotics are left in aquatic products by bioaccumulation, which has a negative impact on the growth of organisms and also the production of antibiotic resistance genes. Exposure to or ingestion of these aquatic products can pose a health risk to people. Methods have been proposed to reduce the adverse effects produced by these drugs. A comparison of relevant regulations in China, and other countries, was conducted to analyze the reasons why drug abuse is very common. Finally, some suggestions are given to policymakers, farmers, and the public for the better development of aquaculture in China.

1. Introduction

The requirement for protein is increasing due to the increase in population worldwide (Melaku & Natarajan, 2019). Fish is one of the most important sources of food for humans as it is a source of high-quality protein, especially in areas where protein from livestock is less available (Tidwell & Allan, 2001). Fish provide humans with approximately 16% of the protein obtained through the consumption of animals. (FAO, 2000). At the same time, the development of society and the occurrence of epidemics have made people more and more concerned about their health. According to Balami et al. (2019), fish contains important macronutrients, and when people consume more fish, it is beneficial for healthy. However, modernization has led to serious marine pollution. Liu et al. (1991) reported that China discharges 2 billion tons of wastewater into its fishing waters, causing excessive levels of heavy metals in the ocean, which can pose a serious threat to aquatic life. Austin (1998) also found that when large amounts of pollutants are released into the ocean, they can cause massive fish kills. Much of this marine pollution occurs in areas of the world where wild marine fish are harvested (Waldichuk, 1974). The demand for protein cannot be met by harvesting wild marine fish alone.

Crops and livestock are also major sources of protein for people. For example, bean plants are rich in protein and so can be a key contributor to human protein intake (Robinson et al., 2019). Also, according to statistics, wheat is an important food for human consumption of protein (Asseng et al., 2018). In Western countries, protein intake is mainly through meat and dairy products (Robinson et al., 2019). Nowadays, however, climate change has had a huge impact on crop production, as changes in temperature, precipitation patterns and other influences. Agriculture and climate change are related. Global climate change has negatively affected crop production in recent years, seriously threatening food security worldwide (Raza et al., 2019). Beebe et al. (2011) found that the distribution of legume crops in some areas is related to temperature changes, and when the temperature increases, the yield of bean crops decreases. In addition, despite the current status of new genotypes of wheat developed to adapt to climate change, their protein concentration is 1.1% less than that of normal varieties of wheat (Asseng et al., 2018). Moreover, Raza et al. (2019) predicted that in 2050 the global population will grow to 9 billion and the demand for food will increase by 85%, while rising temperatures will reduce global crop production, which will lead to deteriorating food security. In addition, increased temperatures due to greenhouse gas emissions will result in lower dairy production, lower animal weights and reduced reproduction, and increased disease rates in livestock, such as cattle, goats and horses that are susceptible to nematode infections, all of which have a significant negative impact on animal protein production (Sejian et al., 2012; Aydinalp & Cresser, 2008).

Therefore, the development of aquaculture is important to compensate for the decline in catchable wild fish due to pollution and the decline in the availability of protein for crops and livestock due to climate change. Integrating agriculture and aquaculture can provide more food and eliminate malnutrition, especially in lesser developed countries (Melaku & Natarajan, 2019; Ahmed & Garnett, 2011).

To prevent and treat infectious diseases in aquatic animals and to improve their production and quality, drugs are widely used in aquaculture. Drugs are chemicals that can induce alterations in organism's physiology after consumed. There are 170 aquaculture diseases, and approximately 500 drugs including antibiotics, pesticides, and disinfectants applied in the water to ensure aquatic food production (He et al., 2016).

However, the irrational use of drugs in aquaculture can cause serious water pollution. Studies have shown that most of the compounds are excreted in the feces and urine of organisms, and incomplete metabolism allows these substances to remain in the water, causing potential contamination of the water (Chen et al., 2022). Moreover, Samuelsen (1989) found that only 20-30% of the antibiotics are absorbed by the fish, while the rest are retained in the water, thus adversely affecting the water environment and the water ecosystem. As the drug residues remain in the water, fish may continue to be exposed and reabsorb the drug to accumulate in their bodies. And these chemicals can cause microorganisms in the water to develop resistance genes and pathogen resistance (He et al., 2016). He et al. (2016) reported that the residual antibiotics had caused the pollution in the Pearl River Delta, and they also found the presence of antibiotic resistance genes (ARGs) in the Beijiang River. In addition, Zou et al. (2011) found that in some cases, ARGs can be transferred in the environment and amplified due to genetic mechanisms. These genes pose risks to humans and animals (Zhang et al., 2009). Meanwhile, a combination of antibiotics can make the overall effect greater than the effect of individual antibiotics (He et al., 2016). Thus, although ARGs may be present in only some aquaculture, they can have an impact on a wider range of aquatic organisms. On the other hand, although studies have shown that low concentrations of these antibiotics are not harmful to humans, the concentration of antibiotics in fish continues to increase as they accumulate over time, and there is a potential health risk for people consuming these fish (Chen et al., 2022).

In this report, I will explain the scope of the study and demonstrate the main fish species and drugs used in the Chinese aquacultural industry. In addition, the effects of drugs on the aquatic environment will also be presented. I will describe some of the measures that can be taken in the future to reduce the negative environmental impacts of drug use. In addition, the existing aquaculture regulations in China, and other countries, will be reviewed to help enforce the management of the aquaculture industry in China.

2. Objectives

- Assess the impact of drugs used in the aquaculture industry on aquatic ecosystems.
- Identify some potential solutions that could mitigate the contamination.

- Provide some suggestions to improve the existing regulations in China by comparison with the management methods of other countries for aquaculture.

