International Food Research Journal 30(6): 1461 - 1470 (December 2023)
Journal homepage: *http://www.ifrj.upm.edu.my*

Multiresidue analysis and health risk assessment of sulfonamides and quinolones from edible Batrachia and other aquatic products

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Article history

Received:
27 June 2022
Received in revised form:
19 July 2023
Accepted:
16 August 2023

Keywords

edible Batrachia, aquatic products, veterinary drugs, risk assessment

Abstract

Tailless amphibians belonging to the order Batrachia are a significant component of human consumption. However, there is limited literature on the consumption of these amphibians by humans. Therefore, the present work aimed to examine the presence of drug residues in edible Batrachia, and compare them with other aquatic products. We assessed 22 veterinary drug residues, including 12 sulfonamides (SAs) and ten quinolones (QNs), in various aquatic products, including edible Batrachia. To provide a comparative analysis, we referenced literature from China between 2005 and 2020 regarding SAs and QNs detected in aquatic products. Additionally, we calculated the food safety index (IFS) of antibiotics, and conducted a health risk assessment. The findings revealed that the detection rate, average residual amount, and over-standard rate of antibiotics in edible Batrachia were higher than most other aquatic products. Furthermore, the systematic cluster analysis demonstrated that edible Batrachia could serve as a potential sentinel animal, distinguishing them from several other aquatic products. The total IFS of all residues obtained from different aquatic products in the present work was less than 1, thus indicating their safety in terms of public health. Nevertheless, it is essential to conduct detailed investigations into the maximum residues of certain antibiotics in specific aquatic products that exceed the safety limits to understand their impact on human health.

DOI
https://doi.org/10.47836/ifrj.30.6.09

Introduction

Veterinary drugs are extensively employed in aquaculture to prevent and control animal diseases, enhance animal growth, and boost production. However, extensive use of these substances during breeding can result in various adverse effects on animals, as well as the accumulation of drug residues in the environment. While only a small fraction of the administered drug accumulates in the tissues and organs of animals, it ultimately enters the human body through the consumption of aquatic food. Furthermore, as animal waste enters the environment, it frequently enters the food chain, thereby posing a risk to human health (Sarmah *et al*., 2006; Kümmerer, 2009a). Based on the FAO Yearbook of Fishery and Aquaculture Statistics 2020 and China Agricultural Outlook 2020 - 2029, China plays a significant role in global aquaculture food production, accounting for 58% of the total aquatic production worldwide in 2018. In 2019, aquaculture production constituted 78.4% of China's overall production. Such a substantial increase in production is closely associated with the extensive use of veterinary drugs. For instance, in 2019, China reported an annual veterinary drug usage of approximately 30,000 tons, making it the second-highest user of diverse antibiotics among Asian countries (Rico *et al*., 2012).

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Among these antibiotics, sulfonamides (SAs) and quinolones (QNs) are widely utilised due to their broad antibacterial spectrum, cost-effectiveness, and therapeutic efficacy. They have relatively high-water solubility and low sorption affinity to soils and sediments, thus making them mobile in the environment (Li *et al*., 2012; Bai *et al*., 2014). Additionally, sulfonamides exhibit poor degradation, and persist in aquatic environments for extended periods (Li *et al*., 2014). Improper use of these antibiotics or inadequate drug withdrawal periods has led to the presence of antibiotic residues in food, thereby increasing the risk of bacterial resistance and potential exposure to carcinogenic and allergenic compounds for consumers (Gentili *et al*., 2005; Kümmerer, 2009b). To ensure food safety and protect human health to the maximum extent, national and international regulatory bodies have established maximum residue limits (MRL) for veterinary drug residues, by considering their detrimental impact on human health.

The issue of food contamination and its impact on human health due to the presence of SAs and QNs veterinary drug residues has gained significant attention. Directly detecting these residues and evaluating their toxicological effects on the human body is impractical. Consequently, researchers have turned to animal models to assess the health risks associated with veterinary drug residues. These drugs enter water bodies through natural or human activities, and adversely affect non-target organisms like algae, fish, and amphibians (Rabinowitz *et al*., 2008).

