การใช้ยาปฏิชีวนะและยาปฏิชีวนะตกค้างในฟาร์มปลานิล: ข้อมูลเบื้องต้นในจังหวัดพะเยา ประเทศไทย
Antibiotic Use and Antibiotic Residue in Nile Tilapia Farms: Preliminary Evidence in Phayao, Thailand

นิพนธ์ต้นฉบับ **Original Article**

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บทคัดย่อ

วัตถุประสงค์: เพื่อสำรวจความรู้และพฤติกรรมการใช้ยาปฏิชีวนะของเกษตรกรผู้เลี้ยงปลานิล และวิเคราะห์สารตกค้างของยาปฏิชีวนะในเนื้อปลาเบื้องต้น **วิธีการศึกษา**: ผู้วิจัยสัมภาษณ์เกษตรกรผู้เลี้ยงปลานิล 28 คนในอำเภอเมือง จังหวัดพะเยา ด้วยแบบสอบถามที่ได้รับการตรวจคุณภาพในเรื่องความรู้และพฤติกรรมการใช้ยาปฏิชีวนะของเกษตรกรผู้เลี้ยงปลานิล พร้อมทั้งใช้ชุดตรวจวิเคราะห์การตกค้างของยาปฏิชีวนะในเนื้อปลาในปลานิลจำนวน 15 ตัวอย่าง **ผลการศึกษา:** เกษตรกรมีความรู้เรื่องข้อบ่งใช้ในการใช้ยาปฏิชีวนะเพื่อการรักษาโรคในปลา แต่มีเกษตรกรที่อ่านเลขทะเบียนยาได้เพียงร้อยละ 42.86 ทราบวันหมดอายุของยาเพียงร้อยละ 32.14 และเข้าใจวิธีใช้ตามคำแนะนำบนฉลากได้อย่างถูกต้องเพียงร้อยละ50.00 เกษตรกรจำนวนมากไม่ทราบเรื่องยาปฏิชีวนะตกค้างในสิ่งแวดล้อม การดื้อยาปฏิชีวนะ และการติดเชื้อดื้อยาปฏิชีวนะ เกษตรกรบางรายไม่ใช้ยาตามฉลากหรือคำแนะนำของเจ้าหน้าที่และสัตวแพทย์ ทิ้งภาชนะบรรจุและกากเคมีไม่ถูกวิธี ทั้งนี้ ไม่พบยาปฏิชีวนะตกค้างในตัวอย่างเนื้อปลาจากฟาร์มทั้ง 15 ตัวอย่าง **สรุป:** เกษตรกรกลุ่มตัวอย่างในพื้นที่ ยังคงขาดความเข้าใจเกี่ยวกับการใช้ยาและให้ข้อมูลพฤติกรรมการใช้ยาที่ไม่เหมาะสมในการเลี้ยงปลานิล เพื่อลดปัญหาการดื้อยาในอนาคต จำเป็นต้องส่งเสริมการดำเนินการเพื่อให้ข้อมูลที่ถูกต้องแก่เกษตรกรเกี่ยวกับการใช้ยาปฏิชีวนะ

คำสำคัญ: การใช้ยาปฏิชีวนะ; การดื้อยาปฏิชีวนะ; ยาปฏิชีวนะตกค้าง; ปลานิล; ไทย

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Abstract

Objective: To determine knowledge and behavior of using antibiotics among tilapia farmers, in addition to a preliminary analysis of antibiotic residues in fish fillets. **Methods:** This study recruited 28 tilapia farmers in Muang district of Phayao Province, Thailand. The questionnaires on knowledge and self-reported practice were validated by experts. Antibiotic residues were quantified in 15 tilapia samples using a field test kit. **Results:** Farmers possessed general knowledge of the objectives of antibiotic applications. However, poor understanding existed. Only 42.86% and 32.14% of farmers could correctly identify drug registration numbers and expiration dates, respectively. Furthermore, 50% reported adhering to label instructions, suggesting a potential disconnect between knowledge and practice. A lack of awareness regarding environmental antibiotic residues, antibiotic resistance, and resistant infections was identified. Inappropriate drug use practices included the dose exceeding recommended dosages and improper disposal of medication containers and waste. No antibiotic residues were detected in the 15 samples of fish fillets. **Conclusion:** There was a knowledge deficit and potential misuse of antibiotics in tilapia farming practices. Interventions and educational initiatives promoting responsible antibiotic use and proper waste management are crucial to address knowledge gaps and ensure sustainable aquaculture practices.