3. Methods

This study highlights the impact of drugs used in Chinese aquaculture on aquatic ecosystems, particularly marine aquaculture, and also includes potential solutions to reduce the continued environmental pollution from drugs in the future.

To achieve these goals, the published literature on aquaculture pollution and the types of drugs used in Chinese aquaculture was reviewed, and evaluated of the influence of pollution on the aquatic ecosystems. Meanwhile, I gathered some information related to existing management practices, and the management and control of aquaculture pollution in other countries. In addition, this project will collect information from statistical websites and government websites. By comparing this information, I provided some recommendations to improve the management of aquaculture in China.

4. Case study

China is one of the most successful countries in the world in aquaculture production and is also a major component of the world aquaculture industry (Farquhar et al., 2017). Since the 1950s, aquaculture has emerged in China and has gradually become an important economic venture. According to Li et al. (2011), China accounted for almost 70% of the global aquaculture industry. The latest statistics from the Food and Agriculture Organization of the United Nations (FAO) show that China's aquaculture production and fishing volume reached almost 60 million tons, the highest in the world (Global Fisheries and Aquaculture at a Glance, n.d.). Global capture fisheries and aquaculture production is shown in Figure 1. Shao et al. (2021) stated that the annual breeding scale of aquaculture in China will reach 30% of the world by 2030.

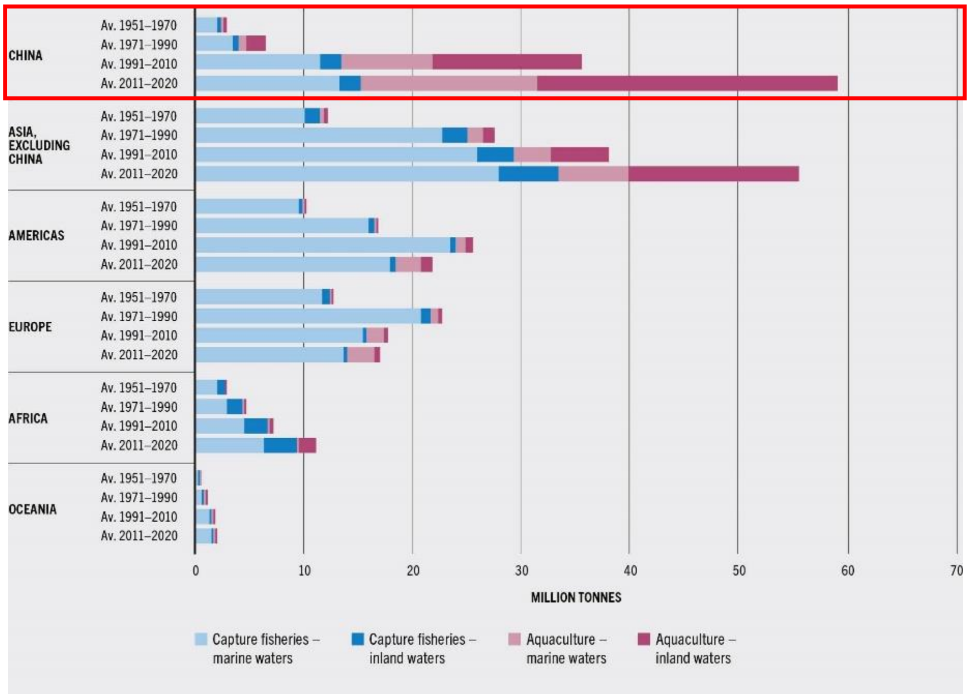

Fig. 1. Global capture fisheries and aquaculture production (Global Fisheries and Aquaculture at a Glance, n.d.)

Intensive aquaculture is common in China, and high stocking densities have increased the incidence of disease, and the use of antibiotics and other drugs has become a requirement in aquaculture (Mo et al., 2015; Zou et al., 2011). In the beginning antibiotics were used to control disease infections in animals. But nowadays they are gradually being used as feed additives, prophylactics and growth promoters, and they are used in large quantities to obtain economic benefits (Shao et al., 2021). However, the misuse of antibiotics led to media coverage, and the U.S. Food and Drug Administration (FDA) issued a warning about the high levels of antibiotics in imported Chinese aquatic products (Mo et al., 2015).

4.1. Scope of project

In China, aquaculture includes freshwater and marine aquaculture. According to statistics, the size of marine aquaculture reached 1,532,152 hectares in 2003, and after 18 years of development, the area of marine aquaculture reached 2,025,510 hectares in 2021 (2021 National Fisheries Statistics Bulletin, n.d.). The aquaculture sites are mainly located in the Bohai Sea, Yellow Sea, East China Sea and South China Sea, as shown in Figure 2 (Cao et al., 2007).

Freshwater aquaculture in China, such as pond, lake and reservoir farming, often adopts low-density culture methods with low disease rates in fish, so it is uneconomical to use drugs to control morbidity (Yulin, 2000; Cao et al., 2007). However, the density of aquaculture in coastal areas of China is high, so fishermen use drugs, especially antibiotics, to limit the occurrence of diseases, and coupled with the large area of culture, the excessive use of drugs has negative effects on the environment as well as on the organisms (Yulin, 2000).

The scope of this study focused on the pollution caused by drug use in the marine aquaculture industry.