Amphibians hold a unique position in the food chain due to their intricate life history, dependence on water, possession of gills and permeable skin in larvae, and high vulnerability of fertilised eggs to drugs. Consequently, drugs present in water can easily enter and accumulate within amphibian bodies. This makes them sentinel organisms for monitoring drug contamination. The term "sentinel animal" is metaphorically used to refer to any non-human animal that can exhibit responses to pollutants before those pollutants significantly impact the ecosystem or human health (Beeby, 2001). By providing early warning signs of potential risks to human health, these animals enable the timely implementation of preventive measures to avoid severe adverse health consequences (García-Fernández *et al*., 2020). Edible Batrachia, being amphibians closely related to humans, are directly bred and consumed. Consequently, drug residues in edible Batrachia are directly transferred to the human body. The characteristics of amphibians make them prone to the accumulation of veterinary drug residues in their bodies.

The food safety index (IFS) is a simple and efficient tool for assessing the health risks associated with contaminants in food samples. It calculates the estimated daily intake (EDI) of residues, and compares them with safe intake values such as acceptable daily intake (ADIs) to evaluate the health risks posed to consumers (Ross and Sumner, 2002; Nie and Li, 2014). Several recent studies have utilised a similar approach to evaluate probabilistic consumer exposure to antibiotic residues in aquatic products (He *et al*., 2016; Piątkowska *et al*., 2017; Wang *et al*., 2017; Zuo and Wang, 2018; Yu *et al*., 2018; Chen *et al*., 2019; Ma *et al*., 2020) and vegetables (Yuan *et al*., 2014). The present work was focused on investigating the occurrence of SAs and QNs in edible Batrachia, and estimating human dietary exposure to these veterinary drug residues. Furthermore, it compared the health risks associated with these two types of residues in other aquatic products.

Materials and methods

Materials and reagents

A total of 101 batches of edible Batrachia (EB) samples were acquired from a domestic market in the Zhejiang Province from 2018 to 2020. The samples consisted of various species including *Lithobates catesbeianus*, *Quasipaa spinosa*, *Pelophylax nigromaculatus*, *Rana chensinensis*, and *Bufo gargarizans*. Additionally, a total of 30 aquatic product (AP) samples, such as *Larimichthys crocea*, *Pelteobagrus fulvidraco*, and *Monopterus albus* were collected. The largest batch of samples (2,251) was obtained from the Zhejiang domestic market between 2018 and 2020. We conducted a literature search using appropriate keywords and retrieved scientific papers (SP) related to SAs, QNs, and aquatic products in China from 2005 to 2020. From these papers, we compiled the largest batch of antibiotic residue data in aquatic products, consisting of 1,476 data points.

The SAs and QNs standards were procured from various pharmaceutical firms. Sigma Aldrich (St. Louis, MO, USA) provided sulfadiazine (SDZ), sulfamethoxazole (SMX), sulfathiazole (STZ), sulfamerazine (SMR), sulfisoxazole (SSZ),

sulfamethizole (SMT), sulfamethazine (SMZ), sulfamonomethoxine (SMM), sulfachloropyridazine (SCP), sulfaquinoxaline (SQX), sulfadoxine (SDX), sulfadimethoxine (SDM), pefloxacin (PEF), and danofloxacin (DAN). NICPBP (Beijing, China) supplied norfloxacin (NOR), ofloxacin (OFL), fleroxacin (FLE), ciprofloxacin (CIP), and lomefloxacin (LOM). Finally, enrofloxacin (ENR), difloxacin (DIF), and sarafloxacin (SAR) were obtained from Dr. Ehrenstorfer (GmbH, Germany).

The McIlvaine buffer solution used in the present work comprised a 0.1 mol/L citric acid solution and a 0.2 mol/L disodium hydrogen phosphate solution with a pH of 4.0. Analytically pure citric acid and disodium hydrogen phosphate were acquired from Sangon Biotech (Shanghai, China), while formic acid, methanol, and acetonitrile of chromatography grade were purchased from Merck.

Equipment

The equipment used in the present work included an API 4000-QTRAPTM Mass Spectrometer from AB SCIEX, USA; an ACQUlTYTM Ultra High-Performance Liquid Chromatograph from Waters, USA; an ULTRA-TURRAX T18 homogeniser from IKA, Germany; a SORVALL RC-6 Plus Supercentrifuge from Thermo, USA; and a MilliQ Ultrapure water Apparatus from Millipore, USA.