Keywords: antibiotic use; antibiotic resistance; antibiotic residue; Tilapia; Thailand

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Introduction

A concern for world health and development is antimicrobial resistance (AMR), which has been named one of the top 10 worldwide public health hazards to humanity. To overcome antibiotic resistance and achieve the Sustainable Development Goals (SDGs) in all countries, urgent multisectoral action is required.[1] Antimicrobial misuse and overuse are the primary causes of infections that are resistant to antibiotics. The economic cost of AMR is high because a protracted illness not only increases the risk of mortality and disability but also lengthens hospital stays, necessitates more expensive medications, and puts a strain on the finances of those affected.[2] AMR infections have caused 38,481 fatalities and at least 3.24 million days spent in hospitals in Thailand. In terms of their financial impact on the economy, antibiotics used to treat AMR infections ranged in price from 2,539 to 6,084 million Baht. At least 40,000 million Baht was spent indirectly on morbidity and mortality as a result of early deaths linked to AMR (in 2010 values). The health and economic impacts of AMR are much higher than the burden of many priority health problems in Thailand. As a result, AMR is a

serious and urgent health issue that requires coordinated and systematic national and local efforts to address.[3]

Environmental change and population growth continue to pose significant difficulties for sustainable global food production. To fulfill rising demand, the meat and fish production sectors are being urged to maintain high growth densities and rely on antimicrobial intervention at all phases of development. Inappropriate antibiotic administration over time creates resistant bacterial species that survive via adaptive pathways using transferrable nucleotide sequences (i.e., plasmids). This is one of the most important pathways for the development of antibiotic resistance in food production systems.[4]

The overuse of antibiotics in aquaculture has led to widespread environmental contamination. This contamination poses potential risks to human health through two main pathways, direct exposure and long-term effects. Traces of antibiotics have been found in children's urine, likely due to contaminated food or water. Chronic exposure to antibiotics can lead to health problems like fatty liver disease and even leukemia in extreme cases.[5] Consuming meat contaminated with antibiotic residues can have significant negative impacts on human health. These effects, which may be direct or indirect, are likely due to the high levels of residues accumulated over a prolonged period.[6] They can manifest as drug hypersensitivity reactions, aplastic anemia, carcinogenic, mutagenic, immunological, and teratogenic effects, as well as nephropathy, hepatotoxicity, disruption of the normal gut flora, reproductive disorders, and the development of antibiotic-resistant bacteria in the gut.[4,6]

Previous studies in Thailand have found widespread use of antibiotics among livestock farmers. Easy access to these drugs, combined with familiarity, likely leads to inappropriate use. A list of the drugs found includes enrofloxacin, erythromycin, sulfadiazine (commonly referred to as union sulfa), amoxicillin, chloramphenicol, tetracycline, amoxicillin-colistin, and gentamycin.[7] Additionally, studies have shown antibiotic resistance in farmed fish. A 2018 study in Ubon Ratchathani and Chiang Rai provinces found that 5% of Salmonella spp. isolated from tilapia were resistant to amoxicillin, ampicillin, and oxytetracycline. Furthermore, residues of enrofloxacin, oxytetracycline, and doxycycline were detected in tilapia meat.[8] Another 2012 study in Phayao Province indicated resistance to amoxicillin, colistin, and amoxicillin-clavulanic acid in *Aeromonas hydrophila* obtained from tilapia in Kwan Phayao Lake.[9]

Phayao Province plays a significant role in Thailand's tilapia industry, supplying both domestic and international markets.[10,11] Concerns regarding antibiotic resistance in farmed fish necessitate further investigation and potentially stricter regulations to ensure consumer safety.

The objectives of this study were to survey the knowledge and behavior of using antibiotics among tilapia farmers and to preliminarily determine antibiotic residues in fish fillet. The results of this study could be useful to the government and private agencies in controlling, supervising, and promoting the rational use of antibiotics in agriculture in the future.