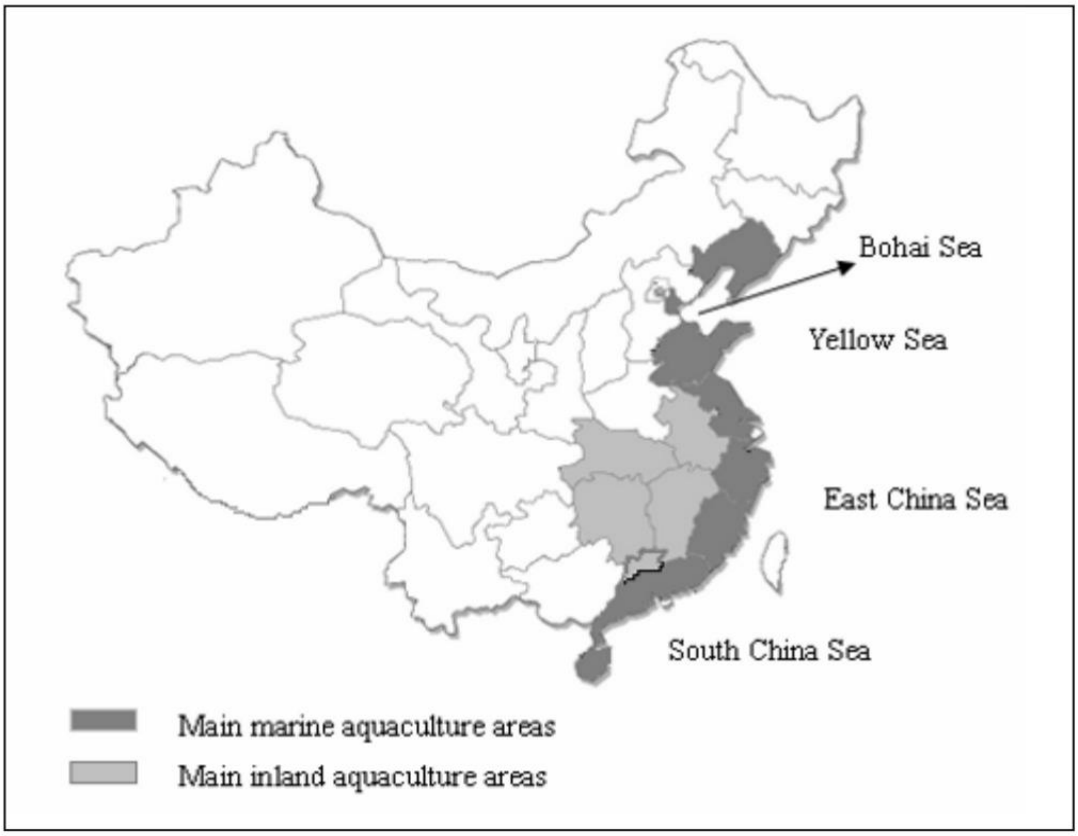

Fig. 2. Map of freshwater aquaculture and marine aquaculture in China (Cao et al., 2007).

5. Results and discussion

5.1. Aquaculture species

The development of China's marine aquaculture industry has expanded very fast. Due to the increase in aquaculture methods, the number of species cultured has increased from a few previously to more than 150 different species as of 2017 (Li et al., 2011; Farquhar et al., 2017). And Yue et al. (2023) stated that up to 280 species are now used for marine aquaculture in 2021. According to Li et al. (2011), the main species in marine aquaculture include fish, shrimps, crabs, mollusks and seaweeds as shown in Table 1. Aquaculture systems are categorized into closed-water aquaculture and open-water aquaculture (Li et al., 2011). Among them, closed water aquaculture includes pond and indoor tank with recirculation water system. Moreover, mollusks account for 70% of total marine aquaculture production (Yue et al., 2023). In addition, in southeast China, large yellow croaker, grouper and sea bream have become the main cultured species (Li et al., 2011). In addition, the development of farming techniques has led to the cultivation of rare species such as abalone, scallops, prawns, turbot and flounder (Li et al., 2011).

Table 1. Major marine aquaculture species in China (Li et al., 2011)

	Culture system	Species
Marine aquaculture	Pond	Shrimp, crab, shellfish, Gracilaria spp., fish
	Floating raft	Seaweed, scallops, oysters, abalone
	Mudflat	Laver, razor clam, hard clams, oysters
	Pen	Abalone, shrimp
	Inshore cage	Fishes
	Offshore cage	Fishes
	Tunnel	Abalone
	Submerged cage	Abalone, fishes
	Indoor tank with recirculation water system	Flounders, turbot and other fishes, abalone
	Sea bottom and sea ranching	Abalone, Japanese scallops, giant cockles, sea cucumbers, sea urchins
	Sea stock enhancement	Chinese shrimp, red sea bream, flounders, large yellow croakers, mullet, jellyfish

5.2. Types of drugs used

5.2.1. Antibiotics

It is widely known that antibiotics are often used for disease prevention and treatment in aquaculture and/or for growth promotion. This is because farmers have found the chemicals to be economical and efficient (Yulin, 2000). In China, with the development of intensive aquaculture, antibiotics have become a necessity in aquaculture activities as the main drug used (Zou et al., 2011). The Chinese average use of antibiotics is 10 times higher than that of the United States (Liu & Wong, 2013). Therefore, the global literature was reviewed to better understand the antibiotics used in the Chinese mariculture industry.

The review concluded that there are six types of antibiotics used in Chinese marine aquaculture, which are sulfonamides (SAs), macrolides (MLs), tetracyclines (TCs), quinolones (QNs), chloramphenicols (CPs) and lincosamides (LNs) (Lyn et al., 2020; Liu et al., 2017; He et al., 2011). However, there are four that were found to be widely used through testing (Lyn et al., 2020), which are QNs SAs, MLs and TCs as shown in Figure 3. Lyn et al. (2020) also claimed that the detection rate of antibiotics in coastal waters was very high, reaching 96.4%. In addition, QNs were the most monitored antibiotics in coastal waters, followed by SAs and MLs, both of which were positively correlated with mariculture in terms of concentration (Liu et al., 2017). Among the QNs include norfloxacin (NOR), ciprofloxacin (CIP) and enrofloxacin (ENR) (He et al., 2011). Meanwhile, Liu et al. (2017) noted that the first two had the highest residue levels.

