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Predicting criteria continuous concentrations of metals or metalloids for protecting marine life by use of quantitative ion characteristic–activity relationships–species sensitivity distributions (QICAR-SSD)

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ABSTRACT

Marine pollution by metals has been a major challenge for ecological systems; however, water quality criteria (WQC) for metals in saltwater is still lacking. Especially from a regulatory perspective, chronic effects of metals on marine organisms should receive more attention. A quantitative ion characteristic–activity relationships–species sensitivity distributions (QICAR-SSD) model, based on chronic toxicities for eight marine organisms, was established to predict the criteria continuous concentrations (CCCs) of 21 metals. The results showed that the chronic toxicities of various metals had good relationships with their physicochemical properties. Predicted CCCs of six metals (Hg^{2+}, Cu^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+} and Zn^{2+}) were in accordance with the values recommended by the U.S. EPA, with prediction errors being less than an order of magnitude. The QICAR-SSD approach provides an alternative tool to empirical methods and can be useful for deriving scientifically defensible WQC for metals for marine organisms and conducting ecological risk assessments.

1. Introduction

With industrialization increasing in coastal cities, metal pollution of the marine environment, especially in estuaries and along coasts, has become a worldwide problem. To strengthen environmental management and to minimize impacts of metals on marine organisms, the U.S. EPA has recommended criteria continuous concentrations (CCCs) for 9 metals or metalloids in saltwater (arsenic (As), cadmium (Cd), hexavalent chromium (Cr(VI)), copper (Cu), lead (Pb), mercury (Hg), nickel (Ni), selenium (Se) and zinc (Zn)) since 1986. However, for other metals, CCCs are still lacking, which limits capabilities of government regulators to assess water quality and to make sound environmental management decisions. Thus, there was a need to derive CCCs for additional metals.

A CCC equals the highest concentration of a toxicant to which aquatic organisms can be exposed indefinitely without causing unacceptable effects. It is determined based on results of chronic toxicity tests (e.g. no observed effect concentrations (NOECs), lowest observed effect concentrations (LOECs) or maximum acceptable toxicant concentrations (MATCs)), but this information is not always easily obtained. Few standard methods for marine toxicity testing are available. In addition, systematic and comprehensive chronic tests of toxicity are costly and difficult due to challenges in maintaining constant toxic exposures and keeping control organisms alive and in good condition. Although use of an acute to chronic ratio (ACR) allows for an estimation of the chronic criteria from acute toxicity data, it was argued to have only a limited predictive value in aquatic ecosystems. Moreover, no ACR correlation was found across trophic levels (Ahlers et al., 2006). The biotic ligand model (BLM) is considered to be a promising method to estimate the activities of dissolved metals and has been used to derive water quality criteria (WQC) for copper in freshwater (U.S. EPA, 2007). However, there still remain limitations for extending the BLM from freshwater to saltwater (Arnold et al., 2005; Pinho and Bianchini, 2010). It has

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been recognized that in silico approaches have potential to become efficient alternative tools to empirical methods to drive WQC.

The quantitative ion characteristic-activity relationship (QICAR) is a mathematical method that is used to predict the biological activities of metal ions based on the assumption that similar electronic configurations should have similar functions. It can be expected to capture the relationships between the "microstructures" of metals, represented by physicochemical properties, and their macroscopic properties, such as biological toxicity, biosorption capacity or accumulation. Also, the QICAR approach is time- and cost-efficient and could reveal mechanisms of toxic potencies of metals. In the last few decades, extensive research has been conducted on QICAR to predict toxic potencies of metal cations (Khangarot and Das, 2009; McCloskey et al., 1996; Mendes et al., 2010; Newman and McCloskey, 1996; Ownby and Newman, 2003; Walker et al., 2007). The most common "descriptors" used in these studies are standard electrode potential (E_0), negative logarithm of the solubility product equilibrium constant (pK_{sp}), standard reduction-oxidation potential (ΔE_0), electronegativity (X, X_{AR}, or X_m) and softness index (σ_p). Additionally, QICAR combined with a species sensitivity distribution (SSD) approach has been used to predict WQC for protecting aquatic life (Chen et al., 2015; Mu et al., 2014; Wu et al., 2012), where linear regression analyses were employed to establish relationships between characteristics of metals and acute/chronic toxicities (log-LC_{50}, log-EC_{50} or log-NOEC) to eight families of selected organisms; the SSD approach was then performed to determine the water quality guidelines. However, there are still challenges in predicting the chronic WQC for metals in saltwater. First, marine ecosystems cover much broader trophic levels than do freshwater ecosystems, making it more difficult to select organisms that are typical, representative and sufficiently sensitive to be protective. Second, speciation and biosorption of metals in saltwater are more complex. Thus, it can be hard to find accurate descriptors. Third, only rarely are chronic experimental data published in the open literature.

This study attempted to predict the CCCs of metal ions for protection of marine life. Eight representative organisms (six phyla) with sufficient toxicity data were selected for deriving numerical WQC under the framework recommended by the U.S. EPA. The toxicity prediction model involves one input variable that describes the characteristics of metal ions. Chronic toxicities and CCCs were predicted by QICAR-SSDs. To validate predicted CCCs, they were compared with values recommended by the U.S. EPA. The QICAR-SSD model can be an alternative method to derive scientifically defensible WQC for metals for marine organisms and to conduct ecological risk assessment for which little or no empirical values are available.