Methods

The survey was conducted in Muang District, Phayao Province, Thailand, a large source of tilapia farming for both domestic consumption and export abroad.

Population and sample

The study population was 80 fish farmers in Muang district, Phayao province, Thailand. Their farms were in 3 out of 8 subdistricts of Muanf district. With a 95% confidence interval, a sample size of 67 participants was required. However, the final number of participants was 28. These 28 fish farmer participants were from three sub-districts of Muang district including Ban Tam (19 farmers), Tha Champee (5 farmers), and Ban Mai (4 farmers). These three sub-districts were the largest fish farming areas in Phayao Province.

Among these 28 farmers, 14 of them reported using antibiotics in the three months preceding the survey. Therefore, the research team selected fish from the ponds of these 14 farms to test whether there were antibiotic residues. One farm also raised fish fry. (i.e., newborn until 1 month old) for sale to other farms. Therefore, 2 samples were collected from this farm, i.e., 1 adult fish and 1 fry. As a result, 15 samples of fish were tested for antibiotic contamination. Fifteen samples of Nile Tilapia were obtained from 11 farms in Ban Tam sub-district, 2 in Tha Champee sub-district, and 2 in Ban Mai sub-district for screening for antimicrobial residues using the Hii-M® test kit.

Questionnaire development

The questionnaire was modified from the questionnaire of a study on the use of antibiotics in livestock farms in Chiang

Mai province.[12] Face validity was tested by 3 experts. The questionnaire consisted of 3 parts. Part 1 collected general information of the farmers including age, sex, and educational level. Part 2 contained 23 closed-ended questions about knowledge and understanding of the use and effects of antibiotics including indication, administration, and duration of administration. The response was “true,” “false,” and “unsured.” Part 3 assessed antibiotic usage practices on farms through two methods. First, researchers asked farmers to show all the medicines they used on their farms. Second, they administered a 10-item questionnaire specifically designed to measure antibiotic use behaviors with the response of “always,” “sometimes,” and “never.”

Hii- M® test kits were used for analyzing of antibiotic residues in fish fillet. This test kit has 95.9% accuracy, 92.6% sensitivity, and 96.9% specificity. This simple test kit can detect penicillins, tetracyclines, and fluoroquinolones.[13]

Participant ethical protection

The study was approved by the institutional review board of the Phayao Provincial Public Health Office.

Data collection procedure

For each of the three sub-districts, the researcher contacted the local officials and farmers for permission and to schedule interview visits. At each interview, the researcher requested farmers' approval to willingly engage in the study. The farmers were informed about objective, process, and voluntary and anonymity of the study. The farmers could withdraw from participation at any time with no negative consequences. Once written informed consent was obtained, the researcher asked the farmers for permission to record audio and photos. The researcher conducted an interview with each farmer using the questionnaire which took about 40 minutes to complete.

At each farm. sample of Nile Tilapia was obtained from the ponds. The meat juice was extracted within 24 hours and tested for antimicrobial residues using the test kit.

Data analysis

Descriptive statistics including mean with standard deviation, interquartile range (IQR) and frequency with percentage were used to summarize demographic characteristics, and study variables of the farmers.

Results

Of the total 28 farmer participants, the majority were men (85.71%). They were at their median age of 56 years old (IQR of 10). About 39% of them graduated from high school and 28% were farm owners. The average experience of tilapia farming was 8.89 ± 7.07 years. The time spent raising each tilapia was 6.42 ± 0.50 months.

Table 1 Characteristics of participants in the study (N = 28).

Characteristics	N (%)
Gender	
Male	24 (85.71)
Female	4 (14.29)
Age (years)	
Median (interquartile range)	56 (10)
Minimum, Maximum	36, 69
Education level, n (%)	
Primary school	11 (39.29)
High school	9 (32.14)
Bachelor's degree	8 (28.57)
Average experience of tilapia farmer (years), mean ± SD	8.89 ± 7.07
Length of time spent in raising fish before selling (months), mean ± SD	6.42 ± 0.50
Fish farming cycle (per year) , mean ± SD	1.86 ± 0.45
Average income in Baht (per cycle), mean	319,285.71
Nursery ponds	11 (39.29)

Knowledge about use and effects of antibiotics

Of the 28 participants, 26 (92.86%) had good knowledge of antibiotics to be used to treat diseases in animals (Table 2). However, this study revealed several areas where farmers lacked adequate knowledge which can be broadly categorized into five main themes namely 1) preventive/prophylaxis use of antibiotics, 2) reading and interpreting medication labels, including aspects such as expiration dates, registration numbers, and dosage instructions, 3) residues of antibiotics, 4) antibiotics resistance, and 5) inappropriate dose and durations, potentially contributing to the development of antibiotic resistance (Table 2).