Analysis of antibiotic residues in samples

The detection method used in the present work was according to Zhang *et al.* (2010) with certain modifications. Initially, 2 g of the sample (edible portions of the aquatic product) were weighed and homogenised using an electric blender. The homogenised sample was then dissolved in 10 mL of McIlvaine buffer in a 50 mL centrifuge tube. To ensure proper mixing, the solution was vortexed for 1 min, and subjected to ultrasound extraction for 10 min. Subsequently, centrifugation was carried out at 18,000 rpm for 10 min at 0°C. The resulting supernatant was transferred to another centrifuge tube, and the extraction process was repeated. The two supernatants were pooled, filtered, and the filtrate was purified using a solid-phase extraction column. For column washing and activation, 3 mL each of methanol, ultrapure water, and McIlvaine buffer were added to a Bond Elut Plexa reversed-phase solid-phase extraction (SPE) column (60 mg, 3 mL). The filtrate was then passed through the column at a rate of 2 to 3 mL/min. Subsequently, the column was rinsed with 2 mL of a 5% methanol-aqueous solution to remove impurities, followed by draining. The target compounds were eluted with 6 mL of methanol, collected, and the eluent was evaporated under a nitrogen atmosphere at 35°C. The sample volume was adjusted to 1 mL using the initial mobile phase, vortexed for 1 min, and filtered through a 0.22 µm filter membrane to prepare the purified sample for UPLC-MS/MS analysis. The UPLC-MS/MS analysis was conducted using a Waters ACQUITY UPLC™ BEH Shield C_{18} reversed-phase column (50 × 2.1 mm [id], 1.7 µm) at a column temperature of 30°C. The injection volume was 1 µL, and the injection temperature was set to 25°C. The mobile phase consisted of liquid A (methanol/acetonitrile solution [4:6, v/v]) and liquid B (0.2% formic acid aqueous solution). The flow rate was 0.45 mL/min with a linear gradient under the following conditions: 0 - 4.0 min, 12% A; 4.1 - 5.0 min, 10 - 17% A; 5.1 - 11.0 min, 17 - 48% A; 11.1 - 11.3 min, 100% A; 11.3 - 11.8 min, 100% A; 11.8 - 12.0 min, 12% A. Electrospray ionisation (ESI) was used to produce ions in the MS. The scanning mode was multiple reaction monitoring (MRM) in positive ion mode, with an ion source temperature of 450°C. The curtain gas (CUR) pressure was 138 kPa (liquid nitrogen), atomisation gas (GS1) pressure was 345 kPa (liquid nitrogen), auxiliary gas (GS2) pressure was 448 kPa (liquid nitrogen), spray voltage (IS) was 5500 V, and collision gas (CAD) pressure was 34 kPa (liquid nitrogen).

Data analysis

We analysed a total of 22 antibiotics, including 12 SAs and ten QNs, in two groups of samples: the edible Batrachia group (EB) and the aquatic products group (AP). To determine the average residual amount of each veterinary drug, we used the formula $C = \sum VA_i/n$, where C = average concentration of antibiotics in the samples (µg/kg, wet weight), VA_i = actual detected content of a specific veterinary drug in the aquatic products (µg/kg, wet weight), and n = total number of samples. Similarly, the average detection rate of each veterinary drug was calculated using the formula $D = \sum VA_j \times 100/n$, where D = detection rate of antibiotics in the samples (%), VA_j = actual detection rate of a specific veterinary drug in the aquatic products, and n = total number of samples. Furthermore, the exceeding rate of each veterinary

drug was estimated using the formula $V = \sum VA_k \times 100/n$, where V = violation rate of antibiotics in the samples (%), VA_k = number of times the veterinary drug exceeded the standard in the aquatic products, and n = total number of samples. The literature data (SP group) were organised statistically based on the reported types and contents of antibiotics.