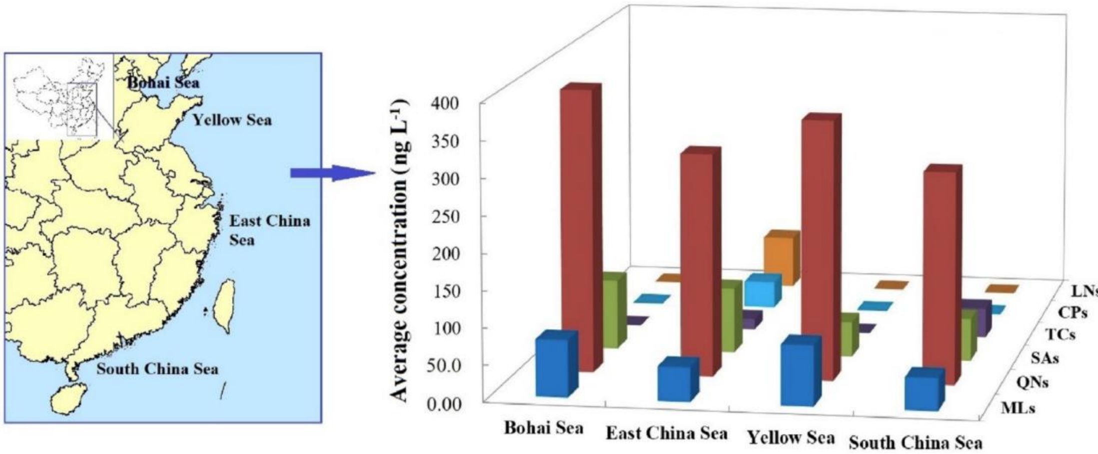

Fig. 3. Average concentrations of six antibiotics detected in coastal areas of China (Lyn et al., 2020)

5.2.2. Metal compounds

Metal compounds are also widely used in the aquaculture industry. People use fertilizers containing metal elements to increase plant nutrient concentrations and improve fish and shellfish production by stimulating phytoplankton production (Emenike et al., 2021). Compounds containing copper are often used as herbicides to control weeds in water (Cao et al., 2016). On the other hand, marine aquaculture uses artificially woven nets and cages. In order to prevent organisms from growing on the surface of these artificial structures, people usually apply paints containing heavy metals to these structures (Emenike et al., 2021). However, over time, these heavy metals can enter the water and, thus, accumulate in the bodies of farmed animals (Kalantzi et al., 2016). According to Boyd and Massaut (1999), the impact on aquaculture products from largest to smallest is lead (Pb), arsenic (As), mercury (Hg), cadmium (Cd), chromium (Cr), cobalt (Co), copper (Cu), zinc (Zn), manganese (Mn), iron (Fe) and nickel (Ni).

5.3. Impacts of drugs

5.3.1. Aquatic organisms

Although antibiotics can effectively reduce the morbidity of fish, promote fish growth, and contribute greatly to the economic growth of the marine aquaculture industry, antibiotics cannot be completely used in the animal's body, and 70% to 80% of antibiotics are re-accumulated in the water, sediment, and animal tissues through the animal's fecal excretion (He et al., 2011; Okeke et al., 2022). On the other hand, farmers only know the efficacy of antibiotics, but lack the knowledge to determine the amount of antibiotics according to the actual situation, thus resulting in the overuse of antibiotics, which will cause antibiotic residues in the water (He et al., 2011). Since water is mobile, these drug residues can have an impact on both farmed and wild animals.

QNs and SAs are widely distributed in fish tissues (Liu et al., 2017). QNs are stable in fish tissues and He et al. (2016) reported 100%, 20% and 40% detection rates for NOR, CIP, and ENR, respectively, in marine fish. The concentration of NOR was the highest, which may be due to its low price and effectiveness, which is widely used by farmers (He et al., 2016). He et al. (2011) examined fish samples collected from the Pearl River Delta in China and found that the concentration of residual QNs in the fish was higher than in fish from Canadian farming areas and even higher than in fish from a sewage-contaminated river in North Texas, USA. Moreover, they also found that higher concentrations of QNs in fish liver tissue than in muscle tissue, most likely because

QNs are mainly metabolized in the liver (He et al., 2011). On the other hand, benthic species have higher concentrations of QNs in their bodies as a result of their living and dietary habits (He et al., 2011). For example, He et al., 2016 and Chen et al. (2020) found that eels and snappers are susceptible to antibiotic residues in sediments, which can lead to cumulative effects in their bodies. The same results were also confirmed by He et al. (2016). Additionally, in some coastal areas, farmers often use frozen fish feed as feed, and some of these antibiotics can precipitate and accumulate in the sediment, allowing benthic species in contact with the sediment to absorb more antibiotics (He et al., 2011).

The concentration of SAs in marine farmed fish is higher than that of QNs and He et al. (2016) pointed out that SAs are less soluble and can persist in water for a long time, while QNs are prone to photolysis in water and are also easily adsorbed by solid particles. According to Chen et al. (2020), the concentration of SAs in carnivorous fish, such as sea bass in the Pearl River Delta of China, is higher than that in herbivorous fish. Meanwhile, He et al. (2011) also stated higher levels of contamination in carnivorous species. The reason for this phenomenon is that carnivorous fish are the top consumers in the aquatic food chain (Okeke et al., 2022; He et al., 2011; Chen et al., 2020). Also, high levels of antibiotics were detected in the gill portion of the fish because the residual antibiotics in the water were reabsorbed into the fish's body through the gills (Chen et al., 2020). The level of antibiotic residues in different animals is different. This is because the rate of metabolism is different and also the stage of growth can have an effect on it (Chen et al., 2020; Bosch et al., 2015). For example, older fish have higher antibiotic accumulation than younger fish.

