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# Occurrence and potential ecological risks of pharmaceuticals and illicit drugs (PhIDs) in the Santos-São Vicente Estuarine System (SSVES), Brazil

Andressa dos Santos Barbosa Ortega [a,e,*], Vinicius Roveri [b,c,d], Marina de Souza Paço [e], Daniel Temponi Lebre [f], Luciane Alves Maranho [a,g], Camilo Dias Seabra Pereira [e,h]

[a] Institute of Bioscience, São Paulo State University (Unesp), Praça Infante Dom Henrique, s/n, 11330-900 São Vicente, São Paulo, Brazil
[b] Metropolitan University of Santos (UNIMES), Avenida Conselheiro Nébias, 536 - Encruzilhada, 11045-002 Santos, São Paulo, Brazil
[c] Interdisciplinary Center for Marine and Environmental Research (CIIMAR/CIMAR), Avenida General Norton de Matos S/N, 4450-208 Matosinhos, Portugal
[d] Natural Products Research Laboratory, Santa Cecília University, Rua Cesário Mota, 8, 11045-040 Santos, São Paulo, Brazil
[e] Federal University of São Paulo (Unifesp), Department of Marine Science, Rua Maria Máximo 168, 11030-100 Santos, São Paulo, Brazil
[f] Center for Applied Mass Spectrometry (CEMSA), IPEN, Av. Prof. Lineu Prestes, 2242, Salas 112 e 113, São Paulo 05508-000, Brazil
[g] Universidade de Ribeirão Preto, UNAERP, Guarujá, São Paulo 11440003, Brazil
[h] Ecotoxicology Laboratory, Santa Cecília University, Rua Cesário Mota, 8, 11045-040 Santos, São Paulo, Brazil

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ABSTRACT

Despite the substantial amount of research on the presence of pharmaceuticals and illicit drugs (PhIDs) in freshwater environments, there is a paucity of data on these contaminants in estuarine systems, particularly in South America. Industries, the biggest port in the Southern Hemisphere, and substantial urban areas surround the Santos-São Vicente Estuarine System (SSVES), located in a Brazilian subtropical area. This study constitutes the first assessment of contamination by PhIDs in this estuarine area. Samples of superficial water, sediments, and oysters were analyzed through liquid chromatography-tandem mass spectrometry (LC-MS/MS). Furthermore, the potential ecological risk to aquatic non-target organisms (i.e., primary producers, primary and secondary consumers) was assessed using the maximum measured environmental concentrations (MEC) of the PhIDs identified in this study. The results revealed the widespread presence of caffeine (MEC = 72.1 $ng{\cdot}L^{-1}$) > losartan (29.6 $ng{\cdot}L^{-1}$) > orphenadrine (25.9 $ng{\cdot}L^{-1}$) > benzoylecgonine (18.6 ng/L-1) > carbamazepine (7.4 $ng{\cdot}L^{-1}$) and cocaine (3.6 $ng{\cdot}L^{-1}$). These findings were obtained from relevant sites at SSVES, near areas with mangroves and anthropogenic activities, such as fishing and swimming. Consequently, the ecological risk assessment indicated significant environmental concern, as our results suggested low to moderate risks of all compounds to algae, crustaceans, and/or fish. Considering the One Health approach, further studies are recommended to investigate the potential human health risks associated with consuming contaminated seafood. Concomitantly, there is an urgent need for improvements in public sanitation, public health care for illicit drug users, and public safety actions against traffic.

## 1. Introduction

Contamination of aquatic ecosystems by pollutants of emerging concern (PECs) has been extensively documented on all continents (Gworek et al., 2020; Roveri et al., 2021a; Morin-Crini et al., 2022). Among the groups of PECs, Pharmaceuticals and illicit drugs (PhIDs) represent a wide range of chemicals, including therapeutic drugs (e.g., antibiotics, analgesics, antiepileptics, anti-inflammatory drugs, antihypertensives, diuretics, and stimulants) (Roveri et al., 2022a, 2022b; Yu et al., 2023), as well as illicit substances such as cocaine and its main metabolite (Pereira et al., 2016; Fontes et al., 2019, 2021). PhIDs are typically found in trace concentrations in the environment, and their daily introduction into ecosystems may pose direct and indirect threats to aquatic ecosystem services, biodiversity, and human health (Yang et al., 2021).

Despite the considerable number of studies on the occurrence of PhIDs in freshwater systems, there is a paucity of data on these contaminants in estuarine systems (mainly in South America) (Adedipe et al., 2024). Estuaries are recognized as ecological biodiversity hotspots due to the interface between marine and freshwater systems (Martínez-

* Corresponding author at: Institute of Bioscience, São Paulo State University (Unesp), Praça Infante Dom Henrique, s/n, 11330-900 São Vicente, São Paulo, Brazil.
*E-mail address:* dressaortega@gmail.com (A.S.B. Ortega).

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Megías and Rico, 2022; Nagarajan et al., 2022; Xu et al., 2022). They are essential for sustaining food supplies for human populations dependent on coastal fisheries and aquaculture activities (Martínez-Megías and Rico, 2022; Nagarajan et al., 2022; Xu et al., 2022). Nevertheless, estuaries are also highly vulnerable due to exposure to several environmental stressors (Martínez-Megías and Rico, 2022; Nagarajan et al., 2022; Xu et al., 2022).

Urbanized estuaries are subject to various human activities, including navigation, commerce, tourism, and leisure. It renders them one of the most impacted ecosystems on the planet due to anthropogenic pollution (Martínez-Megías and Rico, 2022; Nagarajan et al., 2022; Xu et al., 2022). A prime example of an urbanized estuary that has been severely impacted is the Santos-São Vicente Estuarine System (SSVES), which is located in a densely populated area and is surrounded by the largest commercial port in the Southern Hemisphere (Port of Santos) (Buruaem et al., 2013). SSVES is considered one of South America's most economically significant regions, encompassing the municipalities of São Vicente, with a population of 329,911, and Santos, with a population of 418,608 (IBGE, 2024a, 2024b). Nevertheless, slums on stilts represent a major environmental concern in the region (Sampaio et al., 2016; Martins et al., 2021). According to Sampaio et al. (2016), the population residing in irregular dwellings is approximately 130,682 individuals, constituting 17.46 % of the total population. Martins et al. (2021) reported that São Vicente includes 29,079 dwellings in irregular areas, while Santos has 15,732 irregular dwellings. A salient issue with these dwellings is that they are not connected to the sewage systems, meaning that the domestic effluent flows directly to the SSVES. In this context, previous studies have already indicated the presence of different pollutants in this estuarine system. Hortellani et al. (2005) demonstrated that approximately 35 % of the sediment samples from SSVES exhibited concentrations of mercury (Hg) > 0.70 μg.g-1, which is likely to induce adverse effects on the local biota.

Given the context mentioned above, the objectives of this study are as follows. Firstly, to investigate, for the first time, the occurrence of PhIDs (including cocaine and its primary metabolite, benzoylecgonine) in samples of superficial water, sediments, and oysters from the SSVES (São Paulo coastline, Brazil). Secondly, the possible ecological risks to aquatic organisms, including algae, crustaceans, and fish, will be assessed using the maximum measured environmental concentrations (MEC) of these PhIDs (in superficial waters). Given the importance of ecosystem services, enhancing the monitoring of PhIDs in estuaries is imperative. Consequently, the information obtained will facilitate the construction of a database on the influence of PhIDs on the quality of the estuarine aquatic ecosystem of the São Paulo coast. The database will provide a scientific basis to support decision-makers in formulating policies related to these coastal zones' land use, occupation, and

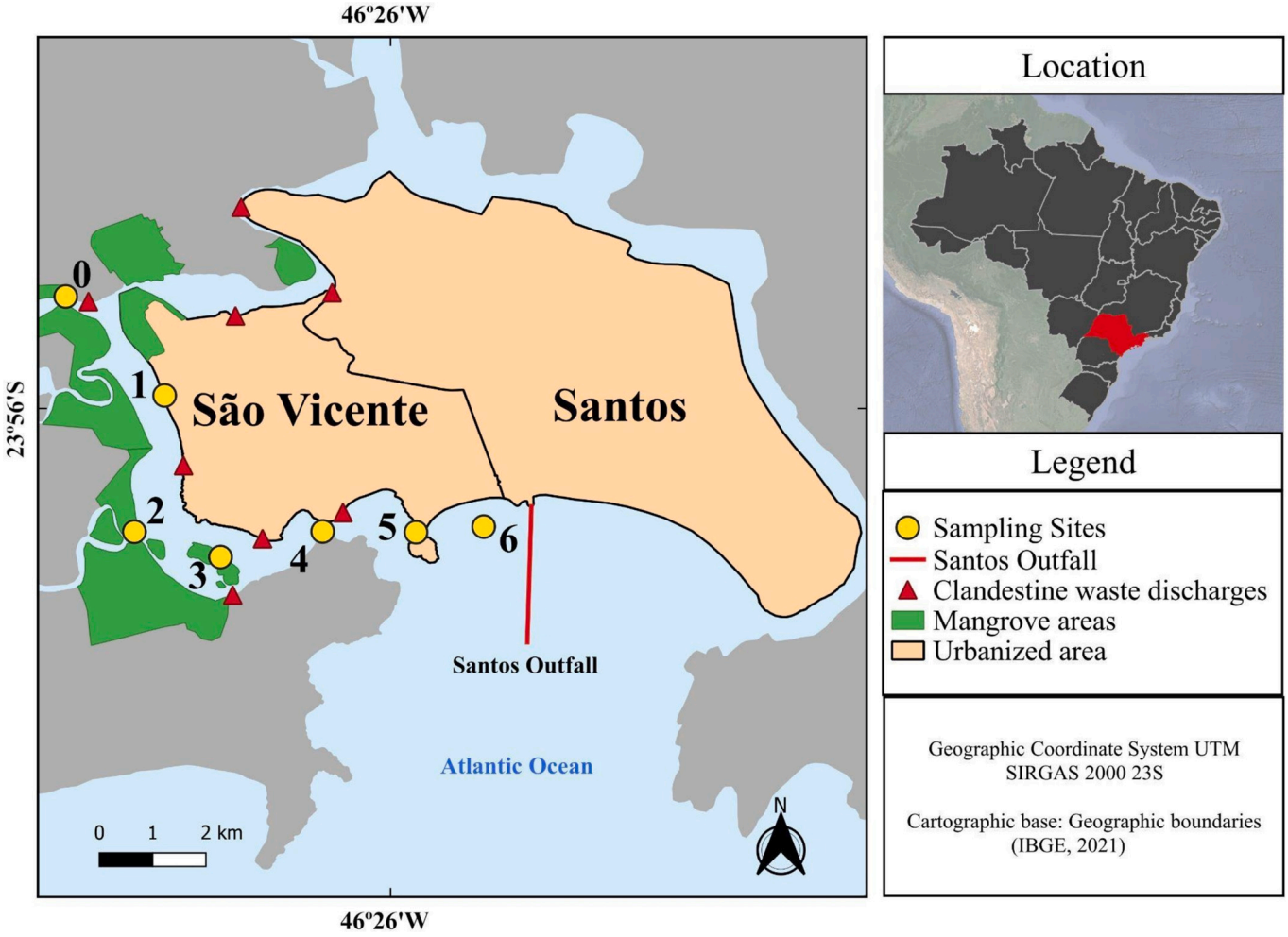


**Fig. 1.** The map of the study area depicts Brazil (top right, marked in black) and the State of São Paulo (marked in red). It also illustrates the location of seven sampling sites (yellow spheres, numbered 0 to 6) situated in the western part of the Santos - São Vicente Estuarine System and São Vicente Bay. In green, the mangrove areas, and in salmon, the two municipalities of Santos and São Vicente with urbanized areas. The red triangles illustrate the clandestine waste discharges across the SSVES. The map was produced based on geographic boundaries provided by IBGE (2021). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

governance, particularly in areas with intense anthropogenic activities.

## 2. Materials and methods

### 2.1. Sampling sites and collection

Seven sampling sites were selected along the western portion of SSVES and São Vicente Bay (see Fig. 1). Sampling sites 0, 1, and 2 are located near the mouths of three rivers: Santana, Mariana, and Piaçabuçu, respectively. Sampling site 3 is situated in an area characterized by irregular housing structures and discharge of domestic effluent. The fourth site is located in the marine zone of Xixová-Japuí State Park, a protected area significantly impacted by adjacent urban zones (Araujo et al., 2013). The fifth site is where people engage in fishing and bathing, and are affected by anthropogenic activities. The final site (sixth) is in São Vicente Bay, near Itararé Beach. Geographical coordinates are available in Supplementary material (Table 1-S).

The water, sediment, and oyster samples were collected on January 4, 2022, during the summer season. The water samples were collected manually using an amber bottle, with the bottle positioned approximately 30 cm from the surface. The oysters were collected from tree trunks or rocks as collection media. Sediment samples were collected using a Van Veen grab sampler and conditioned into plastic bags. During the sampling collection, parameters were measured in the water column (pH, dissolved oxygen, temperature, and salinity). One sample was collected per site for water samples. Sediment and oyster samples, however, were divided into three replicates per site, with three oysters used per replicate. All collected samples were immediately transferred to the laboratory and frozen (−20 °C) until analysis.

### 2.2. Physicochemical characterization of sediment samples

Grain size distribution was determined for an aliquot of each sediment sample and classified using the Wentworth scale (Wentworth, 1922). The sediment samples were initially washed through a sieve with a mesh smaller than 38 μm to remove unwanted particles that could interfere with the granulometric analysis. After drying, the sediment was sieved using a series of sieves with mesh sizes ranging from 38 μm to 1.18 mm. The material retained on each sieve was weighed to calculate the proportion of each granulometric fraction.

To analyze the calcium carbonate content, 30 g of sediment was digested with HCl (15 %) for 24 h. The sediment was then washed with distilled water and dried. The samples were then weighed. The calcium carbonate content was determined based on the difference between the initial and final weights. The procedure followed the protocol outlined by Grant-Groos (1971).

The organic matter in the samples, which had previously undergone decarbonation, was analyzed following the protocol established by Luczak et al. (1997). Five grams of dry sediment were isolated and incinerated in a muffle furnace at 500 °C for four hours. The sediment was then transferred to a desiccator to avoid the effects of ambient humidity before being weighed. The organic matter content in the samples was determined by calculating the initial and final weights of the samples.

### 2.3. Sample preparation

The necessity to lyophilize samples of oysters and sediment for solid-phase extraction (SPE) was imperative. The oysters were divided into three replicates per site, with each replicate comprising a pool of three organisms. The sediment samples were considered as a single sample per site. The samples were then placed in a freeze-dryer LioTop K105 for four days. The SPE procedure followed Method 1694, as outlined by the United States Environmental Protection Agency (USEPA, 2007) and Klosterhaus et al. (2013). Initially, 1 g of each lyophilized sample was weighed. Then, 10 mL of acetonitrile was added, and the samples underwent an ultrasonic bath for 30 min. The samples were filtered after this step, and the filtrate was transferred to a beaker. Subsequently, 10 mL of phosphate buffer was added to each sample and placed under an ultrasonic bath for 30 min. The recovered upper layer was transferred into the beakers used previously. In the final step, 10 mL of acetonitrile was added to each sample, and they were subjected to an additional 30 min of ultrasonic action. Finally, the clarified fractions were pooled, and the resulting mixture was centrifuged. 250 mL of Mili-Q® water was added, giving each sample a total volume of 280 mL.

### 2.4. Solid-phase extraction (SPE)

The SPE procedure was performed following the methods outlined by Wille et al. (2010) and Pereira et al. (2016). In this study, 500 mL of each water sample was separated. 280 mL of the processed sample from the previous stage (see Section 2.3) was used for oysters and sediment. All samples were filtered using a Whatman® GF/C filter (diameter 47 mm; pore size 1.2 μm). The filters were then washed with 2 mL of methanol, after which the pH of the filtered samples was adjusted to 7 ± 0.5 using HCl and NaOH. The SPE was then performed using Chromabond® PP HR-X cartridges (3 mL, 200 mg). The cartridges were then activated by adding 5 mL of methanol and 5 mL of Mili-Q® water. The samples were then passed through the cartridges using a vacuum pump. Thereafter, 5 mL of Mili-Q® water was added, and the cartridges were dried with the flow of the vacuum pump for 15 min. The eluate was then subjected to the addition of 5 mL of acetone and 10 mL of methanol to the cartridges. The eluate was then stored in a glass tube and frozen at −20 °C.

### 2.5. Liquid chromatography-tandem mass spectrometry (LC-MS/MS)

The LC-MS/MS analysis was conducted using the protocol delineated by Shihomatsu et al. (2017). An aliquot of each sample was analyzed by an HPLC Agilent 1260 (Agilent Technologies, CA, USA) combined with a 3200 QTRAP hybrid triple quadrupole/LIT (linear ion trap) mass spectrometer ABSciex, Ontario (Canada). The conditions utilized in this method are consistent with those delineated in the studies of Fontes et al. (2019) and Pereira et al. (2016). Analytes were identified and quantified using ESI ionization (positive and negative modes) and Multiple Reaction Monitoring (MRM) modes. Data analysis was conducted using Analyst® 1.5.2 (ABSciex, Ontario, Canada). The MRM parameters for positive and negative modes for pharmaceuticals, cocaine, and benzoylecgonine are consistent with those described by Pereira et al. (2016). The limit of detection (LOD) and the limit of quantification (LOQ) are shown in the Supplementary material (Table 2-S). The recoveries of SPE extraction for the water matrix ranged from 49 % to 109 %. The recovery rates ranged from 35 % to 40 % in sediment and oyster.

### 2.6. Estuarine ecological risks of PhIDs

The ecological risk assessment was conducted according to Roveri et al.'s (2022b) framework. Different aquatic organisms, including algae, crustaceans, and fish, were used to calculate the Risk Quotient (RQ). The RQ was obtained by dividing the maximum Measured Environmental Concentration (MEC) by the Predicted No Effect Concentration (PNEC) (RQ = MEC/PNEC), both expressed in ng/L-1. The PNEC values were obtained from peer-reviewed literature available in the PubMed database. When acute and chronic experimental data were unavailable, the PNEC was estimated using computational modeling (in silico) methods based on quantitative structure-activity relationship (QSAR) models. The Ecological Structure Activity Relationships Programme (ECOSAR, v. 2.0) (USEPA, 2017) and the VEGA QSAR (Version 1.1.5 beta 48) (Vega, 2021) were utilized as the primary methods. For further details about the applicability domains of both (Q)SAR models, please refer to the Supplementary material (S1). The PNEC values were obtained by

dividing each toxicological endpoint (acute and chronic toxicity) by an assessment factor (AF). For seawater environments, an AF of 10,000 and 100 was applied for datasets covering short- and long-term periods, respectively (ECB, 2003; ECHA, 2008). The RQ for aquatic organisms was then classified into four categories: no (RQ < 0.01; represented in white), low (0.01 ≤ RQ < 0.1; represented in green), moderate (0.1 ≤ RQ < 1.0; represented in yellow), and high ecological risk (RQ ≥ 1.0; represented in red).

## 3. Results

### 3.1. Results of the occurrence of PhIDs in estuarine superficial waters

As outlined in Table 3-S, physicochemical variables analyzed of superficial water exhibited a pH range from 7.33 to 8.30, with the lowest values recorded at sampling site 1, near the mouth of the Santana River. The mean temperature recorded was 27.3 °C. The dissolved oxygen concentrations ranged from 0.7 mg/L. $L^{-1}$ to 3.89 mg. $L^{-1}$. A salinity gradient was observed, ranging from 14 ‰ in sampling sites 1 to 35 ‰ in sampling sites 4, 5, and 6.

Six substances were detected and subsequently quantified in the sampled superficial water: cocaine (COC), benzoylecgonine (BE), caffeine (CAF), carbamazepine (CBZ), orphenadrine (ORP), and losartan (LOS) (see Table 1 for details). The highest measured concentration of COC was 3.66 ng·$L^{-1}$, with an average of 1.64 ± 1.48 ng/L-1. BE was detected and quantified in all site samples, with the highest metabolite concentration recorded being 18.6 ng·$L^{-1}$. The highest concentration found was 118.6 ng·$L^{-1}$ of CAF. The antiepileptic CBZ was found at concentrations between 1.01 and 7.37 ng·$L^{-1}$, while the analgesic ORP and the antihypertensive LOS were found in concentrations of 25.9 and 29.6 ng·$L^{-1}$, respectively.

### 3.2. Results of the occurrence of PhIDs in the sediment and in the samples of oysters

Sediment samples were characterized, and the parameters of calcium carbonate, organic matter, and grain size are shown in Table 4-S. All sampling sites were classified as very fine sand. However, sampling sites 0 and 2 observed a high mud level in the sediment. The humidity of the samples ranged from 19.47 to 47.50 %. The carbonate concentration ranged from 6.56 to 7.42 %, while the organic matter levels ranged from 0.61 to 12.38 %. The occurrence of COC was detected in five of the sediment samples (0, 1, 4, 5, and 6). However, all samples exceeded the detection limit for BE and CAF.

COC was detected in one sample (site 1) in the oyster tissues, but below the quantification limit. Conversely, BE and CAF were below the detection limit in all other samples.

### 3.3. Results of the estuarine ecological risks of PhIDs

The results of the study on the estuarine ecological risks of PhIDs demonstrated the following trend (see Table 2): (i) 47.2 % of the PNEC calculations were achieved using data derived from the scientific peer-reviewed literature; (ii) the remaining 52.8 % of the PNEC calculations were estimated using the VEGA and ECOSAR programs; (iii) a survey of the peer-reviewed literature revealed that only acute toxicity data for estuarine and marine organisms were available for CBZ and ORP (representing only 8 % of the RQ calculations). Consequently, this study adopted toxicity data from freshwater species to calculate the PNEC of the COC, BE, CAF, and LOS (which represent 92 % of the RQ calculations); (iv) concerning acute toxicity, 83.4 % of the results indicated a negligible or low ecological risk for one of the trophic levels tested (0.01 ≤ RQ <0.1). In contrast, 16.6 % of the results (specifically from COC, BE and LOS) indicated moderate toxicity to crustacea (*Daphnia magna*) and/or fish (*Pimephales promelas*) (0.1 ≤ RQ < 1.0) (Table 2); (v) regarding chronic toxicity, 38.9 % of the results indicated low risks, and 61.1 % stated no risks for algae, crustaceans, and fish.

## 4. Discussion

### 4.1. Occurrence of PhIDs in estuarine superficial waters

This study constitutes the first screening for PhIDs on the westside of SSVES and São Vicente Bay. Due to their excretion via urine in metabolized or conjugated forms, COC and BE are reliable markers of domestic wastewater contamination in aquatic environments (Parolini et al., 2018; Maasz et al., 2019). The range observed for COC (non-metabolized or directly discharged fraction) was from 1.41 to 3.66 ng in the superficial water. $L^{-1}$, and for BE (a metabolite of COC use), the range was from 8.89 to 18.6 ng·$L^{-1}$. The highest concentrations of COC and BE were observed in samples collected from sites 0 and 2, located near the mouths of the Santana and Piaçabuçu Rivers within the mangrove areas. It is a matter of concern, given the function of mangroves as providers of ecosystem services (e.g., nursery habitats) and economic resources (e.g., food sources) (Szafranski and Granek, 2023), and the potential consequences of contamination in these areas, which may have adverse effects on biota and human health. This work found a COC/BE ratio between 0.08 and 0.26 (Table 1). Van Nuijs et al. (2009) proposed a cut-off value 0.75 for the metabolic conversion of COC to BE. Therefore, these ratios below 0.75 (observed in 100 % of the samples) indicate high COC consumption along the SSVES. However, this information is unsurprising, with 2.8 million Brazilians using COCs in 2021 (the second-highest global consumption after the USA) (UNODC, 2023).

On a global scale, several studies have reported the occurrence of COC and its main metabolite in aquatic matrices worldwide (Christophoridis et al., 2021; Brieudes et al., 2017; Campestrini and Jardim, 2017; Thomas et al., 2014; Zuccato et al., 2008; Van Nuijs et al., 2009). In this regard, COC and BE have been detected in estuarine water samples across three continents: North America, Europe, and South America (with a high prevalence in Brazil) (Adedipe et al., 2024). COC's average concentration level (WACL) ranged from 0.60 ng·$L^{-1}$ in North America to 143.82 ng·$L^{-1}$ in South America. In the case of BE, the WACL

**Table 1**
Results of the occurrence of six pharmaceuticals and illicit drugs (PhIDs) of different therapeutic classes (i.e. stimulants, antiepileptics, anti-inflammatories and antihypertensives) in surface water samples from the Santos-São Vicente Estuarine System (SSVES), State of São Paulo, Brazil. Note: (i) concentrations are expressed in ng·$L^{-1}$; (ii) bold values represent the maximum measured environmental concentrations (MEC) for each compound; (iii) <LOQ indicates lower than the limit of quantification; and (iv) <LOD indicates lower than the limit of detection. Further details on sampling sites can be found in Fig. 1.

| Sampling site | Cocaine | Benzoylecgonine | Caffeine | Carbamazepine | Orphenadrine | Losartan |
|---|---|---|---|---|---|---|
| 0 | **3.6** | 13.8 | <LOQ | 5.1 | <LOQ | 17.2 |
| 1 | 1.4 | 17.4 | **72.1** | **7.4** | 1.9 | **29.6** |
| 2 | 3.4 | **18.6** | 51.7 | 7.3 | **25.9** | 21.1 |
| 3 | <LOQ | 11.5 | 53.2 | 4.9 | <LOQ | 23.4 |
| 4 | 2.2 | 8.9 | 56.8 | <LOQ | <LOQ | 11.9 |
| 5 | <LOQ | 11.6 | 76.9 | <LOQ | <LOQ | 18.6 |
| 6 | <LOQ | 10.2 | 118.6 | <LOQ | <LOD | <LOQ |
| Mean ± standard deviation | 1.64 ± 1.48 | 13.14 ± 3.66 | 62.48 ± 33.29 | 3.97 ± 2.92 | 4.35 ± 9.52 | 17.86 ± 8.46 |

**Table 2**
Results of ecological risk assessment tests of six pharmaceuticals and illicit drugs (PhID) of different therapeutic classes (i.e. stimulants, antiepileptics, anti-inflammatories and antihypertensives) in surface water samples from the Santos-São Vicente Estuarine System (SSVES) and São Vicente Bay, State of São Paulo, Brazil. The table shows: name of each compound; MEC: measured environmental concentration in the SSVES water body (in ng·L$^{-1}$); acute and chronic toxicity data: [trophic level; organism test, toxicological endpoint and concentration (ng·L$^{-1}$)], assessment factor (AF), predicted no-effect concentration (PNEC, in ng·L$^{-1}$). Toxicological endpoint data were obtained from several published papers (references) available in the ecotoxicology database (ECOTOX) or, in the absence of derived experimental data, estimated using VEGA software. Where the results of the toxicological endpoints were outside the applicability domain of VEGA, the ECOSAR programme was used for in silico prediction. Note: Freshwater (1); seawater (2); EC50: 50 % effective concentration; LC50: 50 % lethal concentration; NOEC: no observed effect concentration; LOEC: lowest observed effect concentration. For further details, please refer to Section 2.6.

| Compound | MEC | Toxicity data | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Trophic level | | Organisms/species | Endpoint | Concentrations (ng.L$^{-1}$) | AF | PNEC (ng.L$^{-1}$) | Reference | RQ |
| Cocaine (COC) | 3.66 | Acute | Algae | *Rhapidocelis subcapitata* (1) | 48h EC50 | 4.35E+06 | 10000 | 4.35E+02 | VEGA | <0.01 |
| | | | Crustacea | *Daphnia magna* (1) | 48h LC50 | 5.48E+06 | | 5.48E+02 | VEGA | 0.10 |
| | | | Fish | *Oryzias latipes* (1) | 96h LC50 | 4.86E+07 | | 4.86E+03 | VEGA | <0.01 |
| | | Chronic | Algae | *Rhapidocelis subcapitata* (1) | NOEC | 1.46E+06 | 100 | 1.46E+04 | VEGA | <0.01 |
| | | | Crustacea | *Daphnia magna* (1) | NOEC | 2.29E+09 | | 2.29E+07 | VEGA | <0.01 |
| | | | Fish | *Danio rerio* (1) | NOEC | 7.18E+06 | | 7.18E+04 | VEGA | <0.01 |
| Benzoylecgonine (BE) | 18.6 | Acute | Algae | *Rhapidocelis subcapitata* (1) | 72h EC50 | 1.20E+10 | 10000 | 1.20E+06 | VEGA | 0.03 |
| | | | Crustacea | *Daphnia magna* (1) | 48h LC50 | 3.14E+12 | | 3.14E+08 | VEGA | 0.06 |
| | | | Fish | *Pimephales promelas* (1) | 96h LC50 | 6.24E+11 | | 6.24E+07 | VEGA | 0.16 |
| | | Chronic | Algae | *Rhapidocelis subcapitata* (1) | NOEC | 3.03E+09 | 100 | 3.03E+07 | VEGA | <0.01 |
| | | | Crustacea | *Daphnia magna* (1) | NOEC | 2.00E+13 | | 2.00E+11 | VEGA | <0.01 |
| | | | Fish | *Danio rerio* (1) | NOEC | 4.92E+09 | | 4.92E+07 | VEGA | <0.01 |
| Caffeine (CAF) | 72.1 | Acute | Algae | *Pseudokirchneriella subcapitata* (1) | 72h LC50 | 3.39E+08 | 10000 | 3.39E+04 | Blaise et al. (2006) | <0.01 |
| | | | Crustacea | *Daphnia dubia* (1) | 48h LC50 | 5.00E+07 | | 5.00E+03 | Moore et al. (2008) | 0.01 |
| | | | Fish | *Pimephales promelas* (1) | 48h LC50 | 8.00E+07 | | 8.00E+03 | Moore et al. (2008) | 0.01 |
| | | Chronic | Algae | *Lemna gibba* (1) | LOEC/2 | 5.00E+05 | 100 | 5.00E+03 | Brain et al. (2004) | 0.01 |
| | | | Crustacea | *Ceriodaphnia dubia* (1) | NOEC | 2.00E+07 | | 2.00E+05 | Brain et al. (2004) | <0.01 |
| | | | Fish | *Pimephales promelas* (1) | NOEC | 3.00E+07 | | 3.00E+05 | Brain et al. (2004) | <0.01 |
| Carbamazepine (CBZ) | 7.37 | Acute | Algae | *Skeletonema marinoi* (2) | 72h EC50 | 1.00E+08 | 10000 | 1.00E+04 | Mínguez et al. (2014) | <0.01 |
| | | | Crustacea | *Artemia salina* (2) | 48h EC50 | 1.00E+08 | | 1.00E+04 | Mínguez et al. (2014) | <0.01 |
| | | | Fish | *Oryzias latipes* (1) | 48h EC50 | 3.52E+07 | | 3.52E+02 | Kim et al. (2009) | <0.01 |
| | | Chronic | Algae | *Lemna gibba* (1) | LOEC/2 | 5.00E+05 | 100 | 5.00E+03 | Brain et al. (2004) | <0.01 |
| | | | Crustacea | *Ceriodaphnia dubia* (1) | NOEC | 2.50E+04 | | 2.50E+02 | Ferrari et al. (2003) | 0.03 |
| | | | Fish | *Danio rerio* (1) | NOEC | 2.50E+07 | | 2.50E+05 | Ferrari et al. (2003) | <0.01 |
| Orphenadrine (ORP) | 25.9 | Acute | Algae | *Lemna minor* (1) | 168h EC50 | 1,20E+07 | 10000 | 1,20E+03 | Kaza et al. (2009) | 0.02 |
| | | | Crustacea | *Artemia salina* (2) | 24h EC50 | 4,50E+07 | | 4,50E+03 | Calleja et al. (1994) | 0.01 |
| | | | Fish | Fish (1) | 96h LC50 | 4,24E+07 | | 4,24E+03 | ECOSAR | 0.01 |
| | | Chronic | Algae | Green algae (1) | 10^([log (LOEC x NOEC)]/2) | 1,32E+05 | 100 | 1,32E+03 | ECOSAR | 0.02 |
| | | | Crustacea | Daphnid (1) | | 6,10E+04 | | 6,10E+02 | ECOSAR | 0.04 |
| | | | Fish | Fish (1) | | 1,37E+05 | | 1,37E+03 | ECOSAR | 0.02 |
| Losartan (LOS) | 29.6 | Acute | Algae | *Lemna minor* (1) | 96h EC50 | 6,46E+07 | 10000 | 6,46E+03 | Godoy et al. (2015) | <0.01 |
| | | | Crustacea | *Daphnia magna* (1) | 48h LC50 | 331000 | | 3,31E+01 | FDA (2012) | 0.89 |
| | | | Fish | *Pimephales promelas* (1) | 48h LC50 | 1,00E+09 | | 1,00E+06 | FDA (2012) | <0.01 |
| | | Chronic | Algae | Green algae (1) | 10^([log (LOEC x NOEC)]/2) | 1,64E+06 | 100 | 1,64E+04 | ECOSAR | <0.01 |
| | | | Crustacea | Daphnid (1) | | 5,55E+05 | | 5,55E+03 | ECOSAR | 0.01 |
| | | | Fish | Fish (1) | | 2,94E+05 | | 2,94E+03 | ECOSAR | 0.01 |

Note: The RQ has been classified into four categories: no ecological risk (RQ < 0.01) is shown in white; low risk (0.01 ≤ RQ < 0.1) is shown in green; moderate risk (0.1 ≤ RQ < 1.0) is shown in yellow; no high risk (RQ ≥ 1.0) was found for aquatic organisms.

ranged from 5.20 ng·L$^{-1}$ in North America to 13.33 ng·L$^{-1}$ in Europe (Adedipe et al., 2024). Specifically in estuarine systems of North America (U.S.), Klosterhaus et al. (2013) detected concentrations ranging from 2.80 to 7.20 ng·L$^{-1}$ of BE and 2.40 ng·L$^{-1}$ of COC. In contrast, Pisetta et al. (2022) reported the detection of COC and BE in estuarine waters from Santa Catarina, Brazil (0.17 and 1.1 ng·L$^{-1}$, respectively). The present study's findings are consistent with extant literature on a regional scale, as a previous study has reported the presence of these substances in the tributaries of the main estuarine channel. Roveri et al. (2022a) observed the presence of COC (2.3–6.7 ng·L$^{-1}$) and BE (10.8–17.2 ng·L$^{-1}$) in draining channels in the municipality of São Vicente, which can introduce COC and BE into the SSVES. In the neighboring city of Santos, Fontes et al. (2019) and Pereira et al. (2016) detected and quantified COC and BE in superficial and bottom marine water, respectively. Fontes et al. (2019) conducted a seasonal study and observed the highest concentration of COC (203.60 ng·L$^{-1}$) in the spring in bottom water. Concurrently, Pereira et al. (2016) documented concentrations of COC ranging from 12.6 to 537 ng·L$^{-1}$ and BE ranging from 4.6 to 20.8 ng·L$^{-1}$. In a subsequent study, Roveri et al. (2020) identified and quantified COC and BE in draining channels in beaches at Guarujá City (COC: 0.2–30.3 ng·L$^{-1}$; BE: 0.9–278 ng·L$^{-1}$). Subsequently, Roveri et al. (2021b) undertook a further study, collecting samples from the Guarujá sewage outfall located on the coast of São Paulo State. COC (0.6 ng·L$^{-1}$) and BE (1.7 ng·L$^{-1}$) were observed. In a similar vein, Fontes et al. (2021) documented comparable concentrations of COC (1.91–12.52 ng·L$^{-1}$) and BE (9.88–28.53 ng·L$^{-1}$) in water samples collected in proximity to the shore and sewage outfalls within the same region as the present study (see Table 3 for details).

**Table 3**
The maximum measured environmental concentrations (MECs) of cocaine (COC) and benzoylecgonine (BE), expressed in ng·L$^{-1}$, were detected in surface water samples taken from the Santos-São Vicente Estuarine System (SSVES) in the Metropolitan Region of Baixada Santista (MRBS), São Vicente, Brazil. The results for these two compounds were compared to concentrations reported by other studies in several aquatic compartments in the MRBS and elsewhere around the world. Note (i) LOQ indicates concentrations lower than the limit of quantification; (ii) (*) cities neighboring São Vicente that belong to the MRBS; (iii) (↑) higher concentrations than in this study; (↓) Lower concentrations than in this study.

| Compound | MEC (ng·L$^{-1}$) | Environmental matrix | Country | Reference | Comparison with this study |
|---|---|---|---|---|---|
| COC | **3.6** | **São Vicente Estuary (SSVES)** | **Brazil (São Vicente)** | **This study** | |
| | 49.3 | São Francisco Bay | USA | Klosterhaus et al. (2013) | ↑ |
| | 6.6 | Seawater | Greece | Borova et al. (2014) | ↑ |
| | 537.0 | Santos Bay | Brazil (Santos)* | Pereira et al. (2016) | ↑ |
| | 43.0 | Coastal waters | Spain | Fernández-Rubio et al. (2019) | ↑ |
| | 203.6 | Santos Bay | Brazil (Santos)* | Fontes et al. (2019) | ↑ |
| | <LOQ | Coastal lagoon | Uruguay | Griffero et al. (2019) | ↓ |
| | 30.3 | Coastal waters | Brazil (Guarujá)* | Roveri et al. (2020) | ↑ |
| | 12.5 | Santos Bay | Brazil (Santos)* | Fontes et al. (2021) | ↑ |
| | 0.2 | Coastal waters | Brazil (Santa Catarina) | Pisetta et al. (2022) | ↓ |
| | 0.6 | Coastal waters | Brazil (Guarujá)* | Roveri et al. (2021a) | ↓ |
| | 1.7 | Santos Bay | Brazil (Santos)* | Roveri et al. (2021b) | ↓ |
| | 6.7 | Coastal waters | Brazil (São Vicente) * | Roveri et al. (2022a) | ↑ |
| | 0.8 | Coastal waters | Brazil (Praia Grande) * | Roveri et al. (2022b) | ↓ |
| | 0.05 | Coastal waters | Brazil (Mongaguá)* | Roveri et al. (2022b) | ↓ |
| | 0.1 | Coastal waters | Brazil (Itanhaém)* | Roveri et al. (2022b) | ↓ |
| | 0.06 | Coastal waters | Brazil (Peruíbe)* | Roveri et al. (2022b) | ↓ |
| BE | **18.6** | **São Vicente Estuary (SSVES)** | **Brazil (São Vicente)** | **This study** | |
| | 54.0 | São Francisco Bay | USA | Nödler et al. (2014) | ↑ |
| | 2.5 | Coastal waters | Spain | Nödler et al. (2014) | ↓ |
| | 16.0 | Coastal waters | Turkey | Nödler et al. (2014) | ↓ |
| | 13.0 | Coastal waters | Italy | Nödler et al. (2014) | ↓ |
| | 2.3 | Coastal waters | Greece | Nödler et al. (2016) | ↓ |
| | 20.8 | Santos Bay | Brazil (Santos)* | Pereira et al. (2016) | ↑ |
| | 152.0 | Coastal waters | Spain | Fernández-Rubio et al. (2019) | ↑ |
| | 38.6 | Santos Bay | Brazil (Santos)* | Fontes et al. (2019) | ↑ |
| | <LOQ | Coastal lagoon | Uruguay | Griffero et al. (2019) | ↓ |
| | 1.1 | Coastal waters | Brazil (Santa Catarina) | Pisetta et al. (2022) | ↓ |
| | 278.0 | Coastal waters | Brazil (Guarujá)* | Roveri et al. (2020) | ↑ |
| | 28.5 | Santos Bay | Brazil (Santos)* | Fontes et al. (2021) | ↑ |
| | 1.7 | Coastal waters | Brazil (Guarujá)* | Roveri et al. (2021a) | ↓ |
| | 4.8 | Santos Bay | Brazil (Santos)* | Roveri et al. (2021b) | ↓ |
| | 17.2 | Coastal waters | Brazil (São Vicente) * | Roveri et al. (2022a) | ↓ |
| | 14.9 | Coastal waters | Brazil (Guarujá)* | Roveri et al. (2022b) | ↓ |
| | 3.4 | Coastal waters | Brazil (Praia Grande) * | Roveri et al. (2022b) | ↓ |
| | 0.6 | Coastal waters | Brazil (Mongaguá)* | Roveri et al. (2022b) | ↓ |
| | 0.8 | Coastal waters | Brazil (Itanhaém)* | Roveri et al. (2022b) | ↓ |
| | 0.3 | Coastal waters | Brazil (Peruíbe)* | Roveri et al. (2022b) | ↓ |

The pharmaceutical compounds CAF (the most abundant in estuarine sample waters worldwide), LOS, CBZ, and ORP were consistently detected in estuarine water samples from six continents: Africa, Asia, Europe, North America, South America, and Oceania (Adedipe et al., 2024). Meanwhile, the WACL values of CAF ranged from 155.98 ng·L$^{-1}$ in North America to 155.98 ng·L$^{-1}$ in Europe, the WACL values for CBZ ranged from 8.94 ng·L$^{-1}$ in North America to 358.04 ng·L$^{-1}$ in Asia. In addition, WACL values for LOS ranged from 18.26 ng·L$^{-1}$ in North America to 61.00 ng·L$^{-1}$ in Europe. ORP was detected only in estuarine waters from Oceania (0.70 ng·L$^{-1}$) (Adedipe et al., 2024). The average global consumption of caffeine is approximately 70 mg per person. In Brazil, the figures are even higher. The daily intake of CAF-based products, including chocolate, coffee, dairy desserts, and several beverages, is estimated at 115.7 mg per person (Korekar et al., 2019). Consequently, due to its high consumption, CAF has been identified as a strong indicator of anthropogenic activity, as shown by previous studies (de Carvalho et al., 2024; Roveri et al., 2022a, 2022b; Pereira et al., 2016). Roveri et al. (2021b) observed a concentration of 118.6 ng·L$^{-1}$ of CAF in superficial water collected at sampling site 6 in São Vicente Bay, which may be influenced by the increase in population during the summer months. In nearby sites, higher concentrations of CAF were reported by Pereira et al. (2016), Roveri et al. (2022a), and Roveri et al. (2021b) (648.9, 568, and 516 ng·L$^{-1}$, respectively).

In Brazil, where self-medication is widely practiced within the population (Arrais et al., 2016), pharmacies and drugstores often sell ORP without requiring a prescription (Abrafarma, 2017; Cmed, 2019). Furthermore, LOS, the second most widely prescribed drug in Brazil, is provided free of charge via the Brazilian Unified Health System (SUS) (Mello et al., 2022). In a country where approximately 70 million inhabitants are affected by hypertension (Ribeiro et al., 2016), LOS is the most frequently prescribed medication (Hanlon et al., 2017). CBZ, an antiepileptic drug, is utilized for the management and treatment of epilepsy, a condition that affects around 2 % of individuals in Brazil (Abrafarma, 2017; Cmed, 2019). The LOS, CBZ, and ORP have also been detected in aquatic matrices from previous studies in the same region, reinforcing the ubiquity of these compounds in the region's coastal and marine systems. Pereira et al. (2016) detected LOS (32 ng·L$^{-1}$) in superficial and bottom marine water collected in Santos Bay, Brazil. In a separate study, Roveri et al. (2022a) observed the presence of CBZ (2.6 ng·L$^{-1}$), ORP (1.1 ng·L$^{-1}$), and LOS (2680 ng·L$^{-1}$) in urban channels from São Vicente city, demonstrating that these channels are important sources of these compounds into the SSVES. Furthermore, the authors observed that CBZ, ORP, and LOS prevalence is notably high among the elderly, constituting 21.67 % of individuals over 60 in Santos and São Vicente (IBGE, 2024a, 2024b). Ultimately, Roveri et al. (2021b) reported the presence of CBZ (4 ng·L$^{-1}$), ORP (0.8 ng·L$^{-1}$), and LOS (218 ng·L$^{-1}$) in the marine waters of Santos City.

### 4.2. Occurrence of PhIDs in the sediment and the samples of oysters

In the sediment samples examined, COC was detected in sites 0, 1, 4, 5, and 6, with concentrations below the quantification limit (ranging

from 2.49 to 8.29 ng.g$^{-1}$). Conversely, Fontes et al. (2021) documented the presence of COC in marine sediment, with concentrations ranging from 0.94 to 46.85 ng.g$^{-1}$. However, it should be noted that, like the present study, the samples collected from Fontes et al. (2021) were below the quantification limit. The low log Kow of organic substances is known to result in their binding to sediments (see Fontes et al., 2020). Given the log Kow of 2.30 for COC, it is plausible that it could be found in sediments. Conversely, due to its polarity, BE is predominantly found in superficial water (López-García et al., 2021). The reduced concentration of COC and the non-detection of pharmaceuticals could be explained by low organic matter contents and the sand constitution of the sediment, decreasing retention.

In the samples of oysters examined, COC was detected in one sampling site (1) in the SSVES (2.49–8.29 ng.g$^{-1}$). Consequently, to our knowledge, the present study constitutes the first documentation of COC in the oyster species from the São Paulo coastal zone. This outcome is a cause for concern, since studies have already demonstrated that environmentally relevant concentrations of BE (the main metabolite of COC) can result in decreased survival of *Crassostrea virginica* oysters, a commercially important seafood on the Brazilian coast, and that thrives in estuaries from the western coast of the Atlantic Ocean (Salcedo et al., 2025). Other studies have reported a potential COC risk for mussel species located along the Brazilian and US coastal regions. For example, Fontes et al. (2021) reported the occurrence of COC in mussels collected in Santos Bay, with levels ranging from 0.914 to 4.58 μg·kg$^{-1}$. In a separate study, Dodder et al. (2014) reported the occurrence of 0.28 ng·g$^{-1}$ in mussels collected on the California coast, USA. In addition, Klosterhaus et al. (2013) detected 0.3 ng·g$^{-1}$ of COC in mussels from San Francisco Bay, CA, USA.

### 4.3. Estuarine ecological risks of PhIDs

As stated by the European Medicines Agency (EMEA), substances with maximum measured environmental concentrations (MEC) exceeding 10.0 ng·L$^{-1}$ requires an ecological risk assessment (EMEA, 2024). In this sense, the MEC values detected in the SSVES estuary [i.e., CAF (MEC = 72.6 ng·L$^{-1}$), LOS (29.6 ng·L$^{-1}$), ORP (25.9 ng·L$^{-1}$), and BE (18.6 ng·L$^{-1}$)], indicate the necessity for a risk assessment of these substances. In this context, the RQs of six quantified PhIDs in SSVES (including COC and CBZ, which had MEC below 10.0 ng·L$^{-1}$) were calculated as MEC/PNEC (corrected by an uncertainty factor of 10,000 and 100 for acute and chronic exposures, respectively) (ECB, 2003; EMEA, 2024). This was achieved by utilizing data derived from the scientific peer-reviewed literature (namely, in Calleja et al., 1994; Ferrari et al., 2003; Brain et al., 2004; Blaise et al., 2006; Moore et al., 2008; Kaza et al., 2009; Kim et al., 2009; FDA, 2012; Minguez et al., 2014; and Godoy et al., 2015) or by estimating the values using the VEGA and ECOSAR programs. It is imperative to acknowledge the limitations and uncertainties intrinsic to VEGA and ECOSAR modeling when interpreting the findings of ecotoxicity assessments. In certain instances, the predicted toxicity levels by both programs have exhibited significant discrepancies compared to the outcomes of experimental research (Roveri et al., 2021a, 2021b, 2022b), which suggests that both VEGA and ECOSAR should be considered initial tools for assessing the ecological risk to aquatic organisms (Roveri et al., 2021a, 2021b, 2022b). For further details, refer to Table 2. As previously reported in several studies (Roveri et al., 2021a, 2021b, 2022b), the lack of toxicity data for estuarine and marine organisms has significantly impeded the practical risk assessment of COC, BE, CAF, and LOS. A survey of the peer-reviewed literature revealed that only acute toxicity data for the algae *Skeletonema marina* and crustacea *Artemia salina* were available for CBZ and ORP (i.e., in Calleja et al., 1994 and Minguez et al., 2014). Consequently, due to the intense interaction between land and sea in the study area, the vast majority of the toxicity data used in the present study to calculate the PNEC were derived from freshwater species, underscoring the necessity for additional ecotoxicological research, particularly with tropical estuarine and marine organisms, for evaluating the short- and long-term toxicity of these PhIDs (Roveri et al., 2021a, 2021b, 2022b).

Specifically, the COC (log Kow = 2.30; pKa = 8.61, and Log BCF = 1.185) is a PhID that may cause harmful effects on non-target organisms (e.g., mussels *Dreissena polymorpha* and *Perna perna*), including toxicity, DNA damage, changes in lysosomal permeability, and bioaccumulation even at trace concentrations (Capaldo et al., 2019; Fontes et al., 2020). In this regard, the MEC of COC in the SSVES estuary was determined to be 3.66 ng·L$^{-1}$, the findings indicate a moderate risk to the crustacean *Daphnia magna*. In comparison with COC, the physico-chemical properties of BE (log Kow = −1.32, pKa = 2.15, and Log BCF = 0.50) indicate a diminished capacity to interact biologically with non-target organisms (Pedriali et al., 2012). Notwithstanding, the result of the MEC of BE in the SSVES estuary was 18.6 ng·L$^{-1}$ suggests a low risk to the algae *Raphidocelis subcapitata* and crustacean *Daphnia magna*, and a moderate risk to fish *Pimephales promelas*. As demonstrated in previous studies, there is a possibility that the discharge of both COC and BE on aquatic ecosystems, in realistic environmental concentrations ranging from 40 to 1000 ng·L$^{-1}$, could result in sublethal effects to freshwater mussels *Dreissena polymorpha* (Binelli et al., 2012), European eel *Anguilla anguilla* (Gay et al., 2015; Capaldo et al., 2019), and crustacean *Daphnia magna* (Parolini et al., 2018; De Felice et al., 2019).

Despite its high solubility (20 g/L), low sorption potential (Log Kow = −0.07 and Log BCF = 0.50), and mobility in water (Log Koc = 1.79), the ubiquity of CAF in aquatic environments raises environmental concerns (Roveri et al., 2022a, 2022b). Studies in tropical waters have shown that CAF is readily biodegradable following microbial exposure (Thomas and Foster, 2005; Gómez et al., 2007). Bacterial strains belonging to the genera *Pseudomonas*, *Serratia*, *Penicillium*, *Phanerochaete*, *Rhizopus*, and *Stemphylium* have been reported to degrade CAF (Beltrán et al., 2006; Yu et al., 2009). However, research has demonstrated that CAF can bioaccumulate in tissues of several fish species, such as the common silver biddy (*Gerres oyena*), mosquitofish (*Gambusia holbrooki*), and milkfish (*Chanos hanos*) (Scott et al., 2018). Furthermore, at realistic environmental concentrations (approximately 500 ng·L$^{-1}$), it has been demonstrated that CAF can induce oxidative stress, lipid peroxidation, and even mortality in annelid *Diopatra neapolitana*, and mollusks *Mytilus galloprovincialis* (Pires et al., 2016; Capolupo et al., 2016; Li et al., 2020). The MEC of CAF in the SSVES estuary was found to be 72.1 ng·L$^{-1}$, which indicates a low acute risk to the crustacean *Daphnia magna* and the fish *Pimephales promelas*, as well as a low chronic risk to the algae *Lemna gibba* (Table 2). Similar findings have emerged from other studies conducted in neighboring cities of São Vicente, such as Praia Grande, Santos, and Guarujá, indicating low ecological risks for crustaceans and fish for both acute and chronic exposures (Roveri et al., 2020, 2021a, 2022a, 2022b).

Notwithstanding the finding that the RQs of CBZ and ORP were equal or below 0.01 (indicating low or no risk) (Table 2), specific key physicochemical characteristics of these PhIDs merit consideration. As demonstrated by the log octanol-water partition coefficient (log Kow) of CAF (log Kow > 2.3) and ORP (log Kow > 3.0), both compounds are hydrophobic and bioaccumulative in the aquatic ecosystems and, thus, can cause ecotoxicity (EMEA, 2024). Recently, CBZ was found in fish and bivalve species commonly consumed by the Brazilian population (Mello et al., 2022). Additionally, considering the kinetic reaction rate (k biol), expressed in grams of suspended solids per day (L/gss day), CBZ is considered resistant to secondary treatment because it is resistant to biodegradation and poorly adsorbable (k biol <0.5 L/gss day) (Arola et al., 2017).

Ultimately, the presence of LOS has previously been identified as a potential risk to the ecosystems of this region (Roveri et al., 2020, 2021a, 2022a, 2022b). In the study by Roveri et al. (2022a), the MEC of LOS detected in urban drainage channels from São Vicente city signaled great environmental concern for the SSVES estuary. The MEC was determined to be 2680.0 ng·L$^{-1}$, i.e., is 268 times higher than the recommended levels by European Union countries (EMEA, 2024).

Consequently, the RQ of LOS indicated a moderate to high ecological risk for algae, crustaceans, and fish, both acute and chronic exposures (Roveri et al., 2022a). It is noteworthy that other studies conducted in neighboring cities of São Vicente (i.e., in Praia Grande, Santos, and Guarujá) have also indicated moderate to high ecological risks across different trophic levels, both for acute and chronic exposures (Roveri et al., 2020, 2021a, 2022b). In the present study, the MEC of LOS was determined to be 29.6 ng·L$^{-1}$. This finding is of significant concern, as it suggests a moderate acute risk to the crustacean *Daphnia magna* and low chronic risks to crustaceans and fish (see Table 2). It is crucial to recognize the lack of environmental data on the potential for bioaccumulation of LOS and its capacity to cause long-term harmful effects within aquatic ecosystems at realistic environmental concentrations. Nevertheless, within the framework of the evaluation stipulated by the European Regulation on the Registration, Evaluation, Authorization and Restriction of Chemicals (Annex IX of REACH regulation), pharmaceuticals exhibiting a Log Kow value exceeding 3.0 and a bioaccumulation factor (BAF) and bioconcentration factor (BCF) falling below 2000 (e.g. LOS: Log Kow: 4.01; BCF and BAF: 316) are deemed to possess the capacity for bioaccumulation and to engender long-term deleterious effects within aquatic ecosystems (EMEA, 2024). In this sense, a recent study conducted in Santos Bay revealed that mussel (*Perna perna*) specimens exposed to concentrations of LOS (up to 3000 ng/L) exhibited cytotoxic effects, which are of concern given that these concentrations are realistic for the environment (Cortez et al., 2018). Concomitantly, other studies have reported toxic effects of LOS in fish (*Pimephales promelas* and *Astyanax altiparanae*), crustaceans (*Daphnia magna* and *Ceriodaphnia dubia*), and algae (*Lemna minor* and *Desmodesmus subspicatus*) (FDA, 2012; Yamamoto et al., 2012; Godoy et al., 2015; Adams et al., 2021; Reque et al., 2021). However, these effects have only been observed at concentrations (in the order of mg/L) that are considered "non-relevant" in the context of environmental concentrations (FDA, 2012; Yamamoto et al., 2012; Godoy et al., 2015; Adams et al., 2021; Reque et al., 2021).

## 5. Conclusions

This study reported, for the first time, the widespread presence of CAF (MEC = 72.1 ng·L$^{-1}$) > LOS (29.6 ng·L$^{-1}$) > ORP (25.9 ng·L$^{-1}$) > BE (18.6 ng·L$^{-1}$) > CBZ (7.4 ng·L$^{-1}$) and COC (3. 6 ng·L$^{-1}$) in the superficial water of the western side of São Vicente Island, a region considered a highly significant aquatic ecosystem of the Brazilian coast. Consequently, the ecological risk assessment revealed significant environmental concerns for this coastal ecosystem, suggesting low to moderate risks from all compounds to algae, crustaceans, and fish. COC was detected in concentrations below the quantification limit in the sediment samples examined. Conversely, in the samples of oysters, COC (2.49–8.29 ng.g$^{-1}$) was detected in one of the sampling sites. In light of the One Health approach and the findings of this study, it is recommended that further studies be conducted to investigate the potential human health risks associated with consuming contaminated seafood. Concomitantly, there is an urgent need for public action, including the improvement of basic sanitation facilities and the regularization of the land in the stilt-house slum in this region.

## CRediT authorship contribution statement

**Andressa dos Santos Barbosa Ortega:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Vinicius Roveri:** Writing – review & editing, Writing – original draft, Validation, Software, Methodology, Formal analysis, Data curation. **Marina de Souza Paço:** Writing – review & editing, Methodology, Investigation. **Daniel Temponi Lebre:** Writing – review & editing, Validation, Software, Methodology, Investigation, Formal analysis, Data curation. **Luciane Alves Maranho:** Writing – review & editing, Visualization, Methodology, Conceptualization. **Camilo Dias Seabra Pereira:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Andressa dos Santos Barbosa Ortega reports financial support was provided by State of São Paulo Research Foundation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.marpolbul.2025.118291.

## Data availability

Data will be made available on request.

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