The calculation of IFS was based on the formula, IFS = EDI/SI, where EDI = (C × K)/BW, where EDI was the estimated daily intake of veterinary drugs (μg/kg body weight per day). In this equation, C = average concentration of antibiotics in the samples (μg/kg, wet weight), K = average consumption rate of aquatic products (kg of wet weight per day), and BW = average body weight of humans (kg). The safe daily intake (SI) was determined based on the acceptable daily intake (ADI) value. If the IFS value was > 1, this indicated a high and unacceptable risk to food safety, thus necessitating the implementation of appropriate prevention and control measures. On the other hand, IFS < 1 indicated an acceptable risk to food safety, with lower IFS values suggesting a lesser impact on food safety (Ross and Sumner, 2002; El Hariri *et al*., 2018; Ma *et al*., 2020). The ADIs of antibiotics and the maximum residue limits (MLRs) refer to the maximum residue limits of veterinary drugs in food set by the Ministry of Agriculture of China. The BW was assumed to be 60.0 kg, based on the mean body weight for Chinese individuals (Zhang *et al*., 2009). The estimated daily consumption of aquatic products was 0.0627 kg per person in Shanghai City (Zhang *et al*., 2013), and since Zhejiang Province is in close proximity to Shanghai City, the consumption data from Shanghai City was used for risk assessment. The intake of edible Batrachia was calculated based on the intake of aquatic products. Additionally, the maximum residual amount of each antibiotic was used to calculate IFS_{max}, considering high food consumption and high pollutant residues to reflect the principle of protecting the majority of the population.

All statistical analyses were conducted using the SPSS software package (version 22), and statistical significance was defined as $p < 0.05$.

Results and discussion

Validation of proposed method

Standard solutions with concentrations ranging from 5 to 250 ng/mL for SAs and QNs were subjected to UHPLC-MS/MS analysis to establish a calibration curve. The correlation coefficients (R^2) of the calibration curve exceeded 0.999, thus indicating strong correlation. The limit of detection (LOD) for the analysed compounds was 1.0 μg/kg, while the limit of quantification (LOQ) was 2.0 μg/kg.

Veterinary drug residues in aquatic products

In the EB group, which consisted 101 sample batches, three types of veterinary drugs were detected: SMX, ENR, and CIP. ENR exhibited the highest detection concentration of 1,960 μg/kg, the highest detection rate of 46.53%, and the highest over-standard rate of 9.90%. In the AP group, which included nearly 2,400 batches of aquatic products, eight types of SAs were detected, including SDZ, SMR, SMZ, SDX, SMX, SMM, SDM, and SMT. SMX showed the highest detection concentration of 1,690 μg/kg, the highest detection rate of 1.31%, and the highest over-standard rate of 0.27%. Additionally, five types of QNs were detected in the AP group: ENR, CIP, NOR, OFL, and PEF. ENR had the highest detection concentration of 9,610 μg/kg and the highest detection rate of 17.81%. NOR, OFL, and PEF were banned by the Ministry of Agriculture of China for use in food animal species, so their detection was considered over-standard, with OFL having the highest over-standard rate of approximately 0.94%. In the SP group, comprising nearly 1,500 batches, 14 types of SAs were reported, including SDZ, SMR, SMZ, SMX, SMM, SDM, STZ, SSZ, SQX, SCP, SMP, SPD, TMP, and SFM. Among them, SDZ exhibited a high detection concentration of 1,261 μg/kg, and SCP had the highest detection rate of 15.89%. Furthermore, 11 types of QNs were reported, including ENR, CIP, NOR, OFL, PEF, LOM, FLE, MAR, SPX, ENO, ORB, and FLU. Among these, ENR had the highest detected concentration (562.2 μg/kg) and the highest detection rate of 15.45%.

A comparison was made between the veterinary drug residues detected in the aquatic products (EB + AP) and those reported in the literature. The average residual amounts and detection rates of each veterinary drug type are illustrated in Figure 1. Figure 1a presents a comparative analysis of the average residues of all veterinary drugs detected in these two groups. The results revealed that the sum of the average residues of veterinary drugs in the SP group (39.88 μg/kg) was approximately 1.9 times higher than that in the EB + AP group (20.76 μg/kg). Correspondingly, the