The impact of TCs on fish cannot be ignored. Amangelsin et al. (2023) found that TCs can cause embryotoxicity in fish, thus hindering embryo development. Economically, this can impede the development of aquaculture. At the same time, Yu et al. (2020) reported damage to the thyroid function of fish due to long-term exposure to TCs, as well as a decrease in body length and body weight with increasing exposure time. In addition, TCs can cause antioxidant stress in fish animals (Amangelsin et al., 2023). Yu et al. (2019) discovered that glucose in fish decreases rapidly after exposure to TCs, which means that fish need more energy to sustain their functions. Another effect of TCs is the alteration of fish behavior, such as changes in swimming patterns due to altered fish photosensitivity (Amangelsin et al., 2023). According to Petersen et al. (2021), TCs also alter the learning process and the propensity for aggressive behavior in fish.

The adverse effects of antibiotics extend beyond fish. QNs and SAs can disrupt early zooplankton developmental processes and reduce chlorophyll production in phytoplankton (Okeke et al., 2022). Also, Song et al. (2016) found that MLs have serious adverse effects on algal growth. Although these changes do not initially cause large effects, the effects are eventually amplified through the food chain. In addition, TCs are harmful to algal communities, and some algae are affected and undergo structural changes (Amangelsin et al., 2023). When the concentration of TCs increases, the transparency of the water decreases and the concentration of dissolved oxygen (DO) also decreases, which will also cause the phenomenon of water bloom, which is harmful to aquaculture animals (Amangelsin et al., 2023). On the other hand, Okeke et al. (2022) found that the roots of aquatic plants can absorb antibiotics, and microorganisms located in the roots can break down antibiotics, thus facilitating the process of antibiotic uptake by the roots. These effects can lead to unbalanced aquatic ecosystems (Cao et al., 2007).

The effects of heavy metals on fish are profound. Due to the accumulation of heavy metals in the water, the organisms in the water are exposed to these elements. And the main elements that cause adverse effects are Pb, As, and Cd. Pb easily enters the bloodstream of fish and accumulates in various parts of the body, such as bones, gills, kidneys, and scales (Bosch et al., 2015). Llobet et al. (2002) found that a large amount of As is present in marine fish, and most of it is in the form of organic arsenic. Also, Cd easily crosses biological membranes and thus enters cells and binds to ligands, for example, in fish muscle tissue cadmium can bind to proteins, so absorbed cadmium cannot be easily excreted, resulting in bioaccumulation (Bosch et al., 2015). Also, Wong et al. (2001) reported the highest concentration of cadmium in the intestine of fish compared to other organs. In addition, Cd is also easily absorbed by plankton and microorganisms into the marine food chain (Bosch et al., 2015).

5.3.2. Microorganisms

The inability to use antibiotics exclusively in aquaculture animals, coupled with repeated and heavy drug use may lead to genetic mutations and pathogen resistance in bacteria, resulting in the development of antibiotic resistance genes (ARG) (Okeke et al., 2022; Zhang et al., 2009 & He et al., 2016). Moreover, ARGs are considered to be emerging pollutants in the environment and are considered to be one of the major environmental issues that people will have to face in the 21st century (Zou et al., 2011). This is mainly due to the rapid development of aquaculture. According to Zhang et al. (2009), ARGs, like other persistent organic pollutants and heavy metals, are 'easy to get but hard to lose'. They also have the characteristic of being easy to spread (Dong et al., 2021).

ARGs are present at all trophic levels in aquatic environments (Okeke et al., 2022). After ARGs are formed, microorganisms in the water are the first to be exposed to ARGs before they are passed on to other organisms at higher trophic levels (Okeke et al., 2022). The main transfer mechanism of ARGs is horizontal gene transfer (HGT), which is a widely recognized adaptive mechanism in bacteria (Soucy et al., 2015). It refers to the sharing of genetic material between organisms that are not related by parentage, so they can be transferred between different species (Dong et al., 2021). And this is why they can disseminate rapidly. In addition, various pollutants can also promote the spread of antibiotic resistance (AR) or ARGs in water, for example, ARs can be induced to change by heavy metal selection, and the HGT of ARGs in microorganisms can be stimulated by environmental stresses caused by pollutants (Li et al., 2021; Sun et al., 2021). More seriously, the range of antibiotics has led to a large variety of ARGs. Liu and Wong (2013) discovered multiple antibiotic resistance integrators, which may contain more than 100 ARGs cassettes. At the same time, these genes can remain in the environment for several years (Naylor et al., 2023).

Aquaculture is a source of antibiotic-resistant bacteria (ARB) production (Dong et al., 2021). The presence of ARGs in water leads to the formation of ARB; however, the genetic material of these bacteria may mutate during the horizontal gene transfer process, leading to the formation of new ARGs and making bacterial resistance more widespread (Okeke et al., 2022). At the same time, the emergence of new bacteria can lead to new infections in aquatic animals, and people have to use more antibiotics, creating a vicious cycle (Dong et al., 2021).