Antibiotics use in tilapia farm

Half of the farmers (50%) had used antibiotics on their farm (Table 3). Six farmers (42.86%) used antibiotics in the past and still discontinued the use while one farmer (7.14%) continued the use. It was found that 14 farmers used antibiotics only when the tilapia in the pond was sick. However, a regular use was found where the drug "oxytetracycline" was frequently added to the diet early in the culture to maintain the health of the fries and prevent mortality.

A combination antibiotic formulation (i.e., amoxicillin plus enrofloxacin) was also used in fish farming (Table 3).

Table 2 Knowledge about use and effects of antibiotics (N = 28).

	Knowledge	N (%)	
		Correct	Incorrect or unsured
1.	**Objectives of antibiotic use**		
1.1	To treat diseases in animals (T)	26 (92.86)	2 (7.14)
1.2	To prevent diseases in animals (F)	8 (28.57)	20 (71.43)
1.3	To accelerate growth in animals (F)	3 (10.71)	25 (89.29)
2.	**How to use antibiotics**		
2.1	Should consult officials or veterinarians before using antibiotics (T)	25 (89.29)	3 (10.71)
2.2	The same antibiotic can be used as long as needed without adverse effects on the animal (F)	9 (32.14)	19 (67.86)
2.3	Antibiotics must be administered daily until the symptoms improve (F)	15 (53.57)	13 (46.43)
2.4	Dose used to treat the disease is in accordance with that stated on the packaging (T)	2 0 (71.43)	8 (28.57)
2.5	Dosage for prophylaxis use is lower and takes longer than treatment (F)	2 (7.14)	26 (92.86)
3.	**Knowledge of drug labels**		
3.1	Always read the drug label before using antibiotics (T)	26 (92.86)	2 (7.14)
3.2*	The word Exp. indicates the expiration date of the antibiotic (T)	12 (42.86)	16 (57.14)
3.3*	Reg no. indicates the antibiotic drug registration number (T)	9 (32.14)	19 (67.86)
3.4*	Able to read the (right/correct) dosage on the label (T)	14 (50.00)	14 (50.00)
4.	**Effects of antibiotics**		
	Residues of antibiotics		
4.1	Use of antibiotics in animals allowing people to receive antibiotics indirectly For example, from eating meat contaminated with antibiotics (T)	11 (39.29)	17 (60.71)
4.2	Antibiotics in animal husbandry can deposit residues in meat (T)	8 (28.57)	20 (71.43)
4.3	Antibiotics in animal husbandry can deposit residues in manure (T)	4 (14.29)	24 (85.71)
4.4	Antibiotic usage in animal husbandry results in medication residues in natural water systems, because of the wastewater generated by the animal husbandry process (T)	8 (28.57)	20 (71.43)
	Antibiotic resistance		
4.5	Antibiotics in animal husbandry cause drug resistance in animals (T)	5 (57.86)	23 (82.14)
4.6	Antibiotics in animal husbandry cause drug resistance in humans. (T) *Antibiotic resistant infection*	4 (14.29)	24 (85.71)
4.7	Antibiotic use in animal husbandry causes contamination of drug-resistant microorganisms in the environment and residential communities (T)	8 (28.57)	20 (71.43)
4.8	Living in an area where antibiotic-treated animals are bred increases the chances of people contracting drug-resistant infections from those animals (T)	6 (21.43)	22 (78.57)
4.9	If there is a drug-resistant infection, the treatment will take longer. The potential for recovery decreases, and the likelihood of death increases. (T)	7 (25.00)	21 (75.00)
5	**Others**		
5.1	The higher the dose, the better the effect. (F)	3 (10.71)	25 (89.29)
5.2	Antibiotics are needed for the entire duration of the animal husbandry (F)	3 (10.71)	25 (89.29)

Note: (T) denotes true statement, (F) denotes false statements.