number of antibiotic types reported in the SP group (25) was about 1.9 times greater than that reported in the EB + AP group (13). Consequently, a Kendall correlation analysis was conducted to assess the relationship between the 22 veterinary drugs detected in the aquatic products and the corresponding 22 veterinary drugs reported in the literature. The analysis revealed significant correlation ($p < 0.01$) between the two datasets. Similarly, the detection rates of the 22 veterinary drugs in the two sample groups (Figure 1b) were analysed using Kendall correlation which also demonstrated significant correlation ($p < 0.01$). Therefore, the veterinary drug residues identified in the aquatic products in the present work were consistent with those reported in the literature. The higher total number of residues reported in the literature could be attributed to investigating a broader range of veterinary molecules. Furthermore, based on our analysis of aquatic products and the literature, veterinary drugs with higher relative detection rate, such as ENR, CIP, SMX, OFL, SDZ, SMZ, SCP, and NOR, were included. The elevated detection of these drugs in aquatic products could be attributed to their higher concentration as veterinary drugs in the aquaculture environment (Li *et al*., 2018). These drugs are commonly used in aquaculture practices (Rico *et al*., 2012; 2013). They are not extensively metabolised or absorbed by non-living objects, but are excreted as parent compounds or biologically active metabolites, which subsequently enter water bodies, sediments, and soils (Tong *et al*., 2011; Jiang *et al*., 2014).

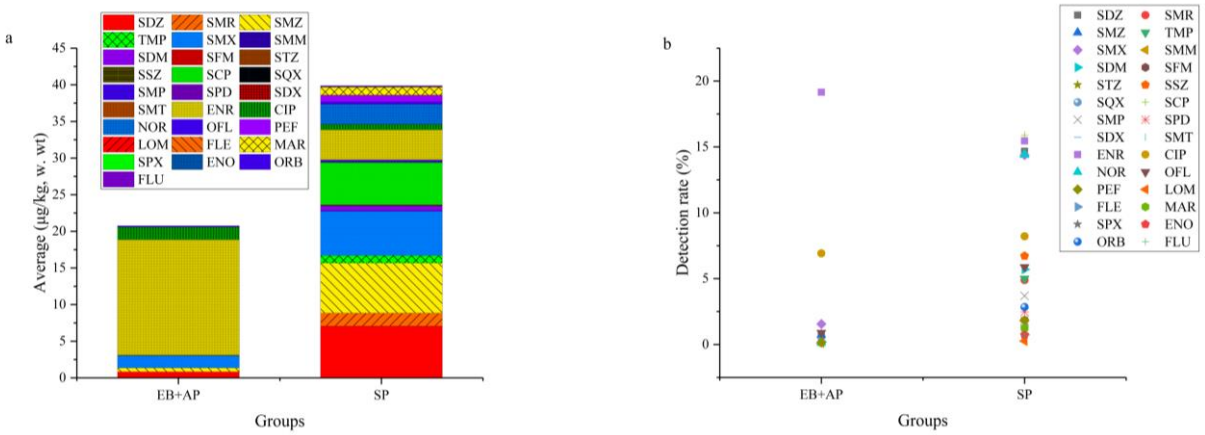

Figure 1. Average residual amounts (**a**; stacked histogram) and average detection rates (**b**; scatter plot) of each type of veterinary drug from all investigated aquatic products.

Comparison of veterinary drug residues in edible Batrachia and other aquatic products

To compare the veterinary drug residues between edible Batrachia and other aquatic products, we assessed the residual amount, detection rate, and over-standard rate of 22 veterinary drugs in edible Batrachia and 30 veterinary drugs in other aquatic products. The results of the cluster analysis based on these parameters are presented in Figure 2. Hierarchical cluster analysis was conducted to classify the 22 antibiotics in 31 aquatic products by considering the residual amount (Figure 2a), detection rate (Figure 2b), and over-standard rate (Figure 2c). Additionally, the comparison of the residual amount, detection rate, and over-standard rate is shown in Figure 2d.

Based on the distribution of veterinary drugs in the AP + EB groups, the clustering results revealed three categories (Figure 2a). *Larimichthys crocea* had the highest concentration of total drug residues (194.1 μg/kg), followed by edible Batrachia with a total residue concentration of 90.92 μg/kg. The distribution differences (Figure 2b) led to the grouping consisted of 27 *Pelteobagrus fulvidraco*, 28 *Monopterus albus*, one edible Batrachia, six *Amydasincnsis*, and 13 *Channa argus*. The results of the drug detection rate indicated that *Pelteobagrus fulvidraco*, *Monopterus albus*, and edible Batrachia exhibited high drug detection rates and cumulative detection rates (sum of detection rates for 22 drugs) of 127.3, 87.5, and 80.2%, respectively. When the distance was about 10, the grouping based on the distribution difference (Figure 2c) was 28 *Monopterus albus*, one edible Batrachia, six *Amydasincnsis*, 20 *Trionyx sinensis*, 13 *Channa argus*, and 15 *Micropterus salmoides*. *Monopterus albus* and edible Batrachia showed high over-standard rates of veterinary drugs, with cumulative

