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Modelling the bioconcentration of Zn from commercial sunscreens in the marine bivalve *Ruditapes philippinarum*

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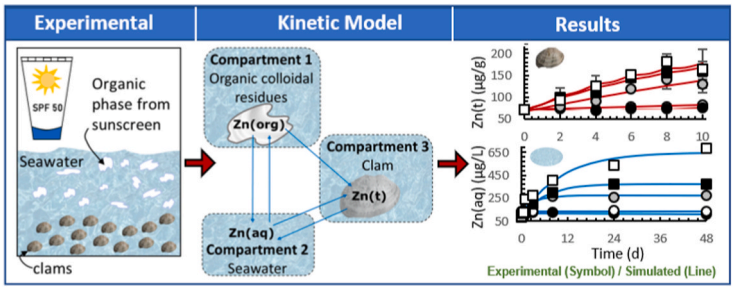
HIGHLIGHTS

- Kinetic model of bioconcentration in clams under varying Zn concentrations
- Sunscreen colloidal residues, seawater and clams as three model compartments
- The model predicts sharp bioaccumulation rates at sunscreen additions up to 200 mg L^{-1}
- Obtained model parameters contribute to ecotoxicological research

GRAPHICAL ABSTRACT



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ABSTRACT

Sunscreens contain ZnO particles used as a UV filter cause adverse effects in the marine environment through the release of this metal into seawater and its bioaccumulation in organisms. A mathematical model using sunscreen colloidal residues, seawater and *R. philippinarum* clams as differentiated compartments, is proposed in order to interpret both the kinetic pattern and the bioaccumulation of Zn in clams. Two kinetic laboratory experiments were conducted, both with and without clams exposed to sunscreen concentrations from 0 to 200 mg L^{-1}. Both the lowest value of uptake rate coefficient obtained when 5 mg L^{-1} of sunscreen is added (0.00688 L g^{-1} d^{-1}) and the highest obtained at sunscreen addition of 100 mg L^{-1} (0.0670 L g^{-1} d^{-1}), predict a lower bioavailability of Zn in a complex medium such as the seawater-sunscreen mixtures, in comparison to those studied in the literature. The efflux rate coefficient from clams to seawater increased from 0 to 0.162 d^{-1} with the sunscreen concentrations. The estimated value of the inlet rate coefficient at all studied concentrations indicates that there is a negligible colloidal Zn uptake rate by clams, probably due to the great stability of the organic colloidal residue. An equilibrium shift to higher values of Zn in water is predicted due to the bioconcentration of Zn in clams. The kinetic model proposed with no constant Zn (aq) concentrations may contribute to a more realistic prediction of the bioaccumulation of Zn from sunscreens in clams.

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1. Introduction

Sunscreens contain many emerging chemicals that could reach the sea and cause adverse ecological effects. Their presence in the marine environment are probably related to the touristic activities and could be evaluated throughout the potential dangers to marine ecology caused by both the organic and inorganic chemical UV filters present in sunscreens (Tovar-Sánchez et al., 2019; Labille et al., 2020). UV filters are released when the product comes into contact with seawater and cause adverse ecological effects in coastal waters (Sánchez-Quiles and Tovar-Sánchez, 2015; Tovar-Sánchez et al., 2020a). ZnO particles (microparticles or nanoparticles-nZnO-) used as UV filter in sunscreen are not stable in the aquatic environment but rather dissociate into its ionic form (de Miranda et al., 2021; Ginzburg et al., 2021). ZnO particles and Zn^{2+} remain in dissolution and some are possibly trapped in the sunscreen complexes (Wong et al., 2020). Several studies identify and evaluate the toxicity and ecotoxicological effects of Zn and nZnO on different aquatic test species (Naasz et al., 2018; Cunningham et al., 2020; Gutierrez et al., 2021; Sellami et al., 2017). It has been suggested that relevant toxicity effects may be induced by both nZnO and Zn^{2+}, highlighting the ion release from nZnO as an important contributor to its toxic effects (Franklin et al., 2007; Lead et al., 2018; Vieira et al., 2021).

Bivalves are considered excellent candidates for use as coastal pollution biomonitors, because they are filter feeders and are exposed to large volumes of water for feeding and respiratory purposes. In these processes, accumulate contaminants in their soft tissues and shells (Sánchez-Marín et al., 2016). Several authors have proposed previously toxikocinetic models to predict the bioaccumulation, biotransformation and toxicity of metals in bivalves (Curis et al., 2009; Sánchez-Marín et al., 2016; Beiras, 2018). Zn bioaccumulation models in clams have been proposed previously (e.g. Lu et al., 2019; O'Mara et al., 2019; Wang and Tan, 2019; Chong and Wang, 2001; Kalman et al., 2014). However, none of these studies which work exclusively with different concentrations of metals, consider the chemical changes in the seawater and the accumulation in organisms due to the addition of a commercial sunscreen. This fact is crucial because the Zn present in solar filters is found initially in its organic matrix, but once the sunscreen is added to the aquatic environment, the Zn is released in the aqueous phase reaching an equilibrium with Zn in stable colloidal residues (Rodríguez-Romero et al., 2019). This process influences the availability of free Zn and its bioaccumulation. Consequently, the changes that are generated in the aqueous medium must be considered. Therefore, the objective of this work is to model the bioaccumulation of Zn in *Ruditapes philippinarum* exposed to different contents of a commercial sunscreen containing ZnO nanoparticles. This bivalve was selected as the test organism in this study according to earlier studies supporting the proposition that *R. philippinarum* could be a useful biomonitor of metal pollution (e.g. Ji et al., 2006; Santana et al., 2017; De Marchi et al., 2017). In order to propose a kinetic model the starting hypothesis of the present work considers the physical-chemical processes of Zn release from the solar protector to seawater and to the organic phase of the sunscreen, as well as the bioaccumulation of Zn in clams. A novel three compartment model with no constant Zn concentrations in water is going to be proposed. Statistical parameters obtained when experimental and simulated values of Zn concentration are compared in parity plots, will be used to check the validity of the model.