5.4. Human health impact assessments

Because aquatic products are contaminated with excessive amounts of drugs, they also pose a health risk when ingested by humans. Human consumption of aquatic products affected by antibiotics (e.g., tetracyclines, sulfonamides) is at risk for adverse drug reactions (ADR) (Liu et al., 2017). These antibiotics can cause allergic symptoms, such as hives, or cause angioneurotic edema, which can lead to shock and death in severe cases (Liu et al., 2017). At the same time, (Wang et al., 2022; Liu et al. (2017) stated that high consumption of fish that are contaminated with quinolones poses potential risks, such as adverse effects on dental development in children. Moreover, some antibiotics become more toxic when metabolized by the body (Liu et al., 2017). Despite the harmful effects of antibiotics on humans, reports comparing estimated daily intake (EDI) with acceptable daily intake (ADI) established by the WHO have found no significant risk to human health from the consumption of these fish products (Chen et al, 2022 & Liu et al., 2017).

However, one study showed that organisms exposed to low levels of contamination for long periods are affected, so long-term human consumption of these aquaculture products can still pose a health risk (Chen et al., 2020; He et al., 2014). He et al. (2016) have demonstrated this by calculating that the EDI of QNs is 2-6% of the ADI, indicating that long-term ingestion of contaminated fish is unsafe. People do not have a health risk if they only consume sea fish, as people also consume other foods, such as seafood shellfish, which have been detected with SAs as well as other antibiotics (He et al., 2014). On the other hand, in addition to the use of antibiotics, people also use some metal-amended feed to meet the demand of fish for some nutrients (Sapkota et al., 2008). For example, higher levels of arsenic, lead, and zinc have been detected in farmed eels than in wild eels. Similarly, there is a report that people in some communities are exposed to heavy metals through the consumption of fish (Rubio et al., 2005). Although arsenic is present in the form of organic arsenic, which is less toxic, human exposure can result in vomiting, muscle weakness, and skin disease symptoms (Bosch et al., 2015). In addition, excessive intake of lead can affect the blood and cause kidney failure as well. Cadmium, on the other hand, has a long biological half-life, and people are unable to reduce the burden on their bodies, causing high blood pressure, neurological disorders, and bone defects (Bosch et al., 2015). Some fish contain mercury, and their ingestion by humans can cause mercury poisoning, resulting in hearing impairment, headaches, motor difficulties, and harm to brain function, especially for children (Bosch et al., 2015). In addition, Rahman et al. (2012) claimed that there may be a correlation between metals, with some metals surviving into the absorption of others by humans. Hence, the intake of some fish can lead to the accumulation of metals in the human body, posing a threat to human health and even causing cancer (Sapkota et al., 2008).

The presence of ARGs and ARBs in water also poses a public health risk. Two ARGs of sulfonamides were found in the Beijiang River, one of southern China's important drinking water sources (Zhang et al., 2023). This means ARGs can enter the body through drinking water and cause infection (Liu et al., 2017). Additionally, long-term intake of foods containing antibiotics can lead to the development of antibiotic resistance in the body. This can increase the number of infections in humans for a given disease, as the pathogen becomes resistant to antibiotics (Rasul & Majumdar, 2017). At the same time, antibiotic resistance prolongs the course of the disease and reduces the success of treatment (Chen et al., 2020). According to the World Health Organization (WHO), drug-resistant diseases will push 24 million people into extreme poverty by 2030. By 2050, drug-resistant diseases will kill 10 million people a year and drive the global economy into crisis (Shao et al., 2021).

The risk posed by drugs to the health of the farmer should also be considered. Because most farmers are unaware of the risks of antibiotics, they don't realize the importance of protection, and long hours of work that expose them to antibiotics by inhalation or through exposure to injured skin which can pose serious health risks and even lead to leukemia (Sapkota et al., 2008).

Due to drug abuse, most of aquatic products are contaminated and these contaminations are undetectable, people cannot recognize them when purchasing and believe that food purchased through legal channels such as supermarkets, dealers, etc. is safe. This shows that people are still not aware of the drug residues in animals and the harm they cause.

5.5. Mitigation methods

In order to reduce the water pollution caused by the drugs used in aquaculture, research should be conducted on the treatment of aquaculture wastewater and finding alternatives to existing drugs, some feasible methods should be derived by reviewing relevant literature.

5.5.1. Wastewater treatment

Differences in farming systems were mentioned above, and treatment of farm wastewater can be adopted for closed-water farming. However, it is difficult to treat mariculture wastewater by conventional processes due to the salinity effect of seawater (Lang et al., 2020). Currently, commonly used wastewater treatment technologies (e.g., nanofiltration and reverse osmosis) can effectively remove some antibiotics, while some studies have shown that aquaculture wastewater filtration using nanofillers can achieve up to 90% antibiotic removal, for example, by removing residual SAs and QNs antibiotics from water (He et al., 2016 & Okeke et al., 2022). These two antibiotics are heavily used in China, so these wastewater treatment technologies can be widely adopted in China. In addition, Okeke et al. (2022) also found that nanoparticles can eliminate some ARBs, thus reducing their threat to aquatic animals and human health.

Filtration leads to high maintenance costs after membrane fouling, so researchers have looked for more efficient and less costly methods. Lang et al. (2020) found that flow-through electrochemical oxidation treatment of marine aquaculture wastewater can improve the removal of pollutants, while the technology has better bactericidal properties and can completely remove SAs antibiotics.

5.5.2. Alternative measures

Vaccination of aquatic organisms can reduce the probability of contracting diseases (He et al., 2016). China currently has six aquatic vaccine products that have passed the national veterinary drug certification (Wang et al., 2020). Vaccines suitable for marine aquaculture include the inactivated vaccine against Aeromonas hydrophila sepsis in fish, the live vaccine against Edwardsiella tarda in turbot, and the genetically engineered live vaccine against V. anguillarum in turbot (Wang et al., 2020). In addition, wang et al. (2020) evaluated the immune response of fish using the vaccine and found that the use of the vaccine had no adverse effects on the fish, while effectively increasing the fish's immunity to the disease. However, a vaccine can control only one disease, and there are many types of diseases in aquatic animals, so it is not feasible to rely on vaccination alone to prevent disease (He et al., 2016). Also, because these animals live in water, vaccination is very difficult. Therefore, more methods need to be explored.