over-standard rates (sum of over-standard rates for 22 antibiotics) of 12.5 and 12.9%, respectively. The investigation of the residual amount, detection rate, and over-standard rate of veterinary drugs in aquatic products (Figure 2d) revealed a grouping of nine *Larimichthys crocea*, one edible Batrachia, 27 *Pelteobagrus fulvidraco*, and six *Amydasincnsis* when the distance was about 5.

The cluster analysis results demonstrated that edible Batrachia differed from most other aquatic products in terms of higher content of veterinary drug residues, higher detection rate, and over-standard rate. This distinction can be attributed to the fact that edible Batrachia larvae live in water and have highly permeable skin which leads to the accumulation of pollutants from their environment (Rabinowitz *et al.*, 2008). This was consistent with previous studies on abnormal frogs and environmental pollutants (Burkhart *et al.*, 2000; Fort *et al.*, 2001; Taylor *et al.*, 2005).

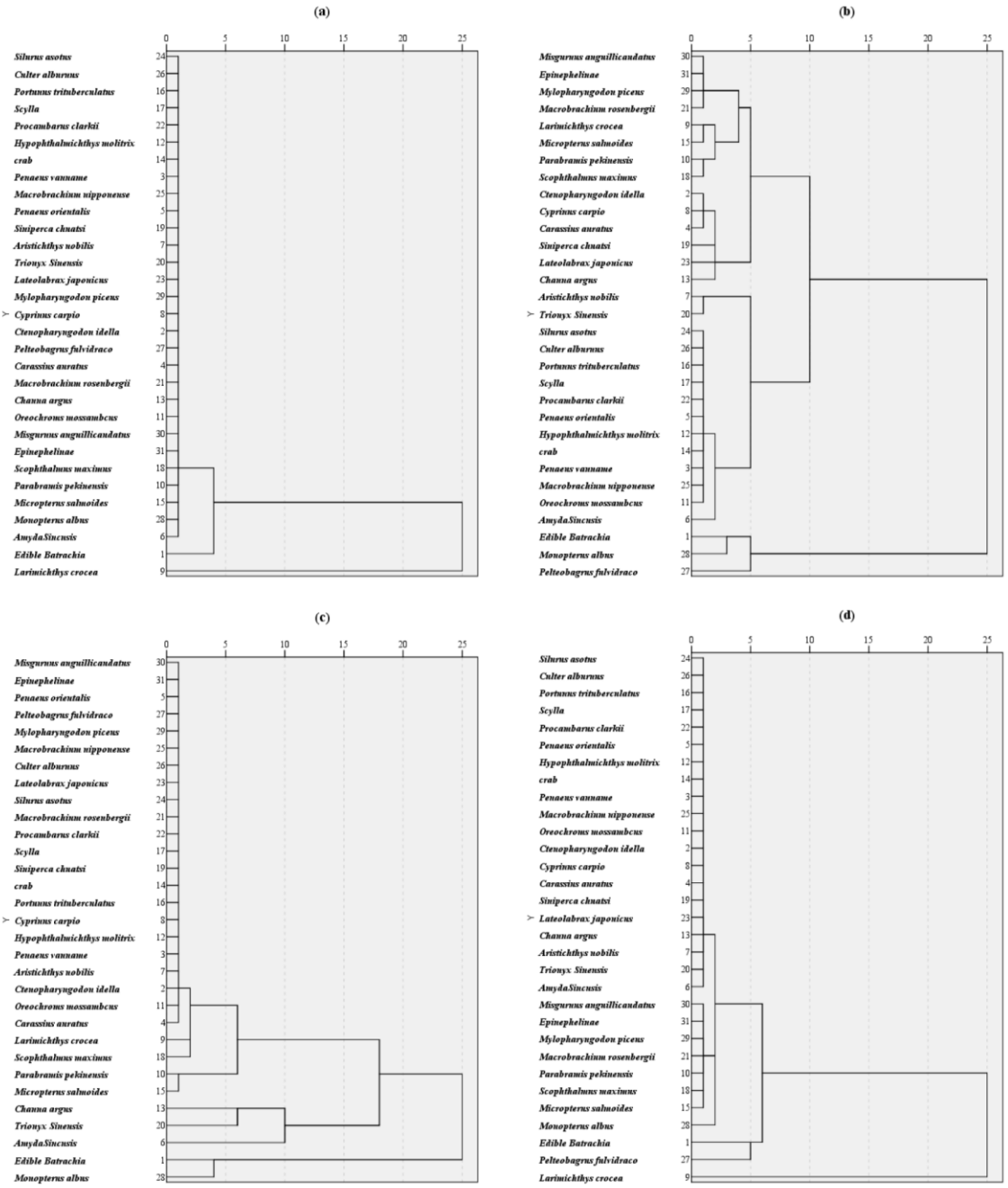

Figure 2. Cluster analysis performed using the residue content of 22 veterinary drugs **(a)**. Cluster analysis performed using the detection rate of 22 veterinary drugs **(b)**. Cluster analysis performed using the over-standard rate of 22 veterinary drugs **(c)**. Cluster analysis based on the residue content, detection rate, and over-standard rate of 22 veterinary drugs **(d)**.