2. Materials and methods

2.1. Sunscreen selected

A commercial sunscreen with an SPF of 50, in a cream gel format widely used in Europe and containing zinc oxide (nano) as the inorganic UV filter, was selected to conduct this study. In order to preserve the anonymity of the brand name, the name of the sunscreen is not disclosed.

2.2. Test organism

Clams of the species *Ruditapes philippinarum* with similar biometric characteristics (length 40±2 mm, width 30±2 mm) were supplied by a commercial aquaculture facility (Cetarea de Sur, S. L, Cadiz, Spain) and transported to the aquaculture facilities of the Instituto de Ciencias Marinas de Andalucía (ICMAN-CSIC) in Puerto Real (Spain). The clams were acclimated in aerated and 0.45 μm filtered clean seawater for 1 week to laboratory conditions (temperature: 17.3 °C ±0.2; salinity: 37‰; pH: 7,92 ± 0.07; dissolved oxygen 89 ± 2% of saturation; photoperiod: 12 h:12 h) before starting the experiment. The natural day/night cycle was recreated with light simulating the solar spectrum (OSRAM, COLOR proof T8).

2.3. Kinetic experiments

In order to assess the kinetic Zn release from sunscreen into the seawater and evaluate the role of *R. philippinarum* (via uptake) on the temporal evolution of Zn concentrations in the environment, two independent laboratory experiments were conducted: 1) without clams and 2) with clams exposed to sunscreens (See Fig. 1). In both kinetic experiments, five different quantities of the selected sunscreen in mg L^{-1} (0, 5, 50, 100, 200) were added to 15 L of seawater in 20 L aquariums. All the treatments were performed in duplicate. The exposure aquariums were continuously aerated. In the first experiment (without clams), the 15 mL water series were collected for Zn analysis at selected time periods (between 0 and 48 h exposure). The time intervals selected were: zero (directly after the addition of sunscreen), 0.25, 0.50, 1, 3, 8, 24 and 48 h. The seawater samples were kept in dark conditions until chemical analysis. Sunscreen concentrations and the time intervals for seawater sampling were selected taking into account previous studies on sunscreen kinetic release and toxicity in marine ecosystems (Sendra et al., 2017; Sureda et al., 2018; Rodríguez-Romero et al., 2019; Araújo et al., 2020).

In the second experiment, after the acclimation period, 15 clams were placed in each sunscreen treatment aquarium in mg L^{-1} (0, 5, 50, 100 and 200) for 10 days. The water treatment was renewed every 48 h. Four individual per treatments (two per tank) were sampled periodically on days 0, 2, 4, 6, 8, and 10 and rapidly dissected at above - 4 °C (all steps were performed on ice). Total biological tissues (group from two individuals) were dissected and then immediately stored at −20 °C for Zn analysis. For each clam taken for sampling, another was added to the tank to keep the number of clams/volume of water ratio constant. Only the clams exposed from the beginning of the experiment were sampled for chemical analysis. The exposure conditions (temperature, salinity, pH, photoperiod and seawater) were the same in both kinetic experiments (see section 2.2 test organism).

2.4. Analytical methods: zinc analysis in the sunscreen, seawater and biological tissues

2.4.1. Zn analysis in the sunscreen

The zinc content in the sunscreen selected was analysed in triplicate by inductively coupled plasma mass spectrometry (ICP-MS PerkinElmer ELAN DRC-e) after prior chemical digestion, following the method described by Páscoa et al. (2011). Briefly, 0.15 g of sunscreen were digested with 8 mL of Trace Metals Grade nitric acid at 65% and 2 mL of 40% hydrofluoric acid. The samples were neutralized with 5 mL of 5% boric acid. Acid digestions were assisted by microwave (MARS5; CEM).

The concentration of zinc determined in the commercial sunscreen used in this study was $(9.35 \pm 0.182) \cdot 10^3$ μg kg^{-1}.

2.4.2. Zn analysis in seawater

Dissolved seawater samples for Zn analysis were filtered through a 0.22 μm pore size filter, as it represents the soluble and bioavailability fraction (e.g. Tovar-Sánchez et al., 2020b; Grand et al., 2019; Wang and

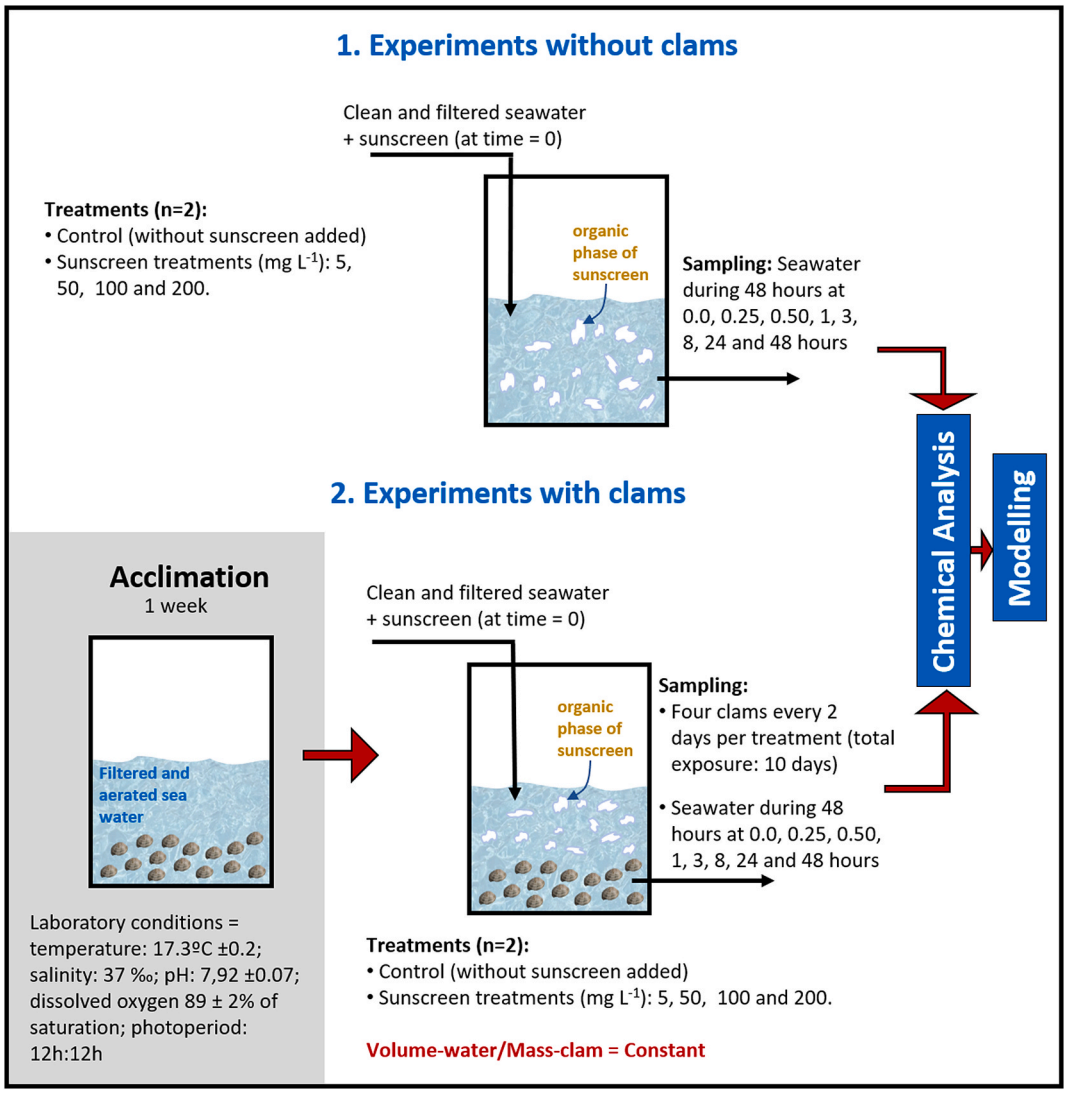

Fig. 1. Schematic diagram of the kinetic experimental design and procedures used in this study.

Liu, 2003). Aliquots (15 mL) were acidified to pH 1.5–2 with 1 M HCl (approximately 1 μL per mL of seawater) before the Zn analysis (Kremling and Brügmann, 1999). In order to decrease the concentration of total dissolved solids and to avoid instrument instability (caused by potential polyatomic interferences during the analysis), the samples were diluted 1:20 (v:v) with Milli-Q water before the determination of Zn using an ICP-MS (Thermo Scientific iCap). All the sampling and analytical operations were carried out in accordance with clean techniques for trace metals. All analyses were measured in duplicate.

2.4.3. Zn analysis in biological tissues

The concentration of Zn was determined following the process described by Amiard et al. (1987). In brief, the organism samples were lyophilized in a freeze dryer (LABCONCO, model 798,030) and subsequently digested (10 mg of sample) with 2 mL HNO_3 using a microwave (MARS5; CEM). The zinc concentration was measured in duplicate by ICP-MS. The accuracy of the Zn analysis in the clam tissues was verified using the following certified reference material: ERM-CE278 – Mussel tissue (Institute for Reference Materials and Measurements, European Commission) with a measured value of 70.8 ± 4.2 μg g^{-1} and a certified value of 71 μg g^{-1}, the recovery obtained was 100%.

2.5. Kinetic model

2.5.1. Kinetic model of Zn release from the sunscreen to seawater

The first column of Fig. 2 shows the kinetic scheme (Fig. 2-Ia) considered to describe the behaviour of Zn release from the sunscreen to seawater, together with the results obtained (Fig. 2-Ib and Fig. 2-Ic).

Sunscreens in seawater are known to form stable colloidal residues that can include macroscopic aggregates, agglomerates, and submicron fractions (Botta et al., 2011; Rodríguez-Romero et al., 2019). Nanoparticles, organic chemicals, and inorganic chemicals in sunscreen formulation can interact through several complex processes at different times and aging conditions (Naasz et al., 2018; Labille et al., 2010; Goswami et al., 2017; Amde et al., 2017). The kinetic scheme shown in Fig. 2-Ia considers that the Zn present in the solar protector is retained in the organic phase of the sunscreen which, once deposited in the seawater, forms colloidal organic residues in equilibrium with the seawater. The release process of Zn from sunscreen in seawater is modelled considering first-order kinetics through an equilibrium reaction (Fig. 2-Ia).

$$\frac{d\ [Zn(org)]}{dt} = -k_1^*\ [Zn(org)] + k_2^*\ LS\ \ [Zn(aq)] \quad (1)$$

$$\frac{d[Zn(aq)]}{dt} = \frac{k_1^*}{LS}[Zn(org)] - k_2^*[Zn(aq)] \quad (2)$$

where [Zn(org)] and [Zn(aq)] are the Zn concentrations in organic colloidal residue and seawater (μg L^{-1}) respectively; k_1^* and k_2^* are rate coefficient of equilibrium release into the seawater from sunscreen (d^{-1}), and LS is the volume-sunscreen mass ratio (L g^{-1}).

The authors, (Rodríguez-Romero et al., 2019), propose a kinetic model to establish the release pattern and the contribution of trace metals and inorganic nutrients from the sunscreen to marine coastal waters in a previous work. They consider that the metals are mainly contained inside the organic material of the sunscreen; subsequently, they are released into the seawater, and finally, after an aging period, they can be adsorbed onto the organic material creating a stable colloidal suspension.

2.5.2. Kinetic model of Zn release from sunscreen and bioaccumulation in the clams

There have been many attempts to develop models to predict the bioaccumulation, biotransformation and toxicity of metals. The bioaccumulation of metals in bivalves can be modelled using toxicokinetic models based on the material balance between influx rate and efflux rate through differential equations that describe the evolution over time (Curis et al., 2009). They combine the uptake of dissolved metals via exposed epithelia (such as gills) and the assimilation of metals from ingested particles into one equation that predicts the concentration of metal in the organism in the steady state (Sánchez-Marín et al., 2016).

Bioaccumulation of Zn in clams from different sources such as that dissolved in water, or in the food and sediment has been previously modelled using mainly a first-order one compartment bioaccumulation model under the well-developed biokinetic model incorporating critical parameters of dissolved uptake, dietary bioavailability and efflux (Beiras, 2018). Lu et al. (2019), establish baseline concentrations of Zn in clams by combined statistical frequency analysis and biokinetic modelling. O'Mara et al. (2019) works with a two compartment (shell and soft tissue) bioaccumulation model; they apply the biokinetic modelling for clams showing that accumulation of Zn is likely to be from the diet in East Australian estuaries of moderate contamination. In the same way, Chong and Wang (2001), highlight that the accumulation of Zn in the clams was dominated by uptake from food ingestion. On the contrary, Chen et al. (2011), propose a two subcellular pool study with the Zn concentration dissolved in water as the only input. Kalman et al. (2014) concludes that dissolved metal is the predominant source of accumulated Zn, in contrast with the input from the sediment, although their relative importance varies with the specific dissolved and sediment concentrations of Zn at each site and with local water and sediment geochemistry.

The second column of Fig. 2 shows the kinetic scheme (Fig. 2-IIa) and the results obtained in the Zn bioaccumulation experiments from sunscreen in clams (Fig. 2-IIb and Fig. 2-IIc) proposed in this work. A three-compartment model was proposed (Fig. 2-IIa) to describe the bioaccumulation kinetics of Zn in clams. This model assumes that once the sunscreen is added to seawater, part of the Zn retained in organic colloidal residues (Compartment 1) is transferred to the seawater (Compartment 2), under an equilibrium reaction. The model also assumes that the Zn from the organic colloidal residues and from the aqueous phase may be transferred to the clams (Compartment 3).

Compartment models generally assume that the transfer between compartments follows first-order kinetics (Barron et al., 1990; Sánchez-Marín et al., 2016; Grech et al., 2017). Therefore, in order to formulate the model, the Zn mass balances are proposed in each compartment, assuming first-order kinetics to describe the inter-compartmental transport of Zn. The differential equations for the organic colloidal residue, seawater and clam compartments are shown in Eqs. (3)–(5) respectively:

$$\frac{d\ [Zn(org)]}{dt} = -k_1\ [Zn(org)] + k_2\ LS\ \ [Zn(aq)] - k_o\ [Zn(org)] \quad (3)$$

$$\frac{d[Zn(aq)]}{dt} = \frac{k_1}{LS}[Zn(org)] - k_2[Zn(aq)] - k_d[Zn(aq)] + \frac{k_e}{LC}[Zn(t)] \quad (4)$$

$$\frac{d[Zn(t)]}{dt} = k_d\ \ LC\ \ [Zn(aq)] + k_o\ \ SC\ \ [Zn(org)] - k_e[Zn(t)] \quad (5)$$

where [Zn(t)] are the Zn concentrations in the organism's tissues (μg g^{-1}); k_1 and k_2 are rate coefficients of the equilibrium release to seawater from sunscreen (d^{-1}), k_o and k_d are the inlet rate coefficients to clams from organic colloidal residue and seawater (d^{-1}) respectively; k_e is the efflux rate coefficients to seawater from clams (d^{-1}), LS is the volume-sunscreen mass ratio (L g^{-1}), LC is the ratio between the seawater volume and the dry tissue mass of clams (g g^{-1}) and SC is the ratio between the mass of sunscreen available and the dry tissue mass of the clams (g g^{-1}).

The uptake rate coefficient k_u, is defined as Eq. (6):

$$k_u = k_d \cdot LC = \ \ k_d \cdot V/Mc \quad (6)$$

where is the volume of seawater (L) and Mc is the dry mass of clams (g). Mc is calculated as the product between the average dry mass of clams (0.38 ± 0.034 g) and the number of clams (n = 15). Both the volume of seawater and the number of clams were kept constant during the experiments, therefore the LC ratio remains constant.

If we consider sunscreen as a food, then the Zn uptake coefficient from the organic colloidal residue from the sunscreen can be expressed as Eq. (7):

$$k_o \cdot SC = IR \cdot AE/Mc \quad (7)$$

where IR is the mass of organic colloidal residue consumed per mass of clam per time and AE is the organic colloidal residue assimilation efficiency in the digestive system.

2.5.3. Modelling

The data obtained from the laboratory experiments were modelled, and the corresponding parameters were calculated using Aspen Custom Modeler software (Bedford, Massachusetts, USA), which solves rigorous models and simultaneously estimates parameters. Furthermore, the Aspen Custom Modeler provides the statistical values that allow us to compare the experimental concentration values with the values from the mathematical model. The correlation coefficient (R^2), standard deviation (σ), coefficient of variation (CV), and relative and absolute error were used to check the validity of the model. This tool has been used previously by the authors to model the release of pollutants from sediments to seawater (Martín-Torre et al., 2016, 2017) as well as to model the release pattern and the contribution of trace metals and inorganic nutrients from sunscreens to coastal marine waters (Rodríguez-Romero et al., 2019). The model's parameters were adjusted using an NL2SOL algorithm for the least-squares minimisation of the deviation between the experimental and theoretical data.

3. Results and discussion

Kinetic experiments were carried out at sunscreen concentrations of 5 mg L^{-1} to 200 mg L^{-1} in seawater, both without the presence of clams and with clams (Fig. 1) to describe the mechanism of Zn release from a sunscreen to seawater and the bioaccumulation of Zn in clams. The kinetic models proposed to interpret the experimental results are shown and discussed in the next subsections.

3.1. Kinetic model of Zn release from the sunscreen to seawater

Aqueous Zn concentrations obtained in the experiments carried out

Table 1
Values of rate coefficients and statistical data for the kinetic modelling of the release of Zn from sunscreen to seawater.

[sunscreen] (mg L^{-1})	Rate coefficients		Ratio k_1^* and k_2^*	Statistical data		
	k_1^* (d^{-1})	k_2^* (d^{-1})	$K^* = \frac{k_1^*}{k_2^*}$	R^2 (%)	σ (μg L^{-1})	CV (%)
5	1.15	0.155	7.39	90.8	3.90	4.36
50	2.01	1.42	1.42	98.0	16.0	8.88
100	1.21	0.905	1.33	97.9	30.1	11.0
200	0.802	0.871	0.920	99.1	32.9	8.01

Table 2
Estimated rate coefficients and statistical data for dynamic modelling of the uptake kinetics of Zn by clams.

		Sunscreen concentration (mg L^{-1})			
		5	50	100	200
Rate coefficients	k_1 (d^{-1})	4.60	3.09	1.47	0.766
	k_2 (d^{-1})	1.10	3.67	2.47	1.52
	k_o (d^{-1})	0	0	0	0
	k_d (d^{-1})	0.00283	0.0168	0.0275	0.0211
	k_e (d^{-1})	0	0.0350	0.122	0.162
	k_u (L g^{-1} d^{-1})	0.00688	0.0409	0.0670	0.0514
Ratio k_1 and k_2	$K = k_1/k_2$	4.18	0.840	0.596	0.502
Statistical data for results in seawater	R^2 (%)	61.0	83.1	98.1	98.0
	σ (μg L^{-1})	4.68	22.9	14.4	26.7
	CV (%)	3.64	11.5	6.95	8.50
Statistical data for results in clams	R^2 (%)	60.2	90.3	97.4	95.4
	σ (μg L^{-1})	2.10	6.35	4.26	6.84
	CV (%)	2.74	6.03	3.45	5.21
Global	R^2 (%)	60.9	84.0	98.1	97.9

without clams are shown in Fig. 2-Ib. The Zn concentration in the water increased sharply during the first 8 h, followed by a slower increase in the concentration until reaching equilibrium. It was observed that the release of Zn into the aquatic environment increased with the amount of sunscreen added. The average concentrations of the eight Zn (aq) concentrations over the time period of 48 h experiments without clams (Fig. 1) when 5 mg L^{-1}, 50 mg L^{-1}, 100 mg L^{-1} and 200 mg L^{-1} of sunscreen are added are respectively in μg L^{-1}: 89.8, 186, 252, 333. The estimated values of the kinetic parameters (k_1^*, k_2^*) and their ratio ($K^* = k_1^*/k_2^*$) obtained from the experimental results, the correlation coefficient (R^2), standard deviation (σ) and coefficient of variation (CV) are shown in Table 1. Curves simulated from the proposed model are shown in Fig. 2-Ib together with the experimental results. Furthermore, the experimental values of the Zn (aq) concentration are represented against the simulated values of the Zn (aq) concentration in a parity plot (Fig. 2-Ic). Both, the statistical data, with R^2 values ranging from 90.8% to 99.1% (Table 1) and the parity plot, where only 3 of the 31 experimental data are more than 20% away from the value estimated by the model proposed, indicate a good correspondence between the experimental and predicted concentrations. The lowest sunscreen addition experiment lead to the lowest R^2 and the lowest CV results too, due to the small variations of the Zn (aq) concentration (86.8–110 μg L^{-1}).

The kinetic rate coefficients k_1^* and k_2^* decrease when added sunscreen concentrations decreases except at the lowest concentrations of 5 mg L^{-1} showing a k_1^*/k_2^* ratio behaviour that satisfy a decreasing power law expression (Fig. 3).

3.2. Kinetic model of bioaccumulation of Zn from sunscreen in clams

Fig. 2-IIb shows the Zn (aq) concentration in the seawater each 48-h water removal cycle in the experiments with clams, showing a behaviour similar to that of the experiments without clams but reaching lower concentrations. The average concentrations of the eight Zn (aq) concentrations over the time period of 48 h experiments with clams (Fig. 1) when 5 mg L^{-1}, 50 mg L^{-1}, 100 mg L^{-1} and 200 mg L^{-1} of sunscreen are added, display results of 84.4 μg L^{-1}, 150 μg L^{-1}, 209 μg L^{-1} and 294 μg L^{-1} respectively.

Fig. 2-IIc shows the graphical representation of the evolution of the Zn(t) concentration over time. The curved lines observed at sunscreen concentrations of 100 mg L^{-1} and 200 mg L^{-1} are due to the variation of the concentration of Zn (aq) with time in each cycle of two days. Time evolution of simulated Zn (aq) concentrations together experimental and simulated concentrations for Zn(t) at four concentrations of added sunscreen are shown in Fig. S1 into the supplementary material.

The concentration of Zn(t) bioaccumulated in the clams exposed to sunscreen, increases over the range of time and concentrations used (Fig. 2-IIc). A similar pattern has been widely demonstrated in laboratory experiments with bivalves, where the metal concentration in the tissue did not reach saturation even with exposure periods of up to two months (Borchardt, 1983; Riisgård et al., 1987; Beiras, 2018; Sánchez-Marín et al., 2011).

The proposed kinetic model (Eqs. (3)–(5)) was applied to the experimental data in order to describe and predict Zn concentration in the water and clams in the sunscreen exposure experiments. The rate coefficients and the statistic values of fitting are presented in Table 2. The parity plots obtained for the validation of the model proposed in terms of the concentrations of Zn (aq) and Zn(t) are shown in Fig. 2-IId and Fig. 2-IIe respectively. The correlation coefficient (R^2) obtained from the experimental and simulated values by the model and taking into account the 52 experimental data is 98%, which indicates that the model proposed describes the bioconcentration of Zn in clams as well as the variation of the Zn concentration in the seawater correctly. The simulated curves from the estimated kinetic parameters are shown in Fig. 2-IIb and Fig. 2-IIc. As in the experiments without clams, the lowest sunscreen addition experiment lead to the lowest R^2 and the lowest CV results too, due to the small variations of the Zn (aq) (122–132 μg L^{-1}) and Zn(t) (70.9–83.0 μg g^{-1}) concentrations.

Table 2 shows the lower rate coefficients at sunscreen concentration of 200 mg L^{-1}. At that concentration, it is visually observed that the clams open less and, consequently, they filter less amount of water probably due to effect of the high concentration of sunscreen in water that lead to high quantity of organic colloidal residue. They protect themselves from the harmful effect caused by the addition of high quantities of sunscreen. At that conditions, the rate coefficients are lower that the obtained at lower sunscreen concentrations.

The seawater used in the experiments has a Zn concentration of 118 ± 10.9 μg L^{-1}. An experiment was carried out, with only seawater, without adding sunscreen. The experimental results are shown in Fig. 2-IIb and Fig. 2. c, obtaining an estimated k_d value of 0.00138 d^{-1}, which is lower than those obtained at the sunscreen concentration of 5 mg L^{-1}, and a value of. $k_e = 0$.

The k ratios obtained in the experiments with clams (Table 2) are lower than those of the k^* ratios obtained in the experiments without clams (Table 1). In both sets of experiments, both ratios decrease through a power law expression with increasing sunscreen concentration (Fig. 3). The power coefficients are similar, which suggests a similar decay rate but reach lower values of k (Table 2) than those of k^* (Table 1) over the range of sunscreen amounts added. This predicts an

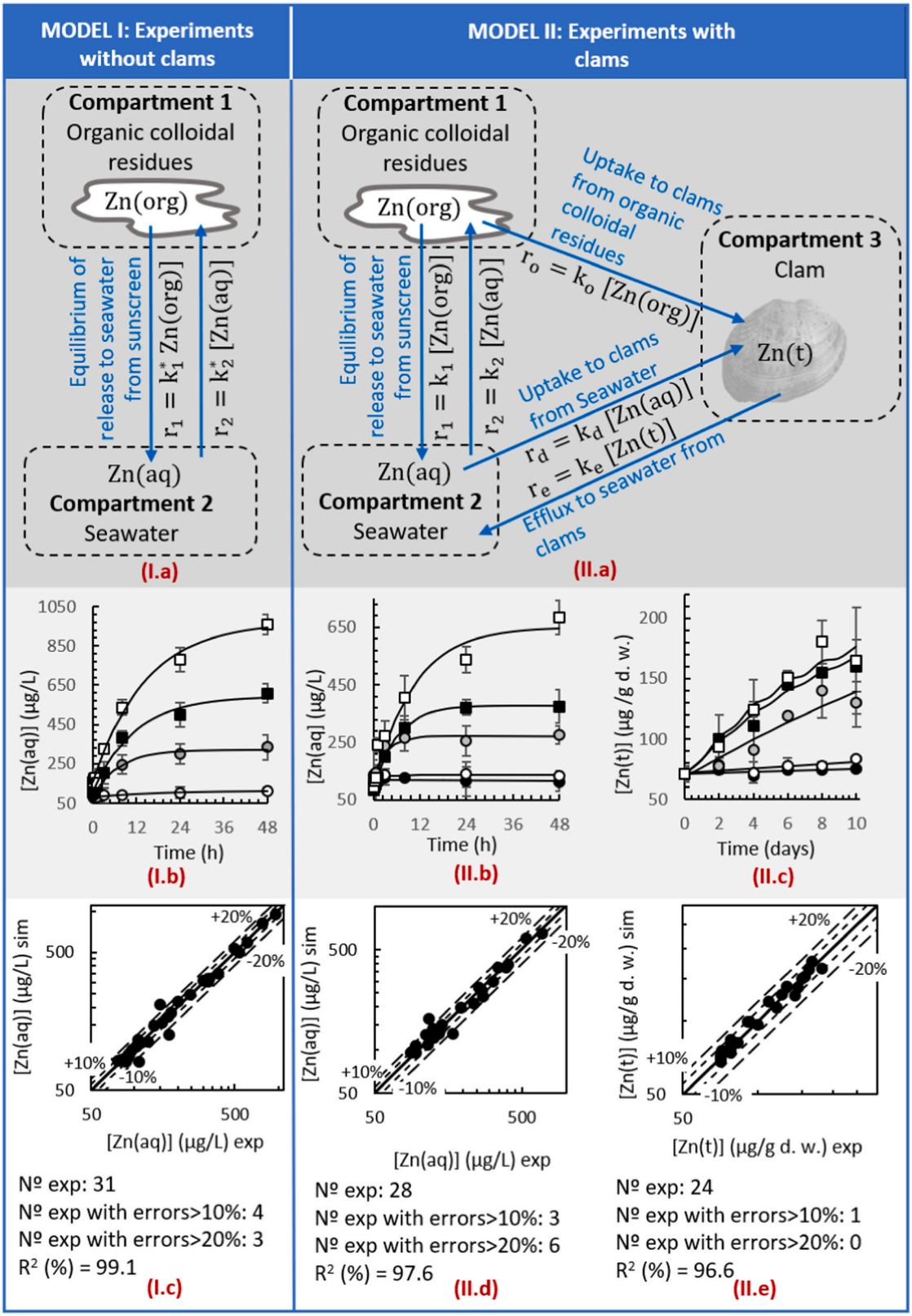

Fig. 2. **(I.a)** and **(II.a)** Kinetic diagram of the compartmental model for the bioaccumulation of Zn from sunscreen. k_1^*, k_2^*, k_1, k_2, k_o, k_d and k_e are the rate coefficients of the kinetic equations 1-5 proposed; **(I.b)** Concentration of Zn (aq) in experiments without clams; **(II.b)** Zn (aq) in experiments with clams; **(II.c)** Zn(t) in experiments with clams: ● 0 mg L^{-1}, ○5 mg L^{-1}, ○50 mg L^{-1}, ■ 100 mg L^{-1}, □200 mg L^{-1}, — simulated curves. Parity plot of the experimental vs. simulated logarithmic concentrations of Zn are showed in **(I.c)** Zn (aq) in experiments without clams, **(II.d)** Zn (aq) in experiments with clams, and **(II.e)** Zn(t) in clam tissues. The data number and percentage variation explained value (R^2) are also shown.

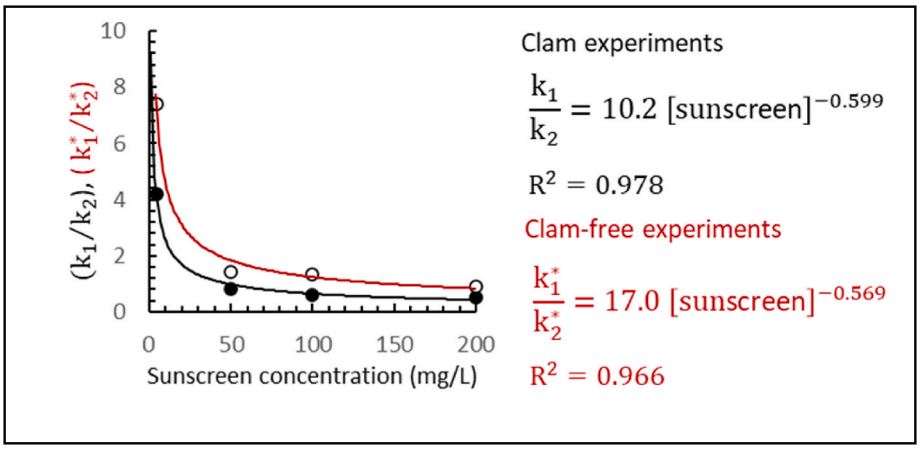

Fig. 3. Rate coefficients of equilibrium release to seawater from sunscreen as a function of the concentration of sunscreen in clams (• k_1/k_2) and in clam-free experiments (k_1^*/k_2^*).

equilibrium shift to higher values of Zn (aq) probably due to the bioconcentration of Zn in the clams.

The estimated value of $k_o = 0$ at all the sunscreen concentrations studied (Table 2) indicates that there is no uptake of Zn in the clam tissues from the organic colloidal residue (Fig. 2-IIa). Several studies have shown that metals in the colloidal phase can be assimilated by marine filter feeding bivalves (Guo et al., 2001; Pan and Wang, 2008; Sánchez-Marín et al., 2016). However, Guo et al. (2001) shows that colloidal complexed metals such as Zn are less bioavailable to oysters compared with low molecular weight dissolved organic carbon which indicates that the uptake of trace metals by the *American oyster* is mostly through the low molecular weight complexed and free ionic metal fractions. Other authors, such as Sánchez-Marín et al. (2011) have shown that dissolved organic matter (DOM) decreases or enhances Pb bioavailability in natural conditions depending on physico-chemical characteristics of the natural DOM and the structural and functional organisation of the epithelial interface for different biological species and exposure conditions. Authors such as Lee et al. (2015) and Kalman et al. (2014), show that the contribution of dissolved Zn to bioaccumulation by different species of bivalves is mainly through the diet, especially for high dissolved Zn concentrations. However, Reinfelder et al. (1998) predicted a route-specific difference in Zn uptake kinetics that states, assuming the equilibrium between the food and the water, that as the dissolved metal concentration increases, the relative importance of water as a route of uptake increases.

Metal uptake is controlled by the chemical properties and speciation of metals, physico-chemical characteristics of the organic matter, the metal-organic matter interactions in seawater as well as the biological species and the contact conditions (Guo et al., 2001; Wang, 2001; Beiras, 2018). The stability of the organic colloidal residue, where nanoparticles, organic chemicals, and inorganic chemicals from the sunscreen formulation can interact through several complex processes depending on different aging times and conditions (Rodríguez-Romero et al., 2019), is likely to be the reason for the negligible uptake rate by the clams of the Zn bound to the complex organic matrix.

The efflux rate coefficient (k_e) values obtained in the present work increase from 0 to 0.162 d^{-1} in the sunscreen concentrations studied with a value of $k_e = 0.0350\ d^{-1}$ at 50 mg L^{-1} of added sunscreen (Zn (aq) concentration = 180–270 μg L^{-1}); this value is within the ranges reported previously for Zn efflux rate coefficients measured in clams that are typically within 0.01–0.05 d^{-1} at seawater Zn exposure concentrations ranging from 1 to 100 μg L^{-1} (Wang, 2002; Chong and Wang, 2001; Lee et al., 1998; Chen et al., 2011). However, the k_e values in the present work were obtained during the sunscreen exposure period; therefore, lower values than those obtained during the depuration period in clean water are expected, taking into account the high Zn concentration in the water.

The uptake rate coefficient of dissolved Zn by the clams (k_u) is metal and species-specific and is used as an indicator of the bioavailability of dissolved metals (Lee et al., 1998; Wang et al., 1996). The work of Chong and Wang (2001) made the comparison of the metal uptake rate constant (ku) for Cd, Cr and Zn among different bivalves (Wang and Fisher, 1999; Chong and Wang, 2001; Lee et al., 1998). The ku values for Zn in clams ranged from 0.091 to 0.425 L g^{-1} d^{-1}, being 0.234 L g^{-1} d^{-1} in the clam *Ruditapes philippinarum* working at 1–100 μg L^{-1} of Zn (Chong and Wang, 2001). Experimental conditions of the referenced previous work are quite similar to the used in the present work in terms of shell length and dry wt. of clams, temperature and salinity. By contrast, the average Zn concentrations used in the present study is 0.85–29 times higher than the work of Chong and Wang (2001); In addition, the presence of organic colloidal residue from sunscreen is specific of the present work leading to very different conditions to the metal uptake. All of this is consistent with our results where ku value predicted is 0.00688 L g^{-1} d^{-1} at 5 mg L^{-1} of sunscreen in seawater reaching an average value of 0.0531 ± 0.0131 L g^{-1} d^{-1} at 50–200 mg L^{-1} added sunscreen equivalent to a maximum of 270–668 μg L^{-1} Zn in seawater. The values obtained from the model are an order of magnitude lower, predicting a lower bioavailability of Zn in a complex medium such as the seawater-sunscreen mixtures and in comparison to those studied in the literature. In this sense, the kinetic model proposed under varying Zn concentrations leads to a good agreement between the experimental and modelled Zn concentration values, which might contribute to a more realistic prediction of the Zn bioaccumulation of sunscreen in clams.

4. Conclusions

This paper presents a three-compartment biokinetic model to interpret the bioaccumulation of Zn in clams exposed to seawater with different concentrations of a commercial sunscreen containing ZnO nanoparticles. The model proposed considers that once the sunscreen is released into the seawater, the Zn retained in the organic colloidal residues (compartment 1) is partly transferred to the seawater (compartment 2) under an equilibrium reaction. The model also assumes that the Zn from the organic colloidal residues and the aqueous phase can also be transferred to the clams (Compartment 3).

The rate coefficients of the reactions are estimated using the Aspen Custom Modeler software. A good agreement between the experimental and modelled concentration values confirms that the model developed can be applied to interpret Zn bioaccumulation in clams from different concentrations of sunscreen in the marine environment. The values of the efflux rate coefficient (k_e) obtained in the present work are within the ranges previously reported for Zn efflux rate coefficients measured in

clams. However, the dissolved source uptake rate coefficient (k_u) is one order of magnitude lower than those previously predicted, probably due to taking the complex medium of the seawater and sunscreen mixtures into consideration, unlike those studied in the literature. The estimated value of the inlet rate coefficient to clams from organic colloidal residue ($k_o = 0$) at all the sunscreen concentrations studied indicates that there is a negligible uptake rate of Zn bound to the complex organic matrix by the clams, probably due to the considerable stability of the organic colloidal residue.

The model proposed and the kinetic parameters obtained could serve as a useful complementary tool within the framework of ecotoxicological research in coastal marine environments where the need to assess the potential environmental effects stemming from the components of sunscreen is of increasing importance. However, in order to increase the range of the applicability of the mathematical model proposed, there is a need for further studies focussing on the other components of sunscreens released into the seawater and the influence of organic matter under environmentally relevant conditions. Further, the role of the substance uptake via food should be quantified by the analysis of the food ingested and faeces excreted.

Author contribution statement

Gema Ruiz-Gutierrez: Conceptualization; Methodology, Formal analysis, Visualization; Validation; Writing – original draft, **Araceli Rodríguez Romero**: Investigation; Formal analysis; Validation; Project administration; Funding acquisition; Writing – review & editing, **Amandine Gaudron**: Investigation; Writing. **Berta Galan Corta**: Writing – review & editing; Methodology; Visualization, **Antonio Tovar-Sanchez**: Writing – review & editing; Methodology; Supervision, **Javier R. Viguri Fuente**: Conceptualization; Writing – original draft; Writing – review & editing; Supervision

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.136043.

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