2. Materials and methods

2.1. Modeling dataset

The chronic toxicity data used in the present study were taken from published literature (Table A.1). According to the U.S. EPA WQC guidelines, a minimum of eight species (three phyla) were required. Specific data screening rules are as follows: (1) All species selected here inhabit North America; (2) The toxicity data of at least five metals are available for each organism; (3) Chronic tests should cover an entire generation or reproductive life cycle. However, exposures during early, sensitive life stages of an organism are also included at times. However, those with mortality >20% in the control sample will be considered invalid; (4) All the toxicity tests should strictly follow the standard methods.

Eight marine species belonging to six phyla were used in this study, including an Echinoderm (*Paracentrotus lividus*), an Arthropod (*Americamysis bahia*), two Annelids (*Ctenodrilus serratus*, *Ophryotrocha diadema*), two Mollusks (*Ilyanassa obsolete*, *Mercenaria mercenaria*), a Chordate (*Cyprinodon variegatus*) and an Ochrophyte (*Skeletonema costatum*). Results of chronic toxicity tests were reported as NOEC, LOEC or MATC. However, considering the scarcity of chronic data, EC_{10} (effective concentration at 10% inhibition) of Ni^{2+} for *Cyprinodon variegatus* and *Skeletonema costatum* were converted into NOEC, by use of previously reported procedures (Durán and Beiras, 2013; Sijm et al., 2002).

2.2. Characteristics of metals and development of predictive relationships

There were 21 physicochemical characteristics of metal ions considered, involving atomic number (AN), atomic weight (AW), atomic radius (AR), Pauling ionic radius (r), ionic charge (Z), ionization potential (ΔIP), standard reduction-oxidation potential (ΔE_0), Pauling electronegativity (X_m), first-order hydroxide complex stability constant (log-$K_1(OH^-)$), logarithmic value of first hydrolysis constant (|log-K_{OH}|), covalent index ($X_m^2 r$), polarization force parameters (Z/r, Z/r^2 and Z^2/r), atomic ionization potential ($AN/\Delta IP$), softness index (σ_p), AR/AW radio, logarithmic value of the largest stability constant of complexes formed between the metal ion and EDTA, CN^- and SCN^- (log-β_n), relative softness (Z/rx) and similar polarization force parameters (Z/AR, Z/AR^2).

For each species, correlation analyses were conducted to investigate relationships between data on chronic toxicity and each characteristic of metals. The magnitude of association was tested using the F-statistic, with the level of significance set to $\alpha = 0.05$. Characteristics with the greatest predictive power were adopted to establish the predictive equations by a linear regression. The predictive potential of QICAR models were evaluated using the adjusted coefficient of determination ($Adj.r^2$), residual sum of squares (RSS), F value from the analysis of variance (ANOVA) and the p value. Meanwhile, internal validation (leave-one-out cross-validation, LOO_{CV}) was performed to assess robustness of predictive models and to limit over-fitting. Under leave-one-out cross-validation, N (the number of data points in the toxicity set) models were trained, each on a different combination of N-1 data points and tested on the remaining datum. The cross-validated correlation coefficient Q^2_{CV}, the sum of squared differences between observed and predicted toxicity, and the difference between r^2 and Q^2_{CV} were used as indicators for judging predictive power of models, with recommended reference criteria of $Q^2_{CV} > 0.6$ and r^2-$Q^2_{CV} \leq 0.3$ (Eriksson et al., 2003).

2.3. SSD construction and HC_5 derivation

Chronic toxicities of each ion to eight representative organisms were predicted from QICAR equations and sorted in ascending order. Cumulative probabilities were then calculated for various species (Eq. (1)).

$$\text{cumulative probability} = (\text{rank}–0.5)/\text{number of species} \tag{1}$$

A Gumbel logistic approach (Gumbel, 1961; Gumbel, 1960) (Eq. (2)) was adopted for fitting functions for development of SSDs with the predicted log-C as the independent variable, while the cumulative probability was the dependent variable. Subsequently, the HC_5 of each metal ion, defined as the concentration to protect 95% species from hazard, was determined by the corresponding SSD equation and taken as the criteria continuous concentration (CCC) (Mu et al., 2014).

$$y = 1-e^{-e^{-\frac{x-a}{b}}} \tag{2}$$

3. Results and discussion

3.1. Predicting chronic toxicities of metals to eight marine organisms

Positive or negative relationships between the logarithmic value of the chronic toxic concentration (log-C) and 21 metal characteristics for each representative species were observed. Six descriptors, X_m, log-

β_n, log-$K_1(OH^-)$, |log-K_{OH}|, AR/AW and σ_p, exhibited the best associations with toxicities to the organisms. Values of these characteristics of 21 metal ions are summarized (Table A.2). Tests of significance and cross-validation of regression models confirmed that all of the predictive equations were satisfactory, with $Adj.r^2 > 0.8$ ($F > 19.455$, $p < 0.022$), $Q^2_{LOO} > 0.635$ and r^2-$Q^2_{LOO} < 0.244$ (Table 1).

The logarithmic value of the chronic toxic concentration of metals to *Paracentrotus lividus* was significantly and negatively correlated with Pauling electronegativity (X_m) with an adjusted coefficient of determination ($Adj.r^2$) of 0.988 ($F = 334.060$, $p = 3.573 \times 10^{-4}$) (Fig. 1(*a*)). Since there is an increasing trend of electronegativity within a period from left to right, this finding is consistent with the fact that transition and post-transition metals generally demonstrate stronger biological toxicity than alkaline earth metals or alkali metals. The parameter of log-β_n exhibited significant, negative correlations with log-C for *Ilyanassa obsoleta* and *Cyprinodon variegatus* ($Adj.r^2 = 0.925$, $F = 50.366$, $p = 0.006$ and $Adj.r^2 = 0.893$, $F = 34.224$, $p = 0.010$, respectively) (Fig. 1(*b*) and 1(*c*)). Previously, there were no QICARs available using log-β_n as a single independent variable for marine species. However, combinations of log-β_n and σ_p and log-β_n and |log-K_{OH}| have been confirmed to best modeled acute toxicities of metal ions to freshwater species (Wu et al., 2012). The magnitude of log-β_n reflects the tendency toward formation of a complex between a metal ion and ligands (EDTA, CN^- and SCN^-) and gives a quantitative measure of the binding affinity of a metal with the O-donor group. The most predictive characteristics of ions for two Annelids (*Ophryotrocha diadema* and *Ctenodrilus serratus*) were log-$K_1(OH^-)$ ($Adj.r^2 = 0.974$, $F = 151.279$, $p = 0.001$) and |log-K_{OH}| ($Adj.r^2 = 0.930$, $F = 53.955$, $p = 0.005$), respectively (Fig. 1(*d*) and 1(*e*)), which suggests that a hydroxyl group (−OH) may mediate toxicity of metals to organisms. Free ions may combine with –OH on the surface of cell membrane and thus affect the permeability and fluidity. Log-$K_1(OH^-)$ represents the formation constant (or stability constant) of the first-order coordination of a ligand L to a metal M to form a complex ML, while the constant for the first hydrolysis (|log-K_{OH}|) describes the attraction of the metal ion to the electron cloud of its water hydration. The connection between log-$K_1(OH^-)$ and |log-K_{OH}| is discussed and shown in the Supplementary data.

The ratio between atomic radius and atomic weight AR/AW, which is a measure of an ion's electron density, exhibited the greatest correlation with the potency of metals to cause toxicity in marine algae (*Skeletonema costatum*), with $Adj.r^2 = 0.822$ ($F = 19.455$, $p = 0.022$) (Fig. 1(*f*)). This is consistent with results of other studies, which found that the AR/AW-form of the predictive equation provided the best fit to metal toxicities for algae (Wolterbeek and Verburg, 2001). For the mollusk (*Mercenaria mercenaria*) and the crustacean (*Americamysis bahia*), strong, positive correlations were obtained between softness index (σ_p) and log-C, with $Adj.r^2 = 0.991$ ($F = 453.562$, $p = 2.265 \times 10^{-4}$) and 0.812 ($F = 26.913$, $p = 0.004$), respectively (Fig. 1(*g*) and 1(*h*)). This is in agreement with experimental observations reported in the literature. For instance, a negative correlation has been reported between σ_p and the percentage of injected metal bound to mollusk hemolymph proteins. That is, softer metals such as Cd^{2+} and Zn^{2+} are bound more stably to plasma proteins than are the harder metals Mn^{2+} and Ca^{2+} (Howard and Simkiss, 1981). Additionally, results of a previous study confirmed that acute toxicities of metals to *Americamysis bahia* were inversely associated with σ_p (Chen et al., 2015). The σ_p is derived from the hard and soft acid and bases theory (HSAB theory) and regarded as a measure of the degree of difficulty for a metal ion to give up its valence electrons (Jones and Vaughn, 1978; Williams and Turner, 1981). Three characteristics, X_m, log-β_n and log-$K_1(OH^-)$, were demonstrated to be significantly and negatively correlated with the log-C of four representative marine organisms, while positive relationships were established for the other species using |log-K_{OH}|, AR/AW and σ_p as descriptors.

3.2. SSD analysis and derivation of predicted CCCs in saltwater

Based on the QICAR equations derived, chronic toxicities of 21 metal ions to each representative organism were predicted (Table A.3). The planktonic algae *Skeletonema costatum* was found to be sensitive to the majority of 21 metal ions, except for Be^{2+}, Mg^{2+} and Al^{3+}. In particular, it appeared most vulnerable to Mn^{2+}, Co^{2+}, Cd^{2+}, Hg^{2+} and Sn^{2+}, which are group VIIB, VIII, IIB and IVA metals. This is consistent with results of a previously reported study, in which algae was demonstrated to be more sensitive (especially to Hg^{2+} and Pb^{2+}) than most phyla (Kong et al., 2011). *Americamysis bahia* exhibited sensitivity to Zn^{2+} and Hg^{2+} in this study. Alternatively, Zn^{2+} can cause a decrease in chitinase activity of crustaceans and inhibit reproduction. Alternatively, it might contribute to lesser stability of the lysosome membrane of the crustacean and subsequently cause cell damage (Koukouzika and Dimitriadis, 2005; Poynton et al., 2007). Hg^{2+} might affect transportation of calcium (Ca) during proecdysis and postecdysis of crustacean, which could affect calcification and decalcification of the exoskeleton (Rodŕiguez Moreno et al., 2003). However, here, *Cyprinodon variegatus* was considered to be relatively tolerant to Hg^{2+}. This is consistent with the finding that fish have repair mechanisms for tissue damage caused by mercury exposure (de Oliveira Ribeiro et al., 2002; Ribeiro et al., 2000). Overall, toxicities of metals predicted by QICAR approach were consistent with empirical results and thus can be used for development of SSDs.

SSDs were fitted using the Gumbel logistic model supported by OriginPro 8.5 (OriginLab, Northampton, MA, USA) software based on the predictive toxicities of metal ions to eight representative organisms (Fig. 2). All regression equations were demonstrated to be satisfactory, with p values of the significance test being $<5.731 \times 10^{-5}$ ($Adj.r^2 > 0.862$, $F > 100.374$). The HC_5 calculation ensued to determine CCC values. Table A.4 presents log-HC_5 values of 21 metal ions, from which it can be concluded that the chronic toxicities generally ranked in the descending order post-transition metals > transition metals > alkaline earth metals. Bi^{3+}, Sn^{2+}, Ag^+, As^{3+}, Hg^{2+}, In^{3+} and Fe^{3+} showed quite strong toxicities, with log-HC_5 values ranging from −3.84 to −2.255, while Mg^{2+}, Ca^{2+} and Mn^{2+} posed the least toxic potencies, with log-HC_5 values of 1.228, 1.019 and 0.348, respectively; those in-between were Ti^{3+}, Cr^{3+}, Co^{2+}, Pb^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Al^{3+} and Zn^{2+}, etc.

Table 1
One-variable regression models based on six characteristics of metal ions X_m, log-β_n, log-$K_1(OH^-)$, |log-K_{OH}|, AR/AW and σ_p, where $Adj.r^2$ is the adjusted coefficient of determination, p is the statistical significance level, and Q^2_{LOO} is the cross-validation correlation coefficient.

Species	Phylum	Predicting equations	n	$Adj.r^2$	F	p	Q^2_{LOO}	r^2-Q^2_{LOO}
Paracentrotus lividus	Echinodermata	$\text{log-C} = (-6.247 \pm 0.342)X_m + (11.534 \pm 0.629)$	5	0.988	334.060	3.573×10^{-4}	0.981	0.010
Americamysis bahia	Crustacean	$\text{log-C} = (41.155 \pm 7.933)\sigma_p + (-4.383 \pm 0.803)$	7	0.812	26.913	0.004	0.635	0.208
Ctenodrilus serratus	Annelida	$\text{log-C} = (0.336 \pm 0.046)\lvert\text{log-}K_{OH}\rvert + (-1.922 \pm 0.342)$	5	0.930	53.955	0.005	0.738	0.209
Ophryotrocha diadema	Annelida	$\text{log-C} = (-0.189 \pm 0.015)\,\text{log-}K_1(OH^-) + (1.765 \pm 0.098)$	5	0.974	151.279	0.001	0.919	0.062
Ilyanassa obsolete	Mollusca	$\text{log-C} = (-0.290 \pm 0.041)\,\text{log-}\beta_n + (5.494 \pm 0.704)$	5	0.925	50.366	0.006	0.700	0.244
Mercenaria mercenaria	Mollusca	$\text{log-C} = (29.868 \pm 1.402)\sigma_p + (-2.014 \pm 0.148)$	5	0.991	453.562	2.265×10^{-4}	0.976	0.017
Cyprinodon variegatus	Chordata	$\text{log-C} = (-0.228 \pm 0.039)\,\text{log-}\beta_n + (4.845 \pm 0.532)$	5	0.893	34.224	0.010	0.767	0.152
Skeletonema costatum	Ochrophyta	$\text{log-C} = (124.161 \pm 28.149)\frac{AR}{AW} + (-3.314 \pm 0.605)$	5	0.822	19.455	0.022	0.666	0.200

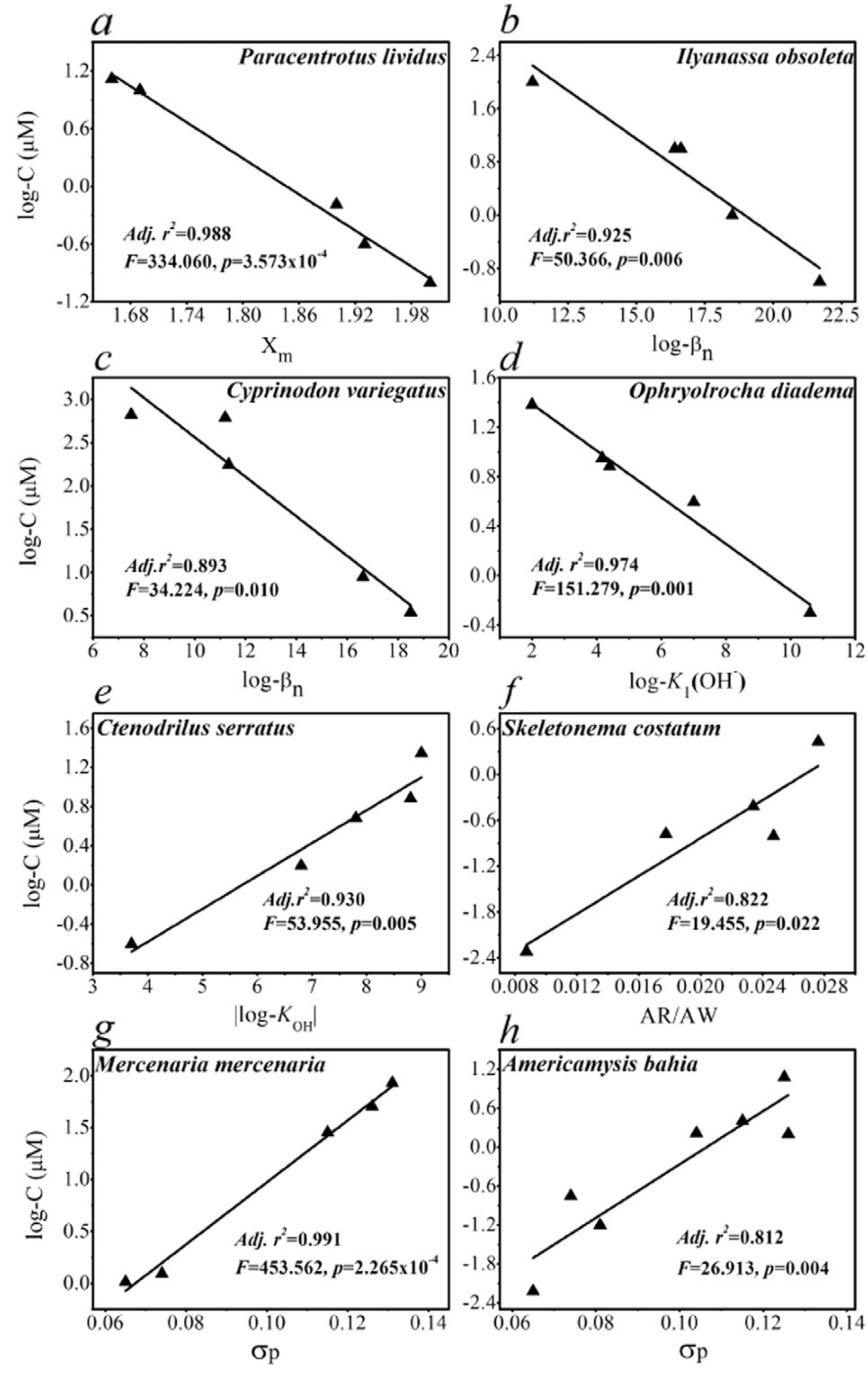

Fig. 1. Regression models of log-C and the six most predictive characteristics of metal ions for eight model organisms.

A comparison was made between the chronic HC_5 obtained in this study and the acute values drawn from previous work (Chen et al., 2015). There was an increasing trend in both acute and chronic toxicities of metal ions from left to right in the periodic table. However, noteworthy differences also existed between them: (1) Cd^{2+} was considered to be highly toxic during a short-term exposure, whereas it showed small long-term adverse effects for marine organisms. (2) In contrast, Be^{2+} had weakly acute toxicities, but relatively significant risk of chronic effect. (3) For the intermediate (or borderline) metals, defined based on the bond stability with various ligand donor atoms, such as O, N and S (Nieboer and Richardson, 1980), chronic toxicities decreased in the order: As^{3+}>In^{3+}>Cr^{3+}>Co^{2+}>Pb^{2+}>Ni^{2+}>Cu^{2+}-+ > In^{3+} > Cr^{3+} > Co^{2+} > Pb^{2+} > Ni^{2+} > Cu^{2+} > Cd^{2+} > Zn^{2+}, while the order of acute toxicity was: Cd^{2+} > In^{3+} > Cu^{2+} > As^{3+} > Cr^{3+} > Zn^{2+} > Ni^{2+} > Co^{2+} > Pb^{2+}.

3.3. Comparison of predicted CCCs and those recommended by the U.S. EPA

To evaluate the predictive capacity of the QICAR-SSD model, predicted CCCs were compared with values recommended by the U.S. EPA for seven metals or metalloids: Hg^{2+}, As^{3+}, Cu^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+} and Zn^{2+}. As for Cr^{6+} (hexavalent chromium) and Se (selenium), predicted

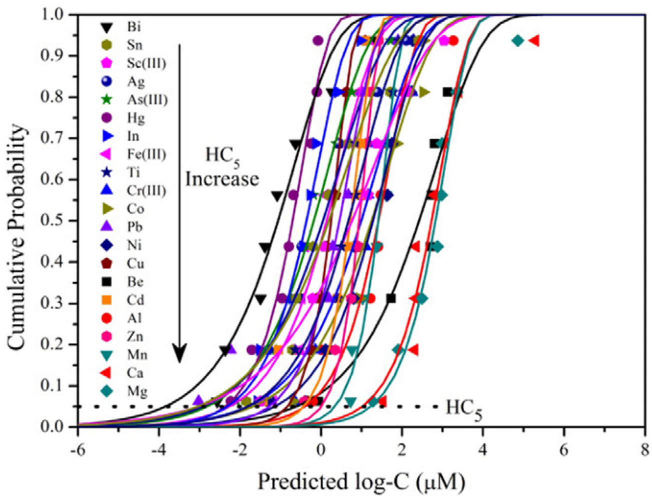

Fig. 2. Species sensitivity distribution analyses and derivation of the predicted log-HC_5 based on the QICAR regressions for 21 metals.

toxicities were missing, because there was insufficient information on certain descriptors. Errors in prediction between predicted values and recommended values were less than a factor of 10, except for As^{3+} (Fig. 3). Discrepancies between recommended values and those predicted by use of the QICAR-SSD model, were mainly caused by different data sources and experimental conditions, including pH, temperature, salinity, dissolved oxygen, etc. The geochemical properties of the saltwater influenced metal speciation, migration and transformation and metabolism of organisms, which might affect toxicities of metal ions. For instance, the toxicities of Cr^{6+} to three invertebrates (*Corophium volutator*, *Macoma balthica* and *Nereis diversieolor*) were greater at higher temperatures (Bryant et al., 1984). Absorption of Cd and Zn by *Mytilus edulis* increased by 150% with a decrease in salinity from 34% to 15% (Wang et al., 1996). However, because detailed and complete descriptions of water geochemical properties in the chronic toxicity tests cited in this study were not provided, it was not possible to quantify effects of these factors on metal toxicities or make corrections.

The predicted CCC for As^{3+}, which was0.118 μg/L, was 300-fold less than that recommended (36 μg/L) by the U.S. EPA. Predicted toxicities of As^{3+} for *Skeletonema costatum*, *Ophryolrocha diadema* (log-C = −1.110 and −0.939, respectively) and *Ctenodrilus serratus*, *Ilyanassa obsolete* (log-C = −0.318 and −0.186, respectively) were similar. This at least

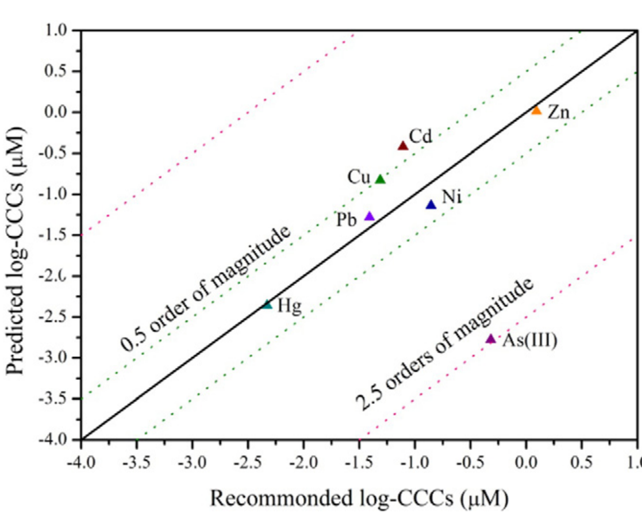

Fig. 3. Comparison between predicted log-HC_5 and the recommended values derived from WQC.

partially accounted for the deviation between predicted CCC and the recommended value. In addition, as a metalloid element, As^{3+} has a relatively high electronegativity. Overestimation might occur when deriving its toxicity by use of a QICAR model with electronegativity as the only independent parameter in the model.

4. Conclusions

This study extended the QICAR-SSD, developed previously for freshwater, to predict CCCs of metal ions for protecting marine life. Relationships between the physicochemical properties of metals and their chronic toxicities (log-C) to marine organisms were investigated. CCCs for 21 metals or metalloids were determined by use of SSD analysis, based on toxicity data derived from QICAR models, and were then compared with the values recommended by the U.S. EPA with satisfactory results except for As^{3+}. However, considering the complexity of interaction of metals with organisms and the multiplicity of influence factors, there still remain some issue that require improvement: (1) Further studies are needed to clarify the toxic mechanisms, which might be diverse among species. (2) The water geochemical properties should be taken into consideration to reduce the uncertainty of the model. One way to do this would be to use chemical activities instead of concentrations for measuring exposure of marine organisms to metals or metalloids. (3) Scope of the application of QICAR models needs to be discussed and how they should be used debated by managers. (4) More data on toxicities to marine organisms, especially chronic toxicity to non-lethal, apical endpoints such as growth and reproduction, are needed to develop more robust prediction models.

Conflicts of interest

The authors declare no competing financial interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.marpolbul.2017.02.055.

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Appendix A. Supplementary Data

Table A.1.

Summary of the chronic data for representative saltwater organisms exposed to metal ions

Species	Ions	Exposure duration	Endpoint	Chronic Values(μM)	Reference
Paracentrotus lividus	Ag^{+}	3d	LOEC	0.250	(Warnau, Temara et al. 1996)
	Cd^{2+}			10.0	
	Cu^{2+}			0.500	
	Hg^{2+}			0.100	
	Cu^{2+}	2d	NOEC	0.798	(Manzo 2004)
	Cr^{6+}			13.1	
Americamysis bahia	As^{3+}	29-51d	LOEC	11.9	(Lussier, Gentile et al. 1985)
	Cu^{2+}			1.64	
	Hg^{2+}			0.006	
	Ni^{2+}			1.59	
	Zn^{2+}			2.54	
	Ag^{+}			0.176	
	Cd^{2+}			0.063	
Ctenodrilus serratus	Cd^{2+}	21d	LOEC	22.2	(Reish and Carr 1978)
	Cu^{2+}			1.57	
	Cr^{6+}			0.962	
	Hg^{2+}			0.249	
	Pb^{2+}			4.83	
	Zn^{2+}			7.65	
Ophryolrocha diadema	Cd^{2+}	21d	LOEC	8.90	(Reish and Carr 1978)
	Cr^{6+}			19.2	
	Cu^{2+}			3.93	
	Pb^{2+}			24.1	
	Hg^{2+}			0.499	
	Zn^{2+}			7.65	
Ilyanassa obsolete	Hg^{2+}	11d	LOEC	0.100	(Conrad 1988)
	Cu^{2+}			1.00	
	Zn^{2+}			10.0	

	Cd^{2+}			10.0	
	Cr^{3+}			100	
Cyprinodon variegatus	Cd^{2+}	7d	LOEC	6.67	(Hutchinson, Williams et al. 1994)
	Cr^{6+}			462	
	Cu^{2+}			2.52	
	Mo^{6+}	28d		666	(Heijerick, Regoli et al. 2012)
	Ni^{2+}	28d	EC_{10}	354	(DeForest and Schlekat 2013)
Skeletonema costatum	Cu^{2+}	15d	LOEC	0.157	(Jensen, Rystad et al. 1976)
	Zn^{2+}	15d		0.382	(Jensen, Rystad et al. 1974)
	As^{5+}	8d		0.167	(Sanders 1979)
	Pb^{2+}	11d		0.005	(Rivkin 1979)
	Ni^{2+}	3d	EC_{10}	5.39	(DeForest and Schlekat 2013)
Mercenaria mercenaria	Hg^{2+}	2d	NOEC	0.012	(Calabrese and Nelson 1974)
	Ag^{+}			0.093	
	Zn^{2+}			1.45	
	Ni^{2+}			1.70	
	Pb^{2+}			1.93	

Table A.2.

Physicochemical properties of 21metals in the QICAR predictive model

Metals ions	$\lvert \log\text{-}K_{OH} \rvert$ [a]	σp [b]	X_m [c]	log-β_n [d]	AR/AW [e]	log-$K_1(OH^-)$ [f]
Be^{2+}	6.2	0.172	1.57	9.3	0.155	9.7
Al^{3+}	5.1	0.136	1.61	14.11	0.053	9.27
Cr^{3+}	3.8	0.107	1.66	11.2	0.036	10.1
Mn^{2+}	10.6	0.125	1.55	14.2	0.033	3.9
Fe^{3+}	2.2	0.097	1.83	15.77	0.023	11.87
Co^{2+}	8.9	0.13	1.88	10.2	0.021	4.3
Ni^{2+}	10.6	0.126	1.91	11.33	0.028	4.97
Cu^{2+}	6.8	0.104	1.9	18.5	0.025	7
Zn^{2+}	8.8	0.115	1.65	16.4	0.023	4.4
As^{3+}	4.78	0.125	2.18	19.6	0.018	14.33
Ag^{+}	12	0.074	1.93	20.6	0.016	2
Cd^{2+}	9	0.081	1.69	16.62	0.015	4.17
Hg^{2+}	3.7	0.065	2	21.7	0.009	10.6
Pb^{2+}	7.8	0.131	2.33	18.3	0.009	7.82
Bi^{3+}	1.6	0.113	2.02	27.8	0.008	12.7
Ca^{2+}	12.7	0.181	1	11	0.049	1.3
In^{3+}	4.4	0.1	1.78	24.37	0.015	10
Mg^{2+}	11.4	0.167	1.31	8.64	0.066	2.58
Sc^{3+}	5.1	0.14	1.36	24.13	0.036	8.9
Sn^{2+}	3.9	0.148	1.96	18.3	0.012	10.4
Ti^{3+}	2.2	0.127	1.54	17.5	0.031	12.71

[a] From the literature reported by J.D. Walker and M.C. Newman, *Fundamental QSARs for metal ions*, (Boca Raton: CRC Press, 2012); and C.F. Baes and R.E. Mesmer, *The hydrolysis of cations*, (New York: John Wiley, 1976).

[b] Data from R.G. Pearson and R.J. Mawby. "The nature of metal-halogen bonds." *Halogen Chemistry.* 3: 55-84.

[c] Adapted from L. Pauling. "The nature of the chemical bond. IV. The energy of single bonds and the relative electronegativity of atoms." *J. Am. Chem. Soc.* 54(9): 3570-3582.

[d] Appeared in F. Wu and Y. Mu. "Predicting water quality criteria for protecting aquatic life from physicochemical properties of metals or metalloids." *Environmental Science & technology*. 47(1): 446-453.

[e] Derived from calculation, where AR represented the atomic radius, AW the atomic weight.
[f] Available online at http://www.hxu.edu.cn/partwebs/huaxuexi/qt/hxsj/cutable2-1.htm.

Table A.3.

Predicted chronic toxicities (log-NOEC) of 21 metal ions to eight representative organisms (μM)

Metal ions	*Paracentrotus lividus*	*Americamysis bahia*	*Ctenodrilus serratus*	*Ophryotrocha diadema*	*Ilyanassa obsolete*	*Mercenaria mercenaria*	*Cyprinodon variegatus*	*Skeletonema costatum*
Be^{2+}	1.727	2.696	0.159	-0.065	2.799	3.123	2.725	15.978
Al^{3+}	1.478	1.214	-0.210	0.016	1.405	2.048	1.628	3.267
Cr^{3+}	1.165	0.021	-0.647	-0.141	2.248	1.182	2.291	1.104
Mn^{2+}	1.852	0.762	1.636	1.029	1.379	1.719	1.607	0.731
Fe^{3+}	0.103	-0.391	-1.184	-0.475	0.924	0.883	1.249	-0.513
Co^{2+}	-0.209	0.967	1.065	0.954	2.538	1.869	2.519	-0.680
Ni^{2+}	-0.397	0.803	1.636	0.827	2.210	1.749	2.262	0.113
Cu^{2+}	-0.334	-0.103	0.361	0.444	0.132	1.092	0.627	-0.247
Zn^{2+}	1.228	0.350	1.032	0.935	0.741	1.421	1.106	-0.409
As^{3+}	-2.083	0.762	1.196	-0.939	-0.186	1.719	0.376	-1.110
Ag^{+}	-0.521	-1.337	2.106	1.388	-0.476	0.196	0.445	-1.300
Cd^{2+}	0.978	-1.049	1.099	0.978	0.677	0.405	1.056	-1.425
Hg^{2+}	-0.959	-1.708	-0.680	-0.235	-0.795	-0.073	-0.103	-2.225
Pb^{2+}	-3.020	1.009	0.696	0.289	0.190	1.899	0.673	-2.235

Bi^{3+}	-1.084	0.268	-1.385	-0.632	-2.563	1.361	-1.493	-2.363
Ca^{2+}	5.288	3.066	2.341	1.520	2.306	3.392	2.337	2.789
In^{3+}	0.416	-0.267	-0.445	-0.122	-1.569	0.973	-0.711	-1.508
Mg^{2+}	3.352	2.490	1.905	1.278	2.990	2.974	2.875	4.858
Sc^{3+}	3.039	1.379	-0.210	0.086	-1.499	2.167	-0.657	1.160
Sn^{2+}	-0.709	1.708	-0.613	-0.198	0.190	2.406	0.673	-1.850
Ti^{3+}	1.915	0.844	-1.184	-0.633	0.422	1.779	0.855	0.499

Table A.4.

SSD fitting, derivation of criteria continuous concentrations (CCCs) for 21 metals or metalloids and comparison with WQC recommended by the U.S. EPA in 2009 (μg/L)

Metal ions	*a*	*b*	*a-SE*	*b-SE*	*Adj.r*^{2}	*RSS*	*F*	*p*	log-HC_5	AW	CCCs	WQC
Be^{2+}	2.846	1.164	0.143	1.164	0.912	0.049	158.891	1.527×10^{-5}	-0.610	9.012	2.212	—
Al^{3+}	1.674	0.698	0.074	0.698	0.942	0.033	241.357	4.501×10^{-6}	-0.397	26.98	10.815	—
Cr^{3+}	1.387	1.075	0.127	1.075	0.921	0.044	176.275	1.129×10^{-5}	-1.808	52.00	0.809	—
Mn^{2+}	1.567	0.410	0.038	0.410	0.943	0.032	244.525	4.332×10^{-6}	0.348	54.94	122.430	—
Fe^{3+}	0.476	0.919	0.113	0.919	0.913	0.049	159.292	1.515×10^{-5}	-2.255	55.85	0.310	—

Co^{2+}	1.662	1.126	0.117	1.126	0.937	0.035	223.191	5.663×10^{-6}	-1.683	58.93	1.223	—
Ni^{2+}	1.623	0.930	0.076	0.930	0.958	0.024	335.147	1.711×10^{-6}	-1.139	58.69	4.262	8.2
Cu^{2+}	0.403	0.414	0.033	0.414	0.969	0.018	449.668	7.170×10^{-7}	-0.827	63.55	9.465	3.1
Zn^{2+}	1.077	0.358	0.020	0.358	0.980	0.011	694.428	1.971×10^{-7}	0.013	65.39	67.377	81
As^{3+}	0.193	1.009	0.069	1.009	0.977	0.013	612.509	2.863×10^{-7}	-2.804	74.92	0.118	36
Ag^{+}	0.466	1.140	0.140	1.140	0.936	0.036	217.390	6.117×10^{-6}	-2.921	107.9	0.129	—
Cd^{2+}	0.887	0.440	0.062	0.440	0.863	0.077	100.374	5.731×10^{-5}	-0.419	112.4	42.832	8.8
Hg^{2+}	-0.467	0.637	0.051	0.637	0.958	0.024	331.578	1.766×10^{-6}	-2.358	200.6	0.880	0.94
Pb^{2+}	0.704	0.668	0.085	0.668	0.914	0.048	161.913	1.445×10^{-5}	-1.280	207.2	10.874	8.1
Bi^{3+}	-0.668	1.068	0.130	1.068	0.941	0.033	235.823	4.818×10^{-6}	-3.840	209.0	0.030	—
Ca^{2+}	2.975	0.658	0.077	0.658	0.936	0.036	218.675	6.012×10^{-6}	1.019	40.08	418.724	—
In^{3+}	-0.082	0.748	0.062	0.748	0.967	0.019	421.138	8.708×10^{-7}	-2.304	114.8	0.570	—
Mg^{2+}	3.054	0.615	0.054	0.615	0.958	0.024	335.905	1.700×10^{-6}	1.228	24.31	410.946	—
Sc^{3+}	1.302	1.459	0.115	1.459	0.967	0.018	431.577	8.098×10^{-7}	-3.032	44.96	0.042	—
Sn^{2+}	0.650	1.244	0.146	1.244	0.943	0.032	245.804	4.266×10^{-6}	-3.044	118.7	0.107	—
Ti^{3+}	1.029	0.957	0.098	0.957	0.942	0.032	242.812	4.422×10^{-6}	-1.812	47.87	0.738	—

Supplemental method

The connection between log-$K_1(OH^-)$ and |log-K_{OH}| was derived as follows:

The coordination of a ligand OH^- to a metal M (hydrated ion) to form the first complex M(OH), could be written as:

$$[M(H_2O)_n] + OH^- \rightleftharpoons [M(OH)(H_2O)_{n-1}] + H_2O \quad (1)$$

The stability constant $K_1(OH^-)$ for this reaction is given by:

$$K_1(OH^-) = [M(OH)(H_2O)_{n-1}][\ H_2O]/[\ M(H_2O)_n][OH^-] \quad (2)$$

It can be simplified as:

$$K_1(OH^-) = [M(OH)]/[M][OH^-] \quad (3)$$

The first hydrolysis step of the hydrated ions can be represented by the reaction:

$$[M(H_2O)_n^{m+}] + H_2O \rightleftharpoons [M(OH)(H_2O)_{n-1}{}^{(m-1)+}] + H_3O^+ \quad (4)$$

The equilibrium constant K_{OH} is:

$$K_{OH} = [M(OH)(H_2O)_{n-1}{}^{(m-1)+}][H_3O^+]/[M(H_2O)_n^{m+}][H_2O] \quad (5)$$

This expression can be simplified as:

$$K_{OH} = [M(OH)][H^+]/[M] \quad (6)$$

$$K_{OH} = [M(OH)]K_w/[M][OH^-] \quad (7)$$

where the K_w represents the ion product of water:

$$K_w = [H^+][OH-] \quad (8)$$

According to above equations, it can be concluded that:

$$K_{OH} = K_1(OH^-)\cdot K_w \quad (9)$$

$$\text{log-}K_{OH} = \text{log-}K_1(OH^-) + \text{log-}K_w \quad (10)$$