Risk assessment for human health

The IFS values were calculated for veterinary drugs detected in edible Batrachia (EB), other aquatic products (AP), and those reported in the literature (SP). The human health risk associated with these drugs was assessed. The findings are presented in Figure 3. For drugs such as NOR, OFL, PEF, LOM, FLE, and other QNs for which ADI values are not currently available, the ADI value of sarafloxacin, the most stringent among all QNs, was utilised (EFSA, 2012). The total IFS values for SAs and QNs in all three sample groups were below 1: $IFS_{EB} = 1.53 \times 10^{-2}$, $IFS_{AP} = 3.08 \times 10^{-3}$, and $IFS_{SP} = 1.97 \times 10^{-2}$. Consequently, the presence of SAs and QNs residues in edible Batrachia, other aquatic products examined in the present work, and those reported in the literature, indicated low risks to food safety and human health. This observation corresponded with recent reports (He *et al.*, 2016; Wang *et al.*, 2017; Yu *et al.*, 2018).

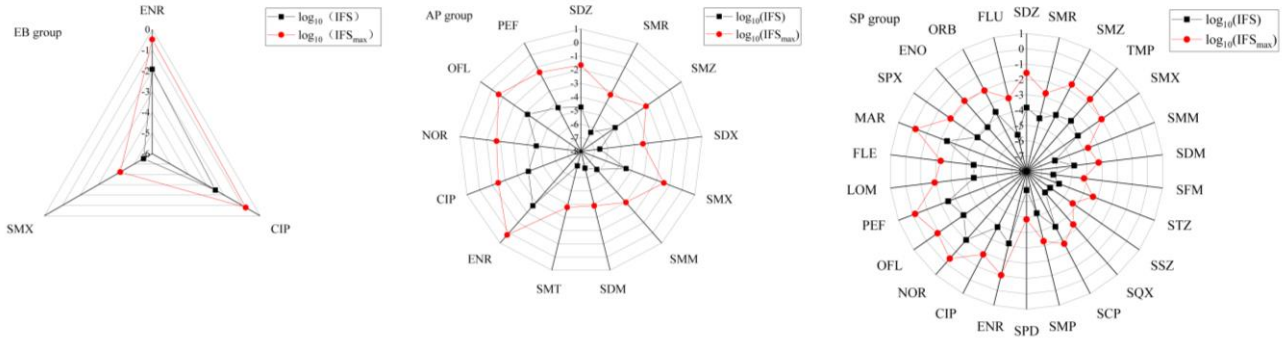

Figure 3. Index of Food Safety (IFS) values of each type of veterinary drug for EB, AP, and SP groups. Black box indicates $\log_{10}$ IFS value, and red circle indicates $\log_{10}$ IFS_{max} value.