Microbial action can effectively prevent and control marine aquaculture diseases (He et al., 2016). According to WHO, probiotics, as a live microbial adjuvant, can alter the microbial community in the host, thus improving the nutritional value of the feed for the host (Hotel & Cordoba, 2001). At the same time, probiotics can improve the host's response to disease and therefore can be used in aquaculture to promote fish growth and prevent disease infections (Mo et al., 2015). For example, Balcázar et al. (2006) found that the use of antagonistic bacteria to control gut bacteria in fish was effective in reducing the probability of opportunistic pathogens. On the other hand, lactic acid bacteria are helpful for the growth of fish and for improving immunity (Mo et al., 2015). The use of lactic acid bacteria can improve the innate immune response as well as the resistance of fish. In addition, since water pollution can suppress the immune system of fish, using bacteria to improve the quality of the water environment can reduce the negative effects of the suppression on fish (Mo et al., 2015; He et al., 2016). Meanwhile, increased immunity to disease means that people can reduce the use of drugs such as antibiotics. Lower drug use is also helpful for resistance gene control, which can greatly reduce the production of ARGs and ARBs in water.

The use of traditional Chinese medicine (TCM) as a potential alternative to antibiotics in aquaculture has been extensively studied (Mo et al., 2015). TCM can improve the ability of fish to have non-specific immunity and disease resistance, while TCM also has antibacterial ability, such as Angelica dahurica (Chinese angelica), Lycium barbarum (Chinese wolfberry), and Scutellaria baicalensis (Chinese skullcap) to inhibit a variety of bacteria. In addition, the Ministry of Agriculture (MOA) has mentioned some specifications for the use of TCM in the Safety Food-Criterion for the usage of Fishery Drugs. Rasul and Ajumdar (2017) reported that natural essential oils extracted from plants are generally recognized as safe substances that have antimicrobial properties and can therefore be used instead of antibiotics to treat diseases present in aquaculture. In addition to its ability to improve immunity and antibacterial properties, Mo (2014) discovered that feeding with TCM can promote the growth capability of fish. TCM has the advantage of no residue and no side effects, so it has great potential to replace antibiotics in the future (He et al., 2016). However, determining the exact dosage of TCM can be challenging because the active ingredients in a plant are influenced by its growth stage and the environment in which it is grown (Pu et al., 2017).

5.6. Regulations

For pollution control, making laws and regulations is often an effective method. From the 1980s to the early 2010s, the Chinese government introduced several regulations for aquaculture, such as the Fisheries Law, Regulations on Aquaculture Quality and Safety, the Marine Environment Protection Law, but they were not strictly enforced (Naylor et al., 2023). In addition, antibiotic abuse is still prevalent despite regulations being issued regarding antibiotic abuse (Shao et al., 2021). Because of the crossover between antibiotics used in aquaculture and those used for medical treatment, only 13 antibiotics are approved for use in China and the use of other antibiotics is prohibited, but aquatic products have been detected to contain 33 antibiotics (Song et al., 2016; Naylor et al., 2023). According to He et al. (2011), CIP is banned by the Chinese Ministry of Agriculture, but reports in recent years have found that CIP is still present in fish, indicating the presence of illegal antibiotic use. Meanwhile, Fang et al. (2020) reported that 89% of farmers in China have easy access to antibiotics, with 83.7% of them able to purchase antibiotics without any permits. On the other hand, antibiotic residues in some fish have been below the guidelines issued by the MOA, but still exceed the U.S. Environmental Protection Agency's (EPA) maximum residue levels (Song et al., 2016). As a result, the United States has banned the import of these fish from China.

Because of the small and inefficient staff regulating antibiotics in China, coupled with the current lack of alternatives to antibiotics, when disease outbreaks occur, farmers are forced to purchase and use antibiotics to treat their animals (Shao et al., 2021). In addition, when animals raised in water are infected with disease, farmers suffer huge economic losses, so they will be more concerned about reducing economic losses rather than ensuring food safety.

In 2017 China issued the National Action Plan to Curb Bacterial Resistance of Animal Origin (2017-2020), which means that China is starting to regulate the use of antibiotics (Shao et al., 2021). However, in other countries, regulations were introduced early on to regulate the use of antibiotics. The U.S. FDA issued the Use of Antibiotics in Animal Feed in 1970. Sweden banned the use of antibiotics to promote animal growth in 1986. The EU required all member states to stop using growth-promoting antibiotics in 2006. In addition, some developed countries have aquaculture regulatory agencies that strictly control the use of antibiotics (Okeke et al., 2022). The Chilean government has adopted the establishment of testing and sanitation zones for marine aquaculture, improved spatial planning for aquaculture, and mandatory environmental impact assessments, with sanctions and fines for industries that do not comply (Naylor et al., 2023). This shows that there is a big gap between China and developed countries in the regulation of animal use of drugs.

6. Recommendation

In order to better prevent the impact of drug abuse in aquaculture on the water environment and aquatic animals, and to raise awareness of food safety, the Chinese government should make efforts in the following aspects:

- The Chinese government should strictly enforce laws and policies regarding antibiotics as well as other drugs, and establish a more direct regulatory authority to regularly monitor the use of drugs in order to limit their abuse. At the same time, the monitoring standards should be the same as the common international standards.

The regulatory authorities should take severe punitive measures for farmers who illegally purchase and abuse drugs.

- The Chinese government should encourage research and development of low-cost and effective water pollution treatment technologies, as well as research into less toxic and degradable alternatives to drugs (promoting the use of TCM).
- It is essential for farmers to develop scientific farming guidelines. The Chinese government should provide relevant course training to farmers so that they can adopt healthy farming patterns instead of relying heavily on drugs.
- The Chinese government needs to step up publicity to make people fully aware of the serious harm caused by drug abuse to the ecological environment as well as human health.

7. Conclusions

Due to climate change and the deterioration of the water environment caused by human activities, the quality and yield of crops have been affected and wild fish have also been contaminated. These soil-based foods alone cannot meet the protein needs of the population. As a result, many countries have developed aquaculture. China is an important part of the world's aquaculture industry, but because of its large number of farmed animals, illness in a single animal can lead to infection of animals in the entire farming area. Farmers use a large number of drugs for this purpose, especially antibiotics, to prevent and treat diseases. The main types of antibiotics used in marine aquaculture are QNs, SAs, MLs and TCs. In addition, farmers also use compounds containing heavy metals to help supplement the animals with elements. However, farmers lack the knowledge and misuse the drugs causing them to remain in the water and thus accumulate in the aquatic animals, which are then passed through the food chain and finally ingested by humans. These antibiotics as well as heavy metals are seriously harmful to both animals and humans. At the same time, the antibiotics in the water can also promote the production of antibiotic resistance genes, and human exposure can lead to aggravation of the disease. Therefore, some treatment technologies and alternative methods have been proposed to reduce the residues of drugs in water. On the other hand, some recommendations are presented in order to prevent drug abuse by farmers and to enhance drug regulation in aquaculture.

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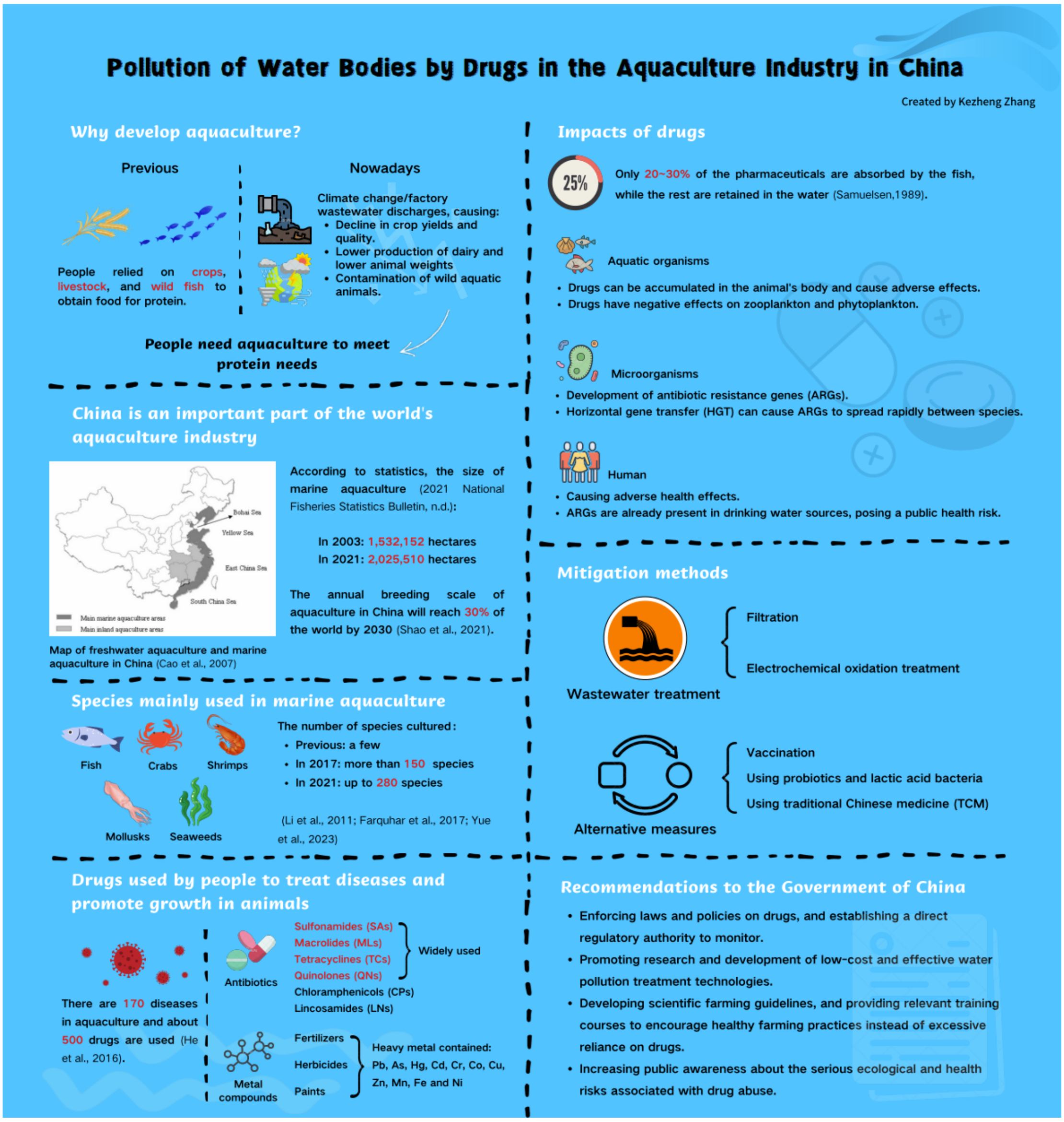
Appendix



URL:

https://www.canva.cn/design/DAFnRD8G9_0/oyiskGaVDdEhas4wRmOS4w/edit?utm_content=DAFnRD8G9_0&utm_campaign=designshare&utm_medium=link2&utm_source=sharebutton