Table 3 Antibiotic use in tilapia farming (N = 14).

Antibiotics	n	Duration of administration	Indication	Administration
Amoxicillin + Enrofloxacin	4	use only when symptomatic	treatment of bruised gums used to treat streptococcosis	mixed with food
Oxytetracycline	3	use at the beginning of raising (2 farms) use only when symptomatic (1 farm)	use to keep the fish healthy (2 farms) use to treat streptococcosis (2 farms)	mixed with food
Enrofloxacin	2	use only when symptomatic	use to treat streptococcosis	mixed with water in the fishpond

Farmer practice of antibiotics use

The majority (more than 50%) of farmers in this study had good antibiotic usage practices before, during, and after antibiotic use (Table 4). More than 80% of the participants always read the drug label before using antibiotics, selected drugs according to indications, cleaned their bodies after using drugs or chemicals, and no drugs or chemicals were used at least 7 days before harvesting. Farmers occasionally or never administered the drug according to the label and the advice of officials and veterinarians, as well as properly disposed of the pharmaceutical containers and chemical waste (Table 4).

Table 4 Antibiotic use behavior (N = 14).

	Antibiotic use behavior	N (%)		
		Always	Sometimes	Never
1.	**Before using antibiotics**			
1.1	Read the label before using antibiotics	12 (85.71)	2 (14.29)	0
1.2	consult officials or veterinarians before using antibiotics	9 (64.29)	5 (35.71)	0
1.3	choose the medication based on the label's indications	12 (85.71)	1 (7.14)	1 (7.14)
2	**While using antibiotics**			
2.1	while using the medicine, use protective equipment such as gloves and a face mask	9 (64.29)	4 (28.57)	1 (7.14)
2.2	administer drugs according to the label and/ or as recommended by officials or veterinarians	7 (50.00)	6 (42.86)	1 (7.14)
2.3	do not eat or drink while using the medicine or agricultural chemicals	11 (78.57)	2 (14.29)	1 (7.14)
3	**After using antibiotics**			
3.1	after providing medicine or agricultural chemicals, cleanse the body	13 (92.86)	1 (7.14)	0
3.2	cleaning equipment used for mixing, spraying, administering drugs or chemicals to animals	10 (71.43)	3 (21.43)	1 (7.14)
3.3	seven days before delivering them to the slaughterhouse/ product collection, cease administering the medication	12 (85.71)	1 (7.14)	1 (7.14)
3.4	safe disposal of empty or expired pharmaceutical and chemical containers	8 (57.14)	6 (42.86)	0

Antibiotic residues in tilapia fillets

The results showed that all 15 fish samples were with a mean weight of 710 ± 298.93 g. The mean age of the fish was 5.40 ± 1.35 months. The youngest fish was three months old while the oldest one was eight months old. No antibiotic residues were detected in any fish fillet samples.

Discussions and Conclusion

The survey of antibiotics use among farmers in Phayao province of Thailand showed that half of the farmers who participated in this study had used antibiotics in their fish farm. The farmers lacked knowledge in drug use and demonstrated inappropriate use of drugs in tilapia farming, despite no antibiotic residues found in the fish fillet. At present, it is the right time to encourage action and pass on the correct knowledge and understanding of antibiotic use to farmers to reduce the problem of drug resistance in the future.

Only 42.86% , 32.14% , and 50.00% of farmers properly read the drug registration number, expiration date, and directions for use as suggested on the label, respectively. The Majority of them were unaware of medication residues,

antibiotic resistance, and antibiotic-resistant infections. This is similar to earlier Thai investigations which indicated that farmers lack adequate awareness about animal drug use.[12] Although farmers successfully answered some knowledge-related questions, they did not act appropriately in their drug-use processes. For example, most farmers knew they should consult officials or veterinarians before using antibiotics, they did not consult anyone when they administered drugs to their fishes.

Most famer participants had incorrect understanding regarding drug use. However, the majority of them maintained appropriate drug use behavior prior to, during, and after drug use. This could be because of the presence of a cooperative system that encourages farmers' practices throughout the fish farming season. The participants we investigated were members of the Phayao province fish farming cooperative group. As a result, they might not necessarily learn how to raise fish on their own. On the other hand, they might raise and harvest the fish as they were impacted by cooperative directives or by mimicking the practices of successful cooperative members. Ultimately, the cooperative followed the checklist from the Department of Fisheries according to Thai GAP standards that guarantee the quality of farming.

The situation we found in this study was similar to that of neighboring countries such as Vietnam[14], where antibiotics were used throughout the fish farming period. Farmers lacked the correct understanding of the use of drugs, and this resulted in incorrect use of drugs in fish farming. For example, the duration of dosing for farmed fish is adjusted according to the farmer' s discretion, which did not comply with the recommended duration of the medication regimen. Farmers changed their drugs and doses once they thought the drugs were not effective for their fish. They also used antibiotics to prevent disease in fish. The administration of antibiotics over a prolonged period may cause drug resistance in animals, and these drug-resistant microbes may also be transmissible to humans.[15]

Amoxicillin plus enrofloxacin, oxytetracycline, and enrofloxacin were used in the farms in our study. These antibiotics were given not only when the fish were sick, but also when raising fries. This was because farmers believed that the antibiotics would prolong the survival rate of the fish. According to the standard practice of aquaculture in Thailand, a combination drug (amoxicillin plus enrofloxacin) is not recommended. It is noted that amoxicillin plus enrofloxacin combination which has been used since 2020 was not approved and has never been certified by the Department of Fisheries.[16] We discovered farmers' medical practices in this investigation were not appropriate. The advice of the Department of Fisheries of Thailand mentioned that before using drugs, the pond water system that raises fish should be managed to have good quality. It is also recommended to use safe chemicals such as probiotics, formalin, and salt before using drugs to reduce antibiotic contamination in the environment. In treating the disease, the diseased fish must first be separated from the pond. The drug must not be mixed with the pond or the food.[17] This study found events of healthy fish receiving antibiotics unnecessarily.

Sources of antibiotic resistance could be from aquaculture, livestock wastewater, effluent discharge, food and feed, agricultural aquatic animals, and poor industrial waste disposal. Eating fish in an antibiotic-contaminated environment is one of the reasons why humans consume antibiotics through food on a daily basis.[18] This study demonstrated that no antibiotic residues were identified in fish grown in soil ponds. From Thailand's tilapia inspection, this differs slightly from the earlier assumption that there was contamination with enrofloxacin, oxytetracycline, or doxycycline. This is because the contamination was at an acceptable level because the retention value did not exceed the standard limit.[8] The list of medications evaluated in this study is consistent with the list of antibiotics used in both domestic and international fish farming, as in Vietnam.[14]

The strength of this study is its investigation of fish-rearing in a natural setting. The fish meat examination was carried out by directly selecting the fish from the pond and testing them within 24 hours of extraction. This provides the most current data and can be used to address knowledge gaps and malpractices by fish farmers in using antibiotics.

Limitation-wise, this research collected data from a small number of fish farmers in Phayao province. The findings are therefore preliminary and could be used to develop a more appropriate antibiotic use management system for fish farming in the province probably not nation-wide. The results of the study should be interpreted with an understanding of the local context. The survey period coincided with a season when fish diseases are less prevalent, so farmers likely had minimal need for antibiotics. This might explain why our study did not detect any antibiotic residues in the fish meat. Consequently, applying these findings should be done cautiously.

Further studies are needed to strengthen the generalizability of these findings. This includes increasing the number of participating fish farmers and conducting research across all seasons. More research on the environmental impact of fish farms could benefit not only public health studies but also other areas of investigation.

By implementing these initiatives, we aimed to empower fish farmers with the knowledge necessary to use antibiotics responsibly, ultimately promoting sustainable and healthy fish farming practices in Phayao province. This approach, combined with existing regulations governing antibiotic use in aquaculture, can create a comprehensive strategy to ensure food safety and preserve the effectiveness of antibiotics for human health.

In conclusion, even though there were no antibiotic traces in the fish fillet, the study concluded that farmers still lacked understanding about drug use and exhibited some inappropriate drug use behaviors for tilapia farming. To lessen the issue of drug resistance in the future, it is essential to promote action and impart accurate information to farmers about the use of antibiotics.

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