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Bioaccumulation of pharmaceuticals and stimulants in macrobenthic food web in the European Arctic as determined using stable isotope approach

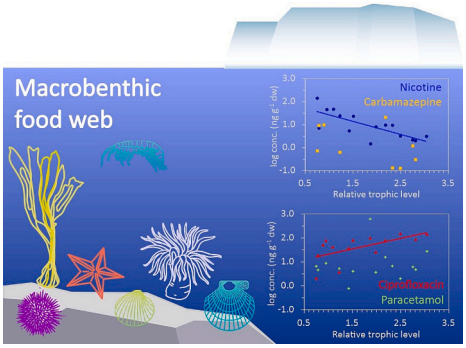
Adam Sokołowski [a,*], Marlena Mordec [a], Magda Caban [b], Ida Beathe Øverjordet [c], Ewa Wielogórska [c], Maria Włodarska-Kowalczuk [d], Piotr Balazy [d], Maciej Chełchowski [d], Gilles Lepoint [e]

[a] University of Gdańsk, Faculty of Oceanography and Geography, Al. Piłsudskiego 46, 81-378 Gdynia, Poland
[b] University of Gdańsk, Faculty of Chemistry, ul. Wita Stwosza 63, 80-308 Gdańsk, Poland
[c] SINTEF Ocean AS, Brattorkaia 17C, NO-7465 Trondheim, Norway
[d] Institute of Oceanology Polish Academy of Sciences, ul. Powstańców Warszawy 55, 81-712 Sopot, Poland
[e] Université de Liège, UR FOCUS, Laboratory of Trophic and Isotope Ecology (LETIS), allée du six Août 11, 4000 Liège 1, Belgium

HIGHLIGHTS

- Bioaccumulation of pharmaceuticals was investigated in the Arctic macrobenthic food web.
- Trophic magnification factor (TMF) ranged from 0.3 to 2.8 and varied among compounds.
- TMFs <1.0 for NIC implied no accumulation with trophic position.
- TMFs >1.0 for CIP indicated biomagnification of this pharmaceutical.
- Trophic transfer of CBZ, DIC, CBZ and CAF was not clear due to large 95 % confidence of their TMFs.
- This study provides the first evidence of drug accumulation in the Arctic food web.

GRAPHICAL ABSTRACT



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ABSTRACT

Although pharmaceuticals are increasingly detected in abiotic matrices in the Arctic, the accumulation of drugs in the resident biota and trophic transfer have not been yet examined. This study investigated the behaviour of several pharmaceuticals in the rocky-bottom, macrobenthic food web in the coastal zone of Isfjorden (western Spitsbergen) using stable isotope analyses (SIA) coupled with liquid chromatography-mass spectrometry (LC-MS/MS). Across 16 macroalgal and invertebrate species the highest average concentration was measured for ciprofloxacin (CIP) (on average 60.3 ng g^{-1} dw) followed by paracetamol (PCT) (51.3 ng g^{-1} dw) and nicotine (NIC) (37.8 ng g^{-1} dw). The biomagnification potential was assessed for six target compounds of 13 analytes detected that were quantified with a frequency > 50 % in biological samples. The trophic magnification factor (TMF) ranged between 0.3 and 2.8, and was significant for NIC and CIP. TMF < 1.0 for NIC (0.3; confidence interval, CI 0.1–0.5) indicated that the compound does not accumulate with trophic position. The dilution of pharmaceutical residues in the food web may result from limited intake with dietary route, poor assimilation efficiency and high

* Corresponding author.
E-mail address: adam.sokolowski@ug.edu.pl (A. Sokołowski).

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biotransformation rates in benthic invertebrates. TMF for CIP (2.8, CI 1.2–6.4) suggests trophic magnification, a phenomenon observed previously for several antibiotics in freshwater food webs. Trophic transfer therefore plays a role in controlling concentration of CIP in the Arctic benthic communities and should be considered in environmental risk assessment. Biomagnification potential of diclofenac (DIC; 0.9, CI 0.5–1.7), carbamazepine (CBZ; 0.4, CI 0.1–2.1), caffeine (CAF; 0.9, CI 0.5–1.9) and PCT (1.3, CI 0.7–2.7) was not evident due to large 95 % confidence of their TMFs. This study provides the first evidence of drug bioaccumulation in the Arctic food web and indicates that behaviour of pharmaceuticals varies among target compounds.

1. Introduction

Pharmaceuticals and stimulants (e.g., caffeine and nicotine) as environmental pollutants and xenobiotics in ecosystems have been the focus of scientific studies for >20 years (Kümmerer, 2009; Świacka et al., 2019; Mezzelani and Regoli, 2022). They are considered emerging contaminants i.e., compounds not routinely monitored, and are suspected to be the cause of adverse effects to the environment and human health (Miller et al., 2018). While a number of studies have addressed the occurrence and fate of pharmaceuticals in freshwaters (e.g., Lahti et al., 2012; Haddad et al., 2018; Zhang et al., 2020), coastal and marine waters have long been neglected under the assumption that dilution would ensure safety, per se (Fabbri and Franzellitti, 2016). Coastal conurbations and industrial hubs have been found, however, to release great amounts of pharmaceuticals (Gaw et al., 2014). Global demographic trends towards coastal conurbations and a subsequent coastal population increase (Neumann et al., 2015) also suggest the potential for increasing discharges of pharmaceuticals into the coastal environments and remote areas, including polar regions in the near future (Claessens et al., 2013; Patel et al., 2019).

The presence of drugs has been broadly confirmed in abiotic matrices in the Arctic, identifying primarily local contaminant sources (largely release from wastewater treatments plants (WWTPs) and households, as well as diffusive seeping from disposal sites; Gunnarsdottir et al., 2013; Vorkamp and Rigét, 2014; Huber et al., 2016). Since they are widespread and bioactive, understanding the fate of pharmaceuticals in the environment, their bioaccumulation, effects on marine biota and their behaviour in the food web is therefore crucial challenge in the pristine locations of the Arctic (Xie et al., 2022).

The potential for trophic transfer of pharmaceuticals in marine food webs has not been well recognised yet, but the preliminary evidence from the lower-latitude freshwater systems indicates that pharmaceuticals tend not to biomagnify (Du et al., 2014; Xie et al., 2015, 2017; Lagesson et al., 2016; Haddad et al., 2018). A certain biomagnification behaviour has been observed, however, for diclofenac (Sathishkumar et al., 2020) and several antibiotics: norfloxacin and enrofloxacin (Zhang et al., 2020), roxithromycin (Xie et al., 2015) and ciprofloxacin (Xie et al., 2017). Heynen et al. (2016) reported increased concentrations of an anxiolytic (oxazepam) in two freshwater predatory species, the Eurasian perch (*Perca fluviatilis*) and the dragonfly larvae (*Aeshna grandis*) relative to their food but failed to detect trophic transfer of other compounds. Elevated concentrations in higher-tropic level marine organisms have also been documented for flumequine in the top predator, the Atlantic sharpnose shark (*Rhizoprionodon terraenovae*) from the Eastern Central Atlantic by Fedorova et al. (2013). Trophic transfer should therefore be a matter of concern for ecological risk assessments of certain pharmaceutical residues in coastal and marine food webs too. Modelling environmental exposures, which neglects to consider dietary uptake and trophic transfer, may underestimate exposure levels and fail to acknowledge intra- and inter-species variability in natural environments (Heynen et al., 2016). This is particularly important in the Arctic regions, where cold temperature slows down degradation rate (Korkmaz et al., 2022; Xie et al., 2022) and organisms' metabolism of the pharmaceuticals. Patterns of accumulation in the trophic chain may therefore differ from those in mid-latitude freshwater systems.

This study set up to investigate the accumulation of several pharmaceuticals and stimulants in the marine food web within the rocky-bottom macrobenthic community in the coastal zone of Isfjorden, western Spitsbergen. By coupling stable isotope analyses (SIA) with quantification of pharmaceutical concentrations using liquid chromatography-mass spectrometry (LC-MS/MS) this pilot study estimated biomagnification potential using a trophic magnification factor (TMF).

2. Material and methods

2.1. Sample collection and pre-treatment

Components of the food web were sampled at one coastal site (78°11.300′N, 15°08.685′E) in the Arctic fjord, Isfjorden, on the western coast of Spitsbergen in the Svalbard archipelago in August 2021. The location of the sampling site was selected based on biocenotic data available in the literature and unpublished repositories of Institute of Oceanology of the Polish Academy of Sciences (IO PAN) to ensure the availability of taxonomically diverse and abundant communities of macrobenthic vegetation and epifauna. The sampling site was west of Adventfjorden, under the Fuglefjella cliff and close to Longyearbyen, Svalbard's most populous, industrialized and touristic settlement, with about 2400 permanent residents in 2021 (Sokolickova, 2022), with an active harbour, marina and an international airport. Thus in proximity of point sources of pharmaceutical residues enter the marine waters and between 10.7 and 15.8 km from the sampling site. There is no sewage treatment plant in the municipality which releases approximately 285,000 m^3 of untreated wastewater into the nearby Adventfjorden (Kalinowska et al., 2020). Samples were taken by hand from a hard bottom below the kelp vegetation belt at water depth ranging between 12 m and 20 m by “IO PAN Scientific Diving TEAM”. A total of 16 macrobenthic species were collected representing the principal trophic categories i.e., producers and consumers from different trophic guilds: suspension feeders, omnivores, carnivores and detritivores (Table 1). The species were sampled in three replicates or in numbers sufficient for SIA and pharmaceutical analyses. The organisms collected were rinsed with seawater, