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Original Research

A Survey and Ecological Risk Assessment of Niclosamide and Its Degradation Intermediate in Wucheng Waters within Poyang Lake Basin, China

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Abstract

Long-term use of niclosamide (NCL) in schistosomiasis control areas may have a certain impact on the regional ecological environment. The purpose of this study is to investigate the NCL residue and its possible degradation intermediates in the Wucheng water in the Poyang Lake Basin of China, and assess its ecological risks. Water samples were collected at twelve sites every month from July 2017 to June 2018, the collected samples were qualitatively and quantitatively analyzed by HPLC and HPLC/MS techniques, and regional ecotoxicological risks were estimated by calculating risk quotients (RQ). The results indicated that due to the use of NCL, the regional water environment contained NCL, 2-chloro-4-nitroaniline, 5-chlorosalicylic acid and 2,5-dihydroxybenzoic acid, etc, and their concentrations were 0.000~0.028 μg/L, 0.000~0.015 μg/L, 0.000~0.019 μg/L, below detectable limit, respectively. The mixed risk quotient (MRQ) for sensitive aquatic organisms algae, invertebrates and fish was 0.000~0.707, 0.000~0.864, 0.000~0.935, respectively. These findings demonstrated that the mixture of NCL residues and their intermediates has a moderate risk to sensitive aquatic organisms such as algae, invertebrates and fish in Wucheng waters. In order to protect the regional water environment, it is necessary to strengthen the supervision and management work after the application of NCL drugs.

Keywords: survey, risk assessment, niclosamide residue, risk quotients, Wucheng water environment

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Introduction

Niclosamide, 5-chloro-N-(2-chloro-4-nitrophenyl)-2-hydroxybenzamide is the most important component of control programs for the freshwater snails that serve as intermediate hosts for the trematodes causing schistosomiasis [1-3] and fascioliasis in humans and domestic animals in many tropical and subtropical countries [4]. In China's schistosomiasi control area, NCL is used to kill snails and schistosomiasis, repel human and animal mites, and the annual usage exceeds 3,200 tons [5] After being used in the application site, NCL does not use any effective technical means for treatment, and discharged arbitrarily, which has a serious impact on the regional ecological environment [6].

The molecular structure of niclosamide is a halogenated phenolic organic substance with a vapor pressure of $9.9*10^{-9}$mm Hg (20ºC) and a solubility of 0.1 mg/L (20ºC) in water. It is a typical polar/ionizable ion. The group (-OH) of halogenated phenolic organic is easy to remain in the environmental solid medium and has high bioaccumulation [7]. For freshwater invertebrates, NCL is a highly toxic substance (EC_{50} 0.034→50 mg/L), a highly toxic substance for freshwater fish (LC_{50} 0.03→0.23 mg/L), and a toxic substance for aquatic plants (EC_{50} 0.04→1450 mg/L) [8]. It has a great influence on algae, invertebrates and freshwater fish in schistosomiasis control areas.

In the natural environment composed of water-suspended particulate matter-sediment, NCL is preferentially adsorbed in solid phase media such as suspended solids and sediment. Under the action of sunlight, plants, microorganisms, etc, NCL migrates and transforms. In the aqueous phase, NCL ionizes the ionization of the group -OH, making NCL molecular and ionic. Under sunlight, NCL undergoes rapid photolysis in the surface waters [9, 10]; Microbial degradation of NCL under the action of aerobic or anaerobic microorganisms [11]; Plant and its root exudates cause migration and transformation of NCL in water-sediment-plant systems [12]. The intermediates of NCL degradation in the natural environment are mainly 5-chlorosalicylic acid, 2-chloro-4-nitroaniline, etc. [13-15], which have higher biological toxicity than the parent compound and have DNA damage effect [16].

In order to study the possible impact on the regional ecological environment after the use of NCL, we conducted a one-year survey and analysis of the water bodies in the lakes and rivers around Wucheng, Poyang Lake Basin, China, selecting 12 sampling points and collecting samples on the 15^{th} of each month. The collected samples were qualitatively and quantitatively analyzed by using HPLC and HPLC/MS techniques, and ecological risk quotients to evaluate the ecological risk of the regional water environment.

Materials and Methods

Chemicals

5-chloro-N-(2-chloro-4-nitrophenyl)-2-hydroxybenzamide [Niclosamide, Analytical reagent, (AR)], 2-chloro-4-nitroaniline (AR), 5-chlorosalicylic acid (AR), 2,5-dihydroxybenzoic acid (AR) were purchased from Sigma-Aldrich (Germany). Ultrapure water was obtained from a Milli-Q system (Millipore, China) and chromatography grade solvents (formic acid and methanol) for HPLC, HPLC/MS were obtained from Sigma-Aldrich (Germany).

Study Area

Wucheng is a town with a long history located in the northeast of Yongxiu County, Jiujiang City, Jiangxi Province. It covers an area of 356 square kilometers, with a population of 15160 and a block area of 2.5 square kilometers at the intersection of Ganjiang River, Xiushui River and Poyang Lake. Wucheng town has $2.7*10^9$ m^2 of water surface, $1.3*10^8$ m^2 of grassland and 42 lakes of different sizes. It is known as the "migrant bird paradise" and is a world-class natural reservation. It is a typical subtropical monsoon climate: The average annual temperature here is 16-17ºC, and the annual precipitation is 1300-1600 mm, more than 40% of which is concentrated in the second quarter. During the rainy season from early summer to June and July, the rainfall is concentrated, heavy rains are frequent. The average annual precipitation in May and June is about 200 mm, which can easily lead to floods; After the rainy season, the weather is hot and dry because it is controlled by the subtropical high pressure. In many years, the high-temperature is higher than 35 degrees Celsius in more than 20 days; Autumn temperatures are milder and there is less rain; Winter is cold but frost is short. Wucheng is the largest market and administrative center of the Poyang Lake Reservation, at the same time, it is the core area of schistosomiasis control in China, the annual use of NCL in this region is about 20 tons.

Field Sampling

In this study, 12 sampling points (See Fig. 1 and Table S1) were selected in Wucheng Town for a field sampling analysis every other month for a period from July 2017 to June 2018. The sampling point is 3~5 m from the shore and the water depth is 0.2~0.5 m. After cleaning the sampler and the brown sampling bottle with the on-site water sample, the water samples are collected according to the sampling standard and saved in number. The survey area includes 7 lakes (site 1#~7#) and 2 rivers (site 8#~12#), of which site 5# and site 7# select the side closer to the residential area, and other lake sampling points are located away from the

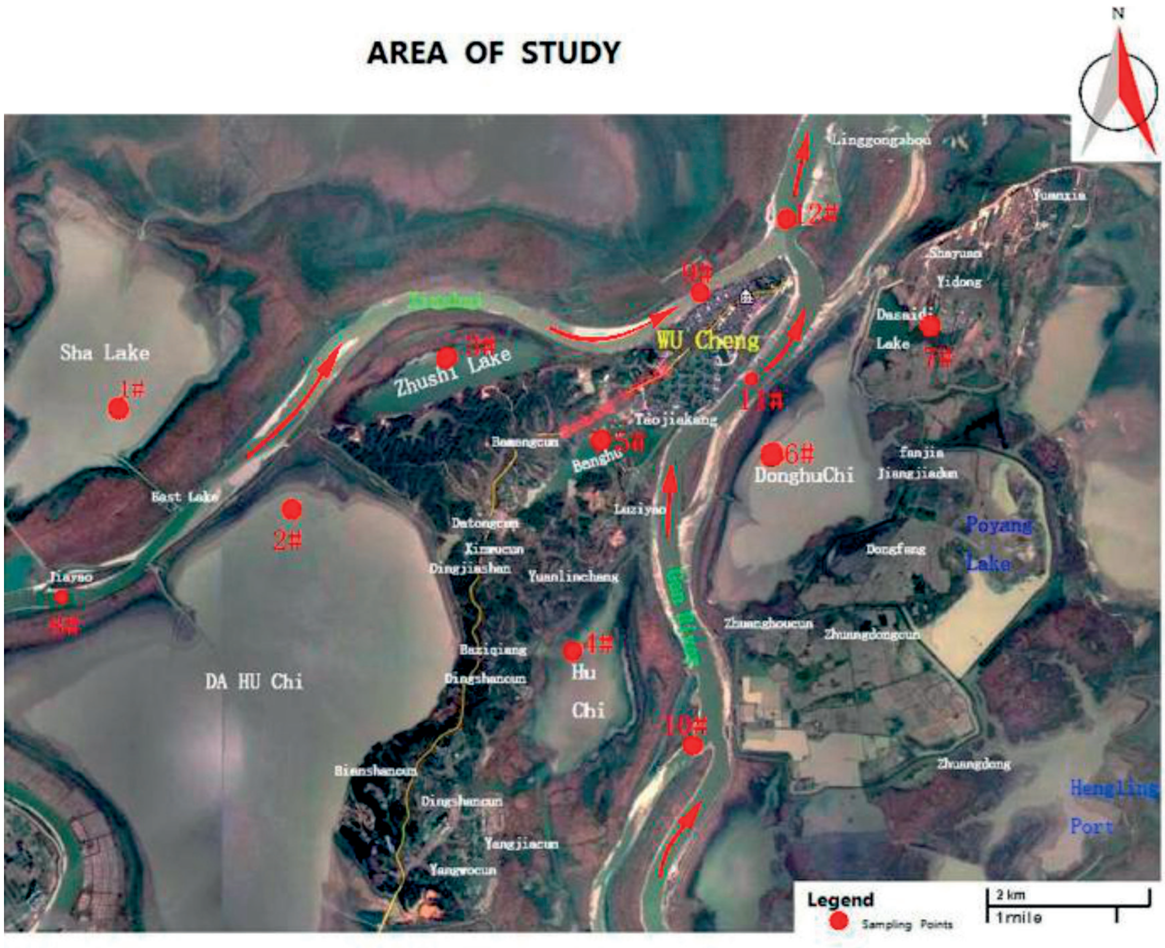

Fig. 1. Map of selected sampling locations in the Wucheng River Basin.

grass beach (molluscicides sparging area) on the near side of the spraying area, the upstream and downstream spacing of the river sampling point is about 8 km, and the 12# sampling point located in the intersection of Xiushui and Ganjiang River. The samples were transported to the laboratory and stored at 4ºC. Detailed information about the coordinates and physicochemical properties of samples was given in Table S2.

Table S1. Coordinates and altitude of the selected sites on Wucheng.

Site No.	Location	Longitude	Latitudes	Altitude
Site 1#	Sha Lake	115°56′15.0″E	29°10′13.3″N	14.89
Site 2#	Da hu Chi	115°57′16.7″E	29°09′18.6″N	15.27
Site 3#	Zhu shi Lake	115°59′05.8″E	29°10′35.8″N	14.02
Site 4#	Hu Chi	115°59′50.7″E	29°08′28.9″N	14.61
Site 5#	Bang hu	115°59′48.9″E	29°10′00.5″N	17.52
Site 6#	Donghu Chi	116°00′57.1″E	29°09′45.6″N	11.51
Site 7#	Dasaidi Lake	116°02′15.0″E	29°10′49.5″N	16.10
Site 8#	Xiushui (upstream)	115°55′47.6″E	29°08′46.5″N	12.58
Site 9#	Xiushui (downstream)	116°00′24.2″E	29°11′00.4″N	12.51
Site 10#	Gan River (upstream)	116°00′27.4″E	29°07′40.6″N	14.39
Site 11#	Gan River (downstream)	116°01′08.6″E	29°10′45.7″N	10.01
Site 12#	Confluence of two rivers	116°01′09.5″E	29°11′34.0″N	12.46

Table S2. Temperature and humidity conditions of Wucheng.

Month	High/Low (ºC)	Humidity
July 15th, 2017	36/28	50
August 15th, 2017	30/25	82
September 15th, 2017	29/20	62
October 15th, 2017	17/15	70
November 15th, 2017	20/13	55
December 15th,2 017	7/3	78
January 15th, 2018	14/6	60
February 15th, 2018	13/6	89
March 15th, 2018	22/8	84
April 15th, 2018	20/10	60
May 15th, 2018	35/27	57
June 15th, 2018	32/21	78

Data sources: China Meteorological Administration and live recording

Sample Preparation and Analysis

Water Sample Preparation

The collected water sample was filtered with filter paper. First, 100 ml filtered water sample was taken in a vacuum rotary evaporator and evaporated to just dry at 60ºC; second, 25 ml methanol was added to the evaporation flask to dissolve the concentrate, and evaporated to just dry in a concentrated evaporator at 60ºC again; third, the second concentrate was dissolved with 4 ml methanol, and the solute was filtered using 0.45 μm membrane, and the resulting solution was used for the analysis of niclosamide residues and its degradation intermediate products.

Sample Analysis

HPLC and HPLC/MS/MS were used to analyze the residual amount of niclosamide and its degradation intermediates in the collected water samples.

Niclosamide and its degradation intermediate products in water samples were qualitatively and quantitatively analyzed by HPLC (W2996/2695, Waters, USA). Samples were separated on a reversed-phase column (Kromasil C18, 250 mm×4.6 mm i.d.) with a guard column (5 μm, 10 mm×4.6 mm i.d.). Mobile phase consisted of 0.2% formic acid methanol solution (A) and distilled water (B) by using a gradient program of 50:50 (A:B, v/v) in 0~4 min, 60: 40 in 4~10 min, 100: 0 in 10~13 min, and 50:50 in 14~16 min. The flow rate was 1 mL/min and column temperature was 20ºC. A photo-diode array (PDA) detector was set at 330 nm for acquiring chromatograms, however, the PDA detector was set at 285 nm for acquiring 5-chlorosalicylic acid chromatograms under the same chromatographic condition.

At the same time, the intermediates products of niclosamide degradation were identified by HPLC/MS/MS (Agilent 6538 Q-TOF System) equipped with an ESI source. As for the HPLC condition in HPLC/MS/MS testing, MeOH: 0.1% methanoic acid = 70: 30 (v/v) was used as mobile phase and flow rate was set to 0.2 $mL{\cdot}min^{-1}$ without a separation column. Full scale MS spectra both in negative ion mode and positive ion mode in the mass range between 50 and 500 m/z was recorded.

Risk Assessment

The potential aquatic ecological risks of NCL and its degradation intermediates were assessed by using the risk quotients (RQ). According to the European technical guidance document on risk assessment (TGD) [17] the RQ value can be calculated by the following formula:

$$RQ = \frac{MEC}{PNEC} = \frac{MEC}{LOEC\ or\ LEC\quad C50/AF} \tag{1}$$

...where MEC and PNEC are the measured environment concentration and predicted no effect concentration for niclosamide, respectively.

PNEC was obtained from short-term/acute toxicity data $L(E)C_{50}$ divided by an assessment factor (AF) of 1000, or from long-term/chronic LOEC divided by 100.

The RQ value of the intermediate products was calculated in the same way.

Aquatic toxicity data of niclosamide were from the USEPA Pesticides and Toxic Substances (7508C), EPA 738-R-99-007. 2-chloro-4-nitroaniline, from the experimental results of Jin [18], Li [19] and EC, aquatic toxicity data of 5-Chloro-2-hydroxybenzoic acid were from the experimental results of Trabalka, et al [20].

$$MRQ = \sum_{i=1}^{n} \frac{MECi}{PNECi} = \sum_{i=i}^{n} \frac{MECi}{\min（PNECalgne，PNECinvertebrate，PNEC\mathit{fish}）} \tag{2}$$

Mixed organic pollutants in water may increase the overall risk through synergistic effects [21]. Concentration addition model [22] was used to assess the mixture risk of niclosamide residues and its degradation intermediate present in natural waters, where MRQ--the mixtures risk quotient was calculated by adding together the highest RQ for the individual chemical material [21, 23].

Environmental risk was divided into three levels based on the calculated RQ value: $RQ<0.1$ is “low risk”, $0.1\leq RQ\leq 1$ mean “moderate risk”, and $RQ>1$ represents “high risk” [24-26].

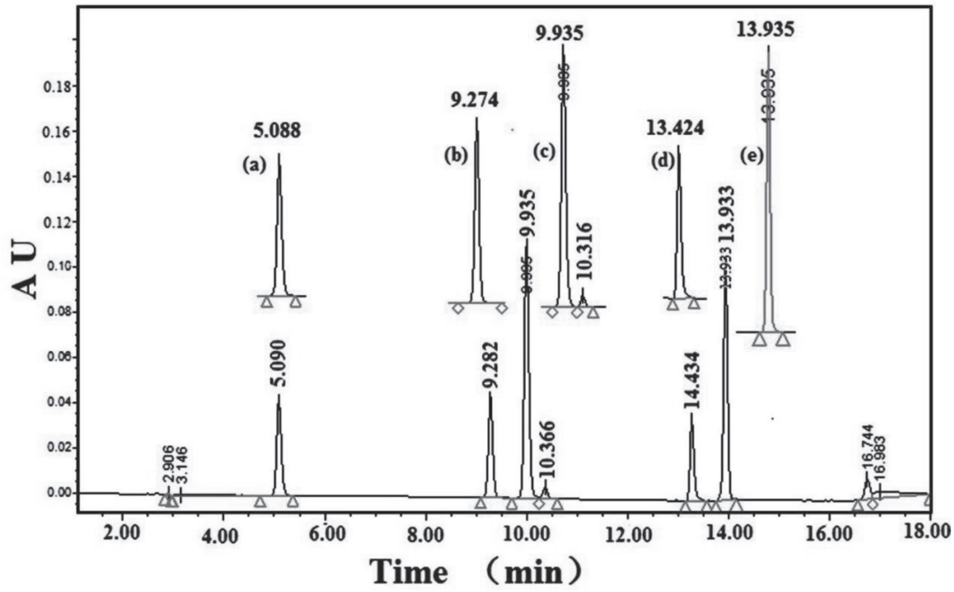

Fig. 2. HPLC spectrogram of niclosamide and possible intermediate standard samples: a) 2,5-dihydroxy benzoic acid (4 mg·L^{-1}), b) 2-chloro-4-nitroaniline (4 mg·L^{-1}), c) 2-chloro-4-nitrophenol (4 mg·L^{-1}), d) 5-chlorosalicylic acid (4 mg·L^{-1}), detection channel 285 nm, e) niclosamid (4 mg·L^{-1}).

Results and Discussion

Niclosamide and its Intermediates in Water

Niclosamide and Its Intermediates Standard Samples HPLC Analysis

The intermediates produced by niclosamide degradation in natural water were mainly 2,5-dihydroxybenzoic acid, 2-chloro-4-nitroaniline, 2-chloro-4-nitrophenol and 5-chlorosalicylic acid [27]. Fig. 2 showed the HPLC chromatogram of niclosamide and possible intermediate standard samples. The retention time of 2,5-dihydroxy benzoic acid, 2-chloro-4-nitroaniline, 2-chloro-4-nitrophenol, 5-chlorosalicylic acid, and niclosamide was 5.088, 9.274, 9.935, 13.424, and 13.935 min, respectively. The results showed that the selected HPLC analytical conditions may be used for qualitative and quantitative analysis of niclosamide residues and its degradation main intermediates.

Niclosamide and Its Intermediates in Water

Water sample concentrates were qualitatively analyzed by HPLC. Fig. 3 was the HPLC chromatogram of water sample concentrates. It can be seen from Fig. 3a) that 2,5-dihydroxy benzoic acid (5.122 min), 5-chlorosalicylic acid (13.436 min) and niclosamide(13.935min) components were detected in some river water samples, and 2,5-dihydroxybenzoic acid (5.124 min), 2-chloro-4-nitroaniline (9.241 min), 5-chlorosalicylic acid (13.434 min) and niclosamide (13.942 min) were detected in some lake waters(as shown in Fig. 3b). The retention times were 1.795, 2.063, 2.942, 16.731, and 17.117 min, which were not qualitatively analyzed.

Fig. 4 was the HPLC/MS/MS of the water sample concentrates. The total ion current (TIC) (See Fig. S1) indicated that there were a number of substances in the water sample. The analysis results of TIC by MS/MS were shown in Fig. 4. Those results showed that there were several molecular ion peaks such as 152.8988, 170.8874, 172.0012, 172.9946, 325.1840, etc. detected at 3.812, 7.325, 2.365, 2.365, and 8.164 min in TIC, respectively.

The analysis results of HPLC/MS/MS indicated that niclosamide (m/z = 325.1840) and its possible natural degradation intermediates (such as: 2,5-dihydroxy benzoic acid (m/z = 152.8988), 5-chlorosalicylic acid (m/z = 170.8831), 2-chloro-4-nitroaniline (m/z = 172.0012), 2-chloro-4 -nitrophenol (m/z = 172.9946) occured in some Wucheng waters of Poyang Lake due to the use of niclosamide.

HPLC and HPLC/MS/MS analysis results showed that after using NCL, there were NCL residues and natural degradation intermediates such as 2,5-dihydroxy benzoic acid, 5-chlorosalicylic acid, 2-chloro-4-nitroaniline, etc. in a certain period of time in the surrounding water environment.

Niclosamide and Its Intermediates Concentration in Water

The concentrations of niclosamide and its intermediates in the water samples were determined by external standard method using HPLC, the test results were shown in Table 1. The results in Table 1 indicated that there were different levels of niclosamide residues

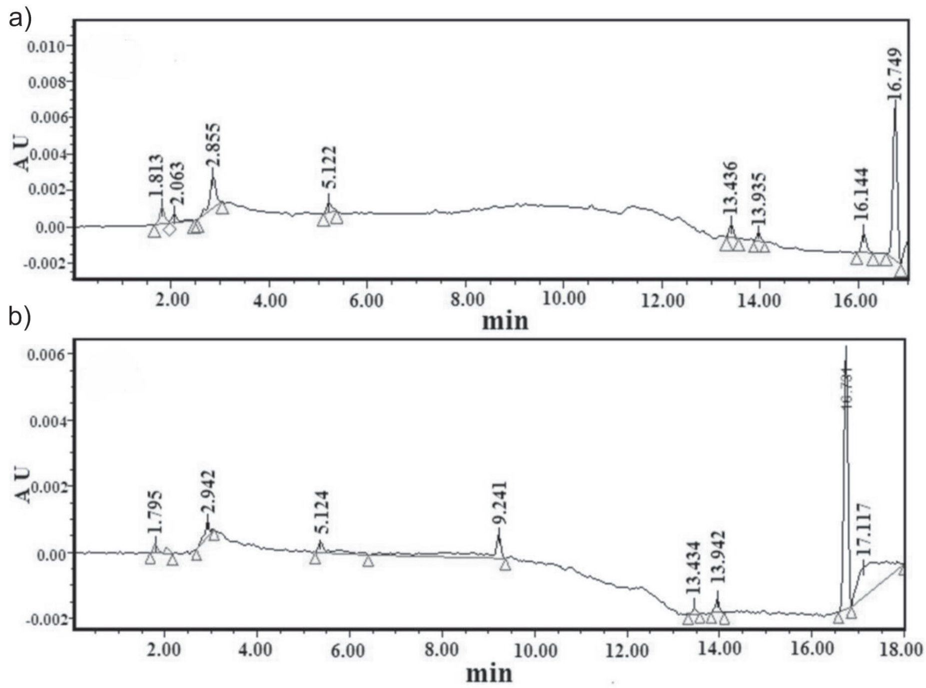

Fig. 3 HPLC spectrogram of water sample concentrates [concentration factor 4.0, a) River water, b) Lake water].

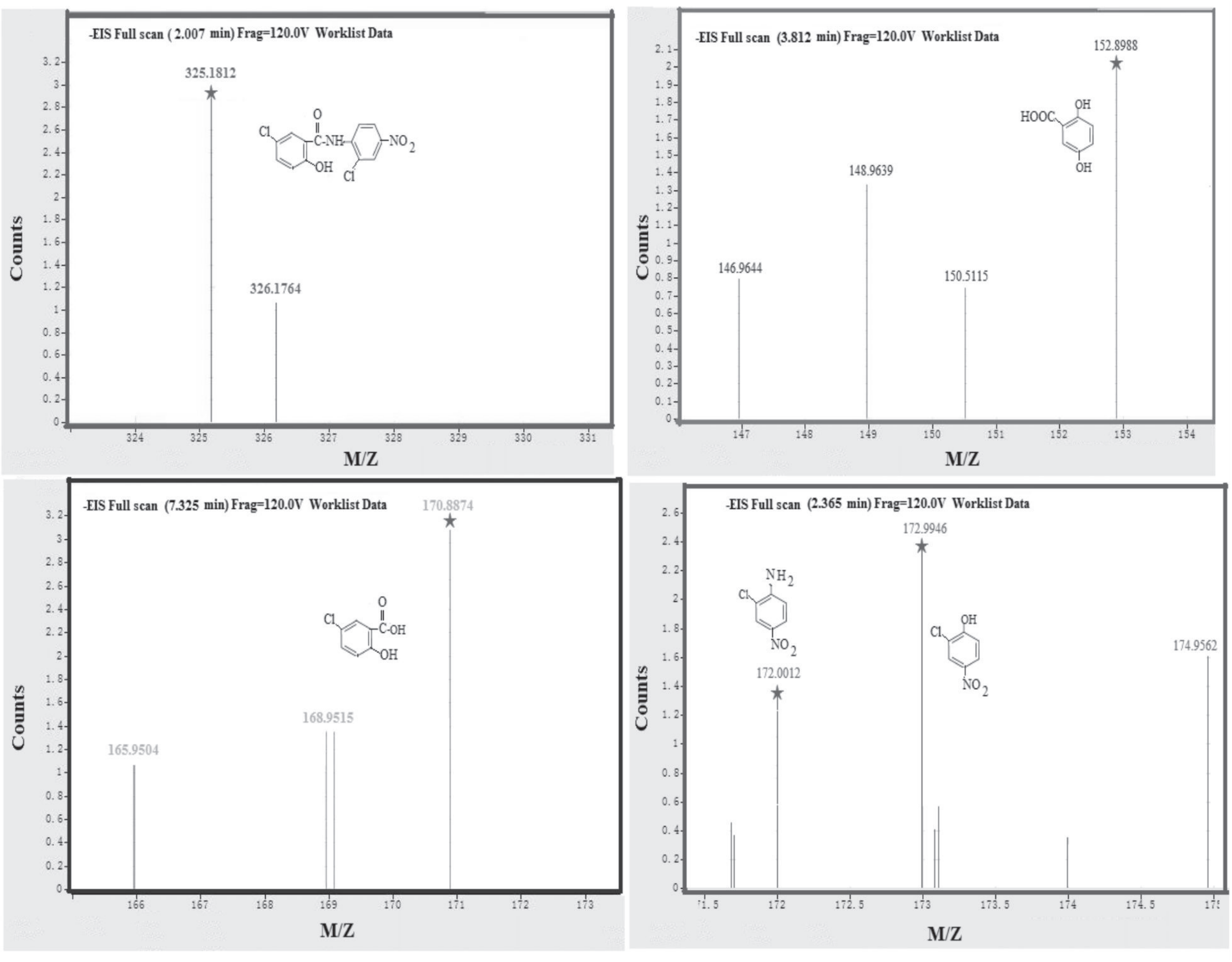

Fig. 4. HPLC−MS/MS analysis sketch of niclosamide and its degradation intermediate products in water sample concentrates.

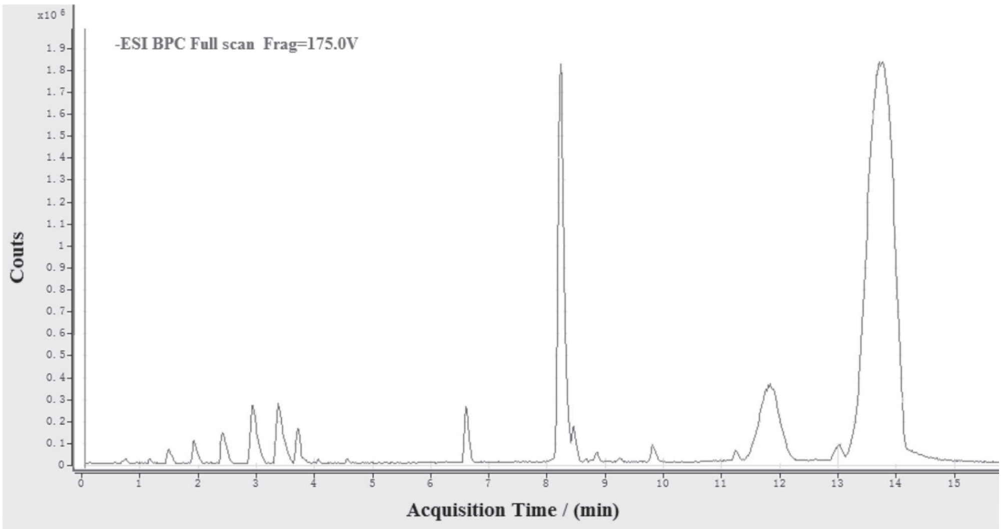

Fig. S1. TIC of water sample concentrate.

in the sampling water of Wucheng, the concentration range was 0.000~0.028 μg/L in Wucheng waters of Poyang Lake Basin.

It can be seen from Table 1 that the residual concentration of NCL in water has time seasonality and geographical location. Due to the dilution effect of the upstream river water, the residual concentration of NCL in the river water is less than that in the lake at the same time. Owing to the application of NCL twice a year, and the amount of rainfall, water temperature, sunlight, water body (organic matter, microorganisms, etc.) are different, the types and concentrations of NCL residues and intermediates are different in the same water body. Every year from March to May is the spawning period of snails. The schistosomiasis control center of Poyang Lake Basin use niclosamide to carry out two phases of snail-killing activities from April to May and from October to November.

Table1. Concentration of niclosamide and its degradation intermediate in water samples from Wucheng ($\mu g \cdot L^{-1}$).

Time / Site		1#	2#	3#	4#	5#	6#	7#	8#	9#	10#	11#	12#
July, 2017	NCL	0.005	0.006	0.013	0.010	0.013	0.011	0.009	ND	ND	ND	ND	ND
	DHBA	ND	ND	ND	BML*	ND	ND	ND	ND	ND	ND	ND	ND
	2C4NA	ND	ND	0.008	0.006	ND	ND	ND	ND	ND	ND	ND	ND
	5-CSA	ND	ND	0.010	0.008	0.012	0.009	0.008	0.008	ND	ND	ND	ND
Aug, 2017	NCL	ND	0.003	0.005	0.008	0.012	0.010	0.004	ND	0.003	ND	ND	ND
	DHBA	ND	ND	ND	BML*	ND	ND	ND	ND	ND	ND	ND	ND
	2C4NA	ND	ND	0.004	ND	0.007	0.006	ND	ND	ND	ND	ND	ND
	5-CSA	ND	ND	ND	0.010	0.009	ND	0.008	ND	0.008	ND	ND	ND
Sept, 2017	NCL	ND	0.005	0.007	0.009	0.009	0.007	0.008	0.005	ND	0.003	ND	ND
	DHBA	ND	ND	ND	ND	ND	BML*	ND	ND	ND	ND	ND	ND
	2C4NA	ND	ND	ND	ND	0.007	0.006	ND	ND	ND	ND	ND	ND
	5-CSA	0.008	ND	0.009	0.010	0.009	ND	0.008	ND	0.008	ND	ND	ND
Oct, 2017	NCL	ND	0.003	0.009	0.013	0.011	0.020	0.005	0.006	0.008	ND	0.005	0.003
	DHBA	ND	ND	BML*	BML*	ND	BML*	BML*	ND	ND	ND	ND	ND
	2C4NA	ND	0.008	0.008	ND	0.009	0.009	0.006	ND	0.006	ND	ND	ND
	5-CSA	ND	ND	0.010	0.013	0.008	0.015	ND	0.008	0.012	ND	ND	0.008
Nov, 2017	NCL	0.008	0.013	0.024	0.022	0.025	0.024	0.028	0.008	0.011	0.006	0.008	ND
	DHBA	ND	BML*	BML*	BML*	BML*	BML*	BML*	ND	ND	ND	ND	ND
	2C4NA	0.006	0.008	0.009	0.010	0.007	ND	0.013	ND	0.006	ND	ND	ND
	5-CSA	ND	ND	0.012	0.009	0.013	0.011	0.015	ND	0.009	ND	0.008	ND

Table1. Continued.

Dec, 2017	NCL	0.006	0.008	0.018	0.018	0.015	0.018	0.015	ND	ND	0.005	ND	ND
	DHBA	ND	ND	BML*	BML*	ND	BML*	ND	ND	ND	ND	ND	ND
	2C4NA	ND	0.006	0.006	ND	0.008	0.007	0.009	ND	ND	ND	ND	ND
	5-CSA	ND	ND	0.012	0.011	0.008	0.010	0.016	ND	0.009	ND	ND	ND
Jan, 2018	NCL	ND	ND	0.005	0.011	0.011	0.010	0.010	ND	ND	0.006	ND	ND
	DHBA	ND	ND	ND	BML*	ND	ND	ND	ND	ND	ND	ND	ND
	2C4NA	ND	ND	ND	ND	0.008	0.006	ND	ND	0.006	ND	ND	ND
	5-CSA	ND	ND	0.010	0.010	0.008	ND	ND	ND	ND	ND	ND	ND
Feb, 2018	NCL	ND	ND	0.007	0.009	0.008	0.009	0.010	0.004	ND	ND	ND	ND
	DHBA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	2C4NA	ND	ND	ND	ND	0.006	ND	ND	ND	ND	ND	ND	ND
	5-CSA	ND	0.008	ND	ND	ND	ND	ND	ND	ND	0.008	ND	ND
Mar, 2018	NCL	0.003	ND	0.008	0.011	0.0013	0.006	0.008	ND	0.003	ND	ND	ND
	DHBA	ND	ND	ND	ND	BML*	ND	BML*	ND	ND	ND	ND	ND
	2C4NA	ND	ND	ND	0.006	0.008	0.006	ND	0.006	ND	ND	ND	ND
	5-CSA	ND	ND	ND	ND	0.0010	ND	0.009	ND	0.008	ND	ND	ND
Apr, 2018	NCL	ND	0.004	0.010	0.013	0.023	0.018	0.007	0.003	ND	ND	0.004	ND
	DHBA	ND	ND	ND	BML*	BML*	BML*	ND	ND	0.006	ND	0.006	ND
	2C4NA	ND	ND	0.006	0.009	0.010	0.008	ND	0.006	ND	ND	ND	ND
	5-CSA	ND	ND	0.008	0.011	0.016	0.010	ND	0.008	0.009	ND	0.008	ND
May, 2018	NCL	0.009	0.013	0.026	0.023	0.015	0.016	0.018	0.005	0.003	0.003	0.003	ND
	DHBA	ND	BML*	BML*	BML*	BML*	BML*	BML*	ND	BML*	ND	ND	ND
	2C4NA	0.006	0.006	0.013	0.015	0.008	0.007	0.009	0.006	0.008	0.006	ND	ND
	5-CSA	0.008	0.010	0.018	0.017	0.019	0.008	0.012	0.008	0.010	ND	0.008	ND
June, 2018	NCL	0.008	0.008	0.018	0.014	0.012	0.006	0.013	ND	ND	0.005	ND	ND
	DHBA	BML*	ND	BML*	BML*	BML*	ND	BML*	BML*	ND	ND	ND	ND
	2C4NA	ND	ND	0.006	0.006	0.007	0.006	ND	ND	ND	ND	ND	ND
	5-CSA	ND	0.008	0.011	0.009	0.008	ND	ND	0.008	ND	ND	ND	ND

Note: BML: Below the monitoring line; ND: not detected;NCL: niclosamide; DHBA: 2,5-dihydroxy benzoic acid; 2C4NA: 2-chloro-4-nitroaniline; 5-CSA: 5-chlorosalicylic acid

The concentration of niclosamide in the water was greatly increased during the application. The concentration of small lakes near the residential area (5#, 7#) is the highest, and the concentration of large lakes such as 1# and Site 2# is relatively low; Two months after the application of NCL, the concentration of niclosamide residue in the water was reduced to a relatively stable state.

In summer, high temperatures and long periods of sunshine favor photolysis and microbial degradation of niclosamide. At the same time, under the action of the upper aerobic microorganisms and the bottom layer anaerobic microorganisms in the water, the NCL adsorbed on the surface of the particles and sludge in the condition of aerobic-anaerobic degradation, and an intermediate product had a larger solubility than NCL is formed. Thereby, the number of intermediate products degraded by NCL in the water body increases and its concentration also increases. In winter, the sun is weak, the water temperature is low, the microbial activity is weak, and the NCL adsorbed on the sediment surface hardly reacts.

During summer, due to the large rainfall, strong sunlight and high water temperature, the residual concentration of niclosamide in the water is lower than that in winter.

At the same time, it can be seen from Table 1 that after using NCL to kill snails in the Wucheng area, the NCL in the water body generates intermediates such as 5-chlorosalicylic acid, 2-chloro-4-nitroaniline, 2,5-dihydroxybenzoicacid under the action of sunlight and microorganisms. 5-chlorosalicylic acid concentrations in water samples collected in 1#~12# were in the range of 0~0.019 μg/L, 2-chloro-4-nitrobenzene concentration in the sample collection points were in the range of 0~0.014 μg/L, and the concentration of 2,5-dihydroxybenzoicacid is less than the detection line of this test instrument.

Table 2. Aquatic toxicity data of niclosamide and its degradation intermediate to the most sensitive aquatic species.

Compound	Non-target organism	Toxicity data (mg /L)	Toxicity	AF[a]	PNEC[b] (ng /L)	Reference
NCL	Aquatic plant (algae)	EC_{50}= 0.04->1.45	Acute	1000	40	EPA 738-R-99-007, (1999) [8]
	Invertebrates (freshwater)	EC_{50} =0.034 ->50	Acute	1000	34~50000	EPA 738-R-99-007, (1999)
	Invertebrates (freshwater)	$NOAE^{C}$ = 0.034	chronic	100	34	EPA 738-R-99-007, (1999)
	Fish (Fresh water)	LC_{50} = 0.03 - 0.23	Acute	1000	30~230	EPA 738-R-99-007, (1999)
5-CSA	Invertebrates (water flea)	LC_{50} >100	Acute	1000	100000	Trabalka,J.R, et al, (1978) [20]
2C4NA	Aquatic plant (algae)	EC_{50}^{d}=1.81	acute	1000	1810	Jin, et al, (2014)[18]
	Invertebrates (daphnia magna)	$NOAEC^{e}$= 3.2	acute	100	320	ECB 121-87-9, (2000) [29]
	Fish (Fresh water)	LC_{50}^{f}=6.99	Acute	1000	6990	Li, et al,(2001) [19]

a. AF: assessment factor; b. b PNEC: predicted no effect concentration. C. NOEC: no observable effect concentration; d. EC_{50}: half maximal effective concentration; e. NOAEC- No Observed Adverse Effect Concentration; f. LC_{50}-Median Lethal Concentration;

Aquatic Ecological Risk

After being used in the Wucheng waters of the Poyang Lake Basin, NCL directly enters the surrounding water, sediment and soil environment, under the influence of factors such as sunlight, plants and microorganisms, NCL migrates and transforms in the water-sediment-soil system, producing many degradation intermediates such as 2-chloro-4-nitroaniline, 5-chlorosalicylic acid, 2,5-dihydroxy benzoic acid, etc. Due to the long-term use of NCL twice a year, the water in Wucheng waters contains NCL residues and intermediates such as 2-chloro-4-nitroaniline, 5-chlorosalicylic acid, 2,5-dihydroxy benzoic acid, and their concentrations were not equal at different times and in different locations (See Table 1).

At the concentration used for snail control, NCL has no effect on important aquatic plants (such as rice, grass, mustard, etc.) [28] in the schistosomiasi control area, however, for aquatic plants (algae), Invertebrates and Fish, NCL is highly toxic due to the lower $L(E)C_{50}$ (or LOEC) values, and their PNEC values are 40, 34, 30 ng/L, respectively (See Table 2). At the same time, 2-chloro-4-nitroaniline was also highly toxic to algae, Invertebrates and Fish due to its lower L(E)C50 (or LOEC) values (See Table 2).

Due to the dilution effect of the upstream water from the river, the environmental risk of NCL residues in the river water in Wucheng is low risk, and the RQ value is less than 0.1 (See Table S3).

NCL residue has moderate environmental risk to algae, invertebrate, and fish in lake water environment in Wucheng waters, and its RQ value is between 0.2 and 0.8, especially in April, May, October and November of the NCL application period, the RQ value in the lake water environment is between 0.5 and 0.8, indicating that the lake water presents moderate ecological risk.

After being degraded by NCL, 2-chloro-4-nitroaniline, 5-chlorosalicylic acid had no effect on algae, invertebrate, and fish in the river water environment of Wucheng, because their corresponding RQ values were less than 0.01. However, for lake water, these intermediates have a minor effect on the algae, invertebrate, and fish in the lake because their corresponding RQ values sometimes reach 0.05.

The risk assessment of the detected NCL residue and its degradation intermediates mixture was conducted based on the classical mixture toxicity concept of concentration addition model. As shown in Fig. 5 and Table S3, the calculated MRQ values of NCL residue, 2-chloro-4-nitroaniline and 5-chlorosalicylic acid mixtures in the lake water sampling sites (1#~7#) for sensitive algae, invertebrates and fish is 0.000~0.707, 0.000~0.864, 0.000~0.935 respectively. MRQ values at all of the lake water sampling sites (1#~7#) were in the range of 0.00 to 0.935, which indicated that the detected NCL residue,2-chloro-4-nitroaniline and 5-chlorosalicylic acid mixtures might pose a moderate ecological risks.

Meanwhile, Table S3 allowed a clear identification of the relative importance of each individual substance. NCL residue and 2-chloro-4-nitroaniline contributed 94.0%~99.0% and 0%~5.8% to the MRQs for each site, respectively, while 5-chlorosalicylic acid only has a negligible contribution.

At the same time, MRQ values of NCL residue, 2-chloro-4-nitroaniline and 5-chlorosalicylic acid mixtures in the river water sampling sites (8#~12#) were in the range of 0.000~0.168. which indicated that the use of NCL is low risk for regional river water.

Table S3. RQ, MRQ values at different times and different sampling points.

Site 1#														
Data / Time	Residual concentration (μg/L)			RQ								MRQ		
	NCL	2C4NA	5-CSA	Algae		Invertebrates			Fish			Algae	Invertebrates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA				
July, 2017	0.0050	0.000	0	0.125	0.000	0.147	0.000	0.000	0.167	0.000		0.125	0.147	0.167
Aug, 2017	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
Sept, 2017	0.0000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
Oct, 2017	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
Nov, 2017	0.0080	0.006	0	0.200	0.003	0.235	0.000	0.019	0.267	0.001		0.203	0.254	0.268
Dec, 2017	0.0060	0.000	0	0.150	0.000	0.176	0.000	0.000	0.200	0.000		0.150	0.176	0.200
Jan, 2018	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
Feb, 2018	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
Mar, 2018	0.0030	0.000	0	0.075	0.000	0.088	0.000	0.000	0.100	0.000		0.075	0.088	0.100
Apr, 2018	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
May, 2018	0.0090	0.006	0.008	0.225	0.003	0.265	0.000	0.019	0.300	0.001		0.228	0.284	0.301
June, 2018	0.0080	0.000	0	0.200	0.000	0.235	0.000	0.000	0.267	0.000		0.200	0.235	0.267
Site 2#														
Data / Time	Residual concentration (μg/L)			RQ								MRQ		
	NCL	2C4NA	5-CSA	Algae		Invertebrates			Fish			Algae	Invertebrates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA				
July, 2017	0.0060	0.000	0	0.150	0.000	0.176	0.000	0.000	0.200	0.000		0.150	0.176	0.200
Aug, 2017	0.0030	0.000	0	0.075	0.000	0.088	0.000	0.000	0.100	0.000		0.075	0.088	0.100
Sept, 2017	0.0050	0.000	0	0.125	0.000	0.147	0.000	0.000	0.167	0.000		0.125	0.147	0.167
Oct, 2017	0.0030	0.008	0	0.075	0.004	0.088	0.000	0.025	0.100	0.001		0.079	0.113	0.101
Nov, 2017	0.0130	0.008	0	0.325	0.004	0.382	0.000	0.025	0.433	0.001		0.329	0.407	0.434
Dec, 2017	0.0080	0.006	0	0.200	0.003	0.235	0.000	0.019	0.267	0.001		0.203	0.254	0.268
Jan, 2018	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
Feb, 2018	0.0000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000

Table S3. Continued.

Mar, 2018	0.0000	0.000	0	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Apr, 2018	0.0040	0.000	0	0.100	0.000	0.118	0.000	0.000	0.133	0.000	0.100	0.118	0.133
May, 2018	0.0130	0.006	0.01	0.325	0.003	0.382	0.000	0.019	0.433	0.001	0.328	0.401	0.434
June, 2018	0.0080	0.000	0.008	0.200	0.000	0.235	0.000	0.000	0.267	0.000	0.200	0.235	0.267
Site 3#													
Data \ Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Invertebrates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0130	0.008	0.010	0.325	0.004	0.382	0.000	0.025	0.433	0.001	0.329	0.407	0.434
Aug, 2017	0.0050	0.004	0.000	0.125	0.002	0.147	0.000	0.013	0.167	0.001	0.127	0.160	0.167
Sept, 2017	0.0070	0.000	0.009	0.175	0.000	0.206	0.000	0.000	0.233	0.000	0.175	0.206	0.233
Oct, 2017	0.0090	0.008	0.010	0.225	0.004	0.265	0.000	0.025	0.300	0.001	0.229	0.290	0.301
Nov, 2017	0.0240	0.009	0.012	0.600	0.005	0.706	0.000	0.028	0.800	0.001	0.605	0.734	0.801
Dec, 2017	0.0180	0.006	0.012	0.450	0.003	0.529	0.000	0.019	0.600	0.001	0.453	0.548	0.601
Jan, 2018	0.0050	0.000	0.010	0.125	0.000	0.147	0.000	0.000	0.167	0.000	0.125	0.147	0.167
Feb, 2018	0.0070	0.000	0.000	0.175	0.000	0.206	0.000	0.000	0.233	0.000	0.175	0.206	0.233
Mar, 2018	0.0080	0.000	0.000	0.200	0.000	0.235	0.000	0.000	0.267	0.000	0.200	0.235	0.267
Apr, 2018	0.0100	0.006	0.008	0.250	0.003	0.294	0.000	0.019	0.333	0.001	0.253	0.313	0.334
May, 2018	0.0260	0.013	0.018	0.650	0.007	0.765	0.000	0.041	0.867	0.002	0.657	0.806	0.869
June, 2018	0.0180	0.006	0.011	0.450	0.003	0.529	0.000	0.019	0.600	0.001	0.453	0.548	0.601
Site 4#													
Data \ Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0100	0.006	0.008	0.250	0.003	0.294	0.000	0.019	0.333	0.001	0.253	0.313	0.334
Aug, 2017	0.0080	0.000	0.010	0.200	0.000	0.235	0.000	0.000	0.267	0.000	0.200	0.235	0.267
Sept, 2017	0.0090	0.000	0.010	0.225	0.000	0.265	0.000	0.000	0.300	0.000	0.225	0.265	0.300
Oct, 2017	0.0130	0.000	0.013	0.325	0.000	0.382	0.000	0.000	0.433	0.000	0.325	0.382	0.433
Nov, 2017	0.0220	0.010	0.009	0.550	0.006	0.647	0.000	0.031	0.733	0.001	0.556	0.678	0.735

Table S3. Continued.

Dec, 2017	0.0180	0.000	0.011	0.450	0.000	0.529	0.000	0.000	0.600	0.000	0.450	0.530	0.600
Jan, 2018	0.0110	0.000	0.010	0.275	0.000	0.324	0.000	0.000	0.367	0.000	0.275	0.324	0.367
Feb, 2018	0.0090	0.000	0.000	0.225	0.000	0.265	0.000	0.000	0.300	0.000	0.225	0.265	0.300
Mar, 2018	0.0110	0.006	0.000	0.275	0.003	0.324	0.000	0.019	0.367	0.001	0.278	0.342	0.368
Apr, 2018	0.0130	0.009	0.011	0.325	0.005	0.382	0.000	0.028	0.433	0.001	0.330	0.411	0.435
May, 2018	0.0230	0.015	0.017	0.575	0.008	0.676	0.000	0.047	0.767	0.002	0.583	0.724	0.769
June, 2018	0.0140	0.006	0.009	0.350	0.003	0.412	0.000	0.019	0.467	0.001	0.353	0.431	0.468
Site 5#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0130	0.000	0.012	0.325	0.000	0.382	0.000	0.000	0.433	0.000	0.325	0.382	0.433
Aug, 2017	0.0120	0.007	0.009	0.300	0.004	0.353	0.000	0.022	0.400	0.001	0.304	0.375	0.401
Sept, 2017	0.0090	0.007	0.009	0.225	0.004	0.265	0.000	0.022	0.300	0.001	0.229	0.287	0.301
Oct, 2017	0.0110	0.009	0.008	0.275	0.005	0.324	0.000	0.028	0.367	0.001	0.280	0.352	0.368
Nov, 2017	0.0250	0.007	0.013	0.625	0.004	0.735	0.000	0.022	0.833	0.001	0.629	0.757	0.834
Dec, 2017	0.0150	0.008	0.008	0.375	0.004	0.441	0.000	0.025	0.500	0.001	0.379	0.466	0.501
Jan, 2018	0.0110	0.008	0.008	0.275	0.004	0.324	0.000	0.025	0.367	0.001	0.279	0.349	0.368
Feb, 2018	0.0080	0.006	0.000	0.200	0.003	0.235	0.000	0.019	0.267	0.001	0.203	0.254	0.268
Mar, 2018	0.0013	0.008	0.001	0.033	0.004	0.038	0.000	0.025	0.043	0.001	0.037	0.063	0.044
Apr, 2018	0.0230	0.010	0.016	0.575	0.006	0.676	0.000	0.031	0.767	0.001	0.581	0.708	0.768
May, 2018	0.0150	0.008	0.019	0.375	0.004	0.441	0.000	0.025	0.500	0.001	0.379	0.466	0.501
June, 2018	0.0120	0.007	0.008	0.300	0.004	0.353	0.000	0.022	0.400	0.001	0.304	0.375	0.401
Site 6#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0110	0.000	0.009	0.275	0.000	0.324	0.000	0.000	0.367	0.000	0.275	0.324	0.367
Aug, 2017	0.0100	0.006	0.000	0.250	0.003	0.294	0.000	0.019	0.333	0.001	0.253	0.313	0.334

Table S3. Continued.

Sept, 2017	0.0070	0.006	0.000	0.175	0.003	0.206	0.000	0.019	0.233	0.001	0.178	0.225	0.234
Oct, 2017	0.0200	0.009	0.015	0.500	0.005	0.588	0.000	0.028	0.667	0.001	0.505	0.617	0.668
Nov, 2017	0.0240	0.000	0.011	0.600	0.000	0.706	0.000	0.000	0.800	0.000	0.600	0.706	0.800
Dec, 2017	0.0180	0.007	0.010	0.450	0.004	0.529	0.000	0.022	0.600	0.001	0.454	0.551	0.601
Jan, 2018	0.0100	0.006	0.000	0.250	0.003	0.294	0.000	0.019	0.333	0.001	0.253	0.313	0.334
Feb, 2018	0.0090	0.000	0.000	0.225	0.000	0.265	0.000	0.000	0.300	0.000	0.225	0.265	0.300
Mar, 2018	0.0060	0.006	0.000	0.150	0.003	0.176	0.000	0.019	0.200	0.001	0.153	0.195	0.201
Apr, 2018	0.0180	0.008	0.010	0.450	0.004	0.529	0.000	0.025	0.600	0.001	0.454	0.555	0.601
May, 2018	0.0160	0.007	0.008	0.400	0.004	0.471	0.000	0.022	0.533	0.001	0.404	0.493	0.534
June, 2018	0.0060	0.006	0.000	0.150	0.003	0.176	0.000	0.019	0.200	0.001	0.153	0.195	0.201
Site 7#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0090	0.000	0.008	0.225	0.000	0.265	0.000	0.000	0.300	0.000	0.225	0.265	0.300
Aug, 2017	0.0040	0.000	0.008	0.100	0.000	0.118	0.000	0.000	0.133	0.000	0.100	0.118	0.133
Sept, 2017	0.0080	0.000	0.008	0.200	0.000	0.235	0.000	0.000	0.267	0.000	0.200	0.235	0.267
Oct, 2017	0.0050	0.006	0.000	0.125	0.003	0.147	0.000	0.019	0.167	0.001	0.128	0.166	0.168
Nov, 2017	0.0280	0.013	0.015	0.700	0.007	0.824	0.000	0.041	0.933	0.002	0.707	0.864	0.935
Dec, 2017	0.0150	0.009	0.016	0.375	0.005	0.441	0.000	0.028	0.500	0.001	0.380	0.469	0.501
Jan, 2018	0.0100	0.000	0.000	0.250	0.000	0.294	0.000	0.000	0.333	0.000	0.250	0.294	0.333
Feb, 2018	0.0100	0.000	0.000	0.250	0.000	0.294	0.000	0.000	0.333	0.000	0.250	0.294	0.333
Mar, 2018	0.0080	0.000	0.009	0.200	0.000	0.235	0.000	0.000	0.267	0.000	0.200	0.235	0.267
Apr, 2018	0.0070	0.000	0.000	0.175	0.000	0.206	0.000	0.000	0.233	0.000	0.175	0.206	0.233
May, 2018	0.0180	0.009	0.012	0.450	0.005	0.529	0.000	0.028	0.600	0.001	0.455	0.558	0.601
June, 2018	0.0130	0.000	0.000	0.325	0.000	0.382	0.000	0.000	0.433	0.000	0.325	0.382	0.433

Table S3. Continued.

Site 8#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Aug, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Sept, 2017	0.0050	0.000	0.000	0.125	0.000	0.147	0.000	0.000	0.167	0.000	0.125	0.147	0.167
Oct, 2017	0.0060	0.000	0.008	0.150	0.000	0.176	0.000	0.000	0.200	0.000	0.150	0.177	0.200
Nov, 2017	0.0080	0.000	0.000	0.200	0.000	0.235	0.000	0.000	0.267	0.000	0.200	0.235	0.267
Dec, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Jan, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Feb, 2018	0.0040	0.000	0.000	0.100	0.000	0.118	0.000	0.000	0.133	0.000	0.100	0.118	0.133
Mar, 2018	0.0000	0.006	0.000	0.000	0.003	0.000	0.000	0.019	0.000	0.001	0.003	0.019	0.001
Apr, 2018	0.0030	0.006	0.008	0.075	0.003	0.088	0.000	0.019	0.100	0.001	0.078	0.107	0.101
May, 2018	0.0050	0.006	0.008	0.125	0.003	0.147	0.000	0.019	0.167	0.001	0.128	0.166	0.168
June, 2018	0.0000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Site 9#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Aug, 2017	0.0030	0.000	0.008	0.075	0.000	0.088	0.000	0.000	0.100	0.000	0.075	0.088	0.100
Sept, 2017	0.0000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Oct, 2017	0.0080	0.006	0.012	0.200	0.003	0.235	0.000	0.019	0.267	0.001	0.203	0.254	0.268
Nov, 2017	0.0110	0.006	0.009	0.275	0.003	0.324	0.000	0.019	0.367	0.001	0.278	0.342	0.368
Dec, 2017	0.0000	0.000	0.009	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Jan, 2018	0.0000	0.006	0.000	0.000	0.003	0.000	0.000	0.019	0.000	0.001	0.003	0.019	0.001
Feb, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Table S3. Continued.

Mar, 2018	0.0030	0.000	0.008	0.075	0.000	0.088	0.000	0.000	0.100	0.000	0.075	0.088	0.100
Apr, 2018	0.0000	0.000	0.009	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
May, 2018	0.0030	0.008	0.010	0.075	0.004	0.088	0.000	0.025	0.100	0.001	0.079	0.113	0.101
June, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Site 10#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Aug, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Sept, 2017	0.0030	0.000	0.000	0.075	0.000	0.088	0.000	0.000	0.100	0.000	0.075	0.088	0.100
Oct, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Nov, 2017	0.0060	0.000	0.000	0.150	0.000	0.176	0.000	0.000	0.200	0.000	0.150	0.176	0.200
Dec, 2017	0.0050	0.000	0.000	0.125	0.000	0.147	0.000	0.000	0.167	0.000	0.125	0.147	0.167
Jan, 2018	0.0060	0.000	0.000	0.150	0.000	0.176	0.000	0.000	0.200	0.000	0.150	0.176	0.200
Feb, 2018	0.0000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Mar, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Apr, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
May, 2018	0.0030	0.006	0.000	0.075	0.003	0.088	0.000	0.019	0.100	0.001	0.078	0.107	0.101
June, 2018	0.0050	0.000	0.000	0.125	0.000	0.147	0.000	0.000	0.167	0.000	0.125	0.147	0.167
Site 11#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Aug, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Sept, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Oct, 2017	0.0050	0.000	0.000	0.125	0.000	0.147	0.000	0.000	0.167	0.000	0.125	0.147	0.167

Table S3. Continued.

Nov, 2017	0.0050	0.000	0.008	0.125	0.000	0.147	0.000	0.000	0.167	0.000	0.125	0.147	0.167
Dec, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Jan, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Feb, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Mar, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Apr, 2018	0.0040	0.000	0.008	0.100	0.000	0.118	0.000	0.000	0.133	0.000	0.100	0.118	0.133
May, 2018	0.0030	0.000	0.008	0.075	0.000	0.088	0.000	0.000	0.100	0.000	0.075	0.088	0.100
June, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Site 12#													
Data / Time	Residual concentration (μg/L)			RQ							MRQ		
	NCL	2C4NA	5-CSA	algae		Invertebrates			Fish		algae	Inverte-brates	Fish
				NCL	2C4NA	NCL	5-CSA	2C4NA	NCL	2C4NA			
July, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Aug, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Sept, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Oct, 2017	0.0030	0.000	0.008	0.075	0.000	0.088	0.000	0.000	0.100	0.000	0.075	0.088	0.100
Nov, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Dec, 2017	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Jan, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Feb, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Mar, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Apr, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
May, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
June, 2018	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

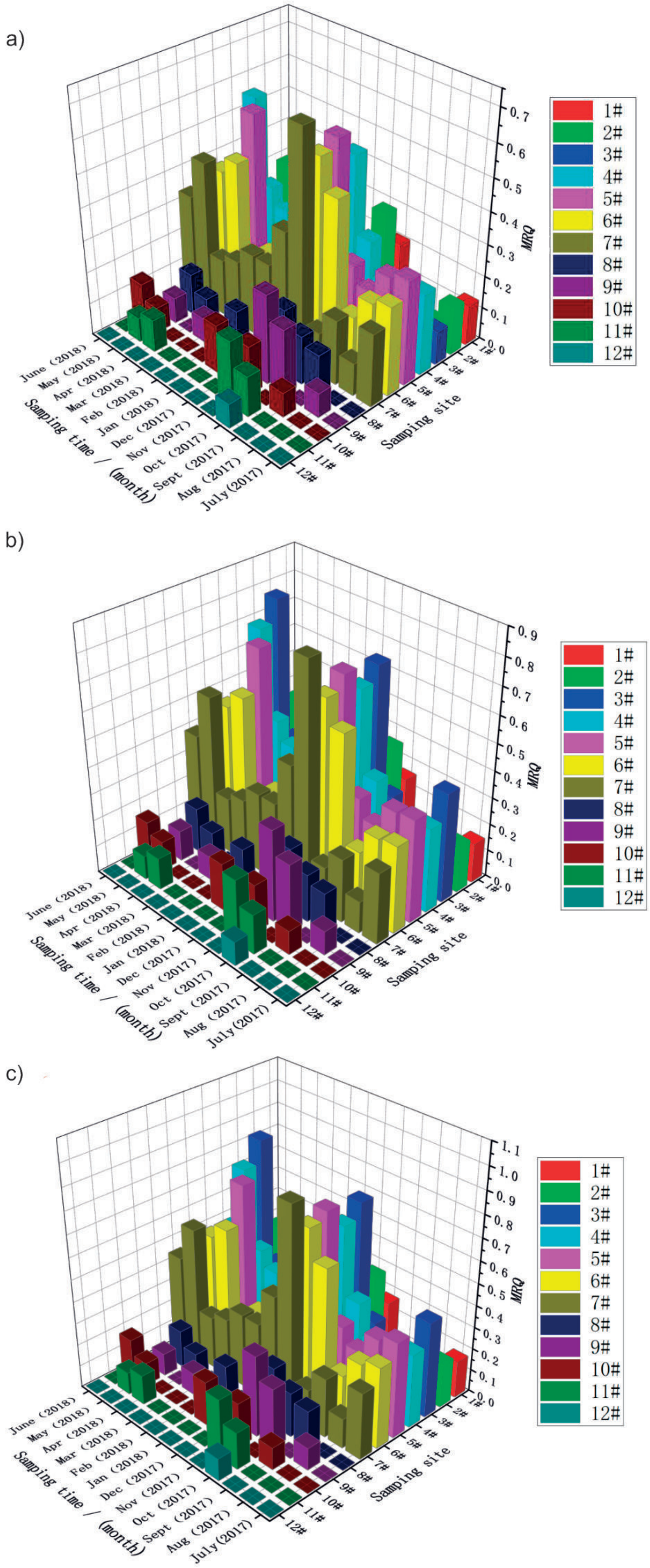

Fig. 5. Calculated mix risk quotients (MRQs) for the detected niclosamide and its degradation intermediate to aquatic organisms: a) algae; b) invertebrates; c) fish.

Overall, MRQ value of each sampling sites mainly contributed by NCL residue, followed by 2-chloro-4-nitroaniline, and 5-chlorosalicylic acid has basically no contribution. The use of NCL has a moderate ecological risk to the lake water in Wucheng waters, but the ecological risk to the river water is low risk.

Conclusions

This study conducted a one-year sampling analysis of the water environment in Wucheng waters of the Poyang Lake Basin. It was found that due to the use of the molluscicide NCL, the regional water environment contained NCL residues, 2-chloro-4-nitroaniline and 5-chlorosalicylic acid, etc, and their concentrations were 0.000~0.028 μg/L, 0.000~0.015 μg/L, 0.000~0.019 μg/L, respectively. According to the MRQ calculation results, there was a moderate ecological risk in the Wucheng waters, which had certain influence on sensitive aquatic organisms such as algae, invertebrate, and fish in the water environment.

Owing to the lack of long-term monitoring, it is not possible to compare NCL residue levels in different years, under different meteorological and hydrological conditions in the same month. Continuous monitoring is necessary to guide the avoidance of ecological risks caused by making use of niclosamide to control schistosomiasis.

Thus, in the schistosomiasis control area, the problem of the snail-killing agent niclosamide residue pollution should cause the attention of the relevant departments, and more frequent monitoring should be encouraged and focused on lake farming areas to protect the water environment and improve the quality of aquatic products.

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Conflict of Interest

The authors declare no conflict of interest.

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