We compared the IFS values of SAs and QNs, and calculated their total values. In the EB group, the IFS values were $IFS_{SAs} = 3.03 \times 10^{-6}$ and $IFS_{QNs} = 1.53 \times 10^{-2}$. In the AP group, the values were $IFS_{SAs} = 6.78 \times 10^{-5}$ and $IFS_{QNs} = 3.01 \times 10^{-3}$. In the SP group, the values were $IFS_{SAs} = 8.58 \times 10^{-4}$ and $IFS_{QNs} = 1.89 \times 10^{-2}$. The IFS of QNs was 2 to 4 orders of magnitude higher than that of SAs in the samples investigated. Hence, the residual risk associated with QNs in aquatic products was greater than that of SAs. This can be explained by two factors. Firstly, the concentration of QNs in the aquatic tissues was higher than that of SAs due to their stability in edible animal tissues (Juan-García *et al.*, 2006). Additionally, the usage of QNs in China for humans and farmed animals is higher as compared to SAs (Rico *et al.*, 2012; 2013). Secondly, QNs exhibit greater toxicity than SAs owing to their lower ADIs.

When comparing the IFS (individual food safety) of each drug (Figure 3, black box), ENR and CIP were found to pose a relatively higher risk in the EB group. Sulfonamides such as SDZ, SMZ, and SMX indicated a higher relative risk in the AP group. Quinolones with higher relative risk included ENR, CIP, and OFL. In the SP group, SAs with higher relative risk were SDZ, SMZ, SMX, TMP, and SCP, while QNs with higher risk were NOR, OFL, PEF, and MAR. However, their $\log_{10}$ (IFS) values were less than 0, thus indicating IFS < 1. This suggested that the residue of a single drug will have no impact on human health. Considering the worst-case scenario where IFS_{max} was calculated based on the maximum detected value of drugs (Figure 3, red circle), the connection shape of the red circle and the black box was quite similar. The Kendall correlation analysis revealed a significant positive correlation among the IFS_{max} of various drugs, with IFS of $p_{EB} < 0.01$, $p_{AP} < 0.01$, and $p_{SP} < 0.01$, thus indicating that higher value of the maximum residual risk of a certain drug was associated with higher value of the average residual risk. The $\log_{10}$ (IFS_{max}) of ENR in the AP group was > 0. Therefore, when considering the highest detected value, an individual batch of drug residue in the tested aquatic products posed a threat to human health. Furthermore, there are reports of high drug content detection in aquatic products in the literature (Kong *et al.*, 2018; Yu e*t al.*, 2018; Huang *et al.*, 2020). Although the probability of such occurrences was extremely low, it also suggested that veterinary drug residues in aquatic products might have an impact on human health, which, therefore, should not be overlooked.

Conclusion

In the present work, we investigated the presence of SAs and QNs residues in both edible Batrachia and other aquatic products. We compared these findings with the results of recent research on aquatic products. Our analysis revealed that edible Batrachia had higher number of veterinary drug residues and higher detection rate as compared to other aquatic products. Cluster analysis further highlighted the distinctiveness of edible Batrachia from other aquatic products. Edible Batrachia, with their unique characteristics such as complex amphibian life history, high skin permeability, and position in the food chain, can serve as valuable sentinel animals. They can provide insights into the potential risks associated with veterinary drug residues in aquatic products and their impact on human health. The current levels of SAs and QNs residues in aquatic products do not pose a threat to human health. However, the detection of certain veterinary drugs serves as a reminder of the historical and ongoing use of large drug doses in aquaculture practices. Therefore, the potential food safety risks associated with veterinary drug residues in aquatic products should be carefully studied. It is important to note that an individual batch of aquatic products with an IFS > 1 can indeed pose health risks to humans. This finding emphasised the need for aquaculture practitioners to regulate the use of veterinary drugs, and for relevant authorities to enhance supervision of aquatic food safety. The safety concern regarding QNs residues is higher as compared to SAs, as indicated by their higher IFS and IFS_{max} values. Based on a comprehensive analysis of the drug detection rate, over-standard rate, residue amount, and IFS value, particular attention should be given to ENR, CIP, and SMX drugs.

Acknowledgement

The present work was financially supported by "School-Enterprise Cooperation Project" for Domestic Visiting Engineers of Institutions of Higher Learning, Department of Education, Zhejiang Province (grant number FG2019023), Jinhua City scientific and technological projects (grant number KZ22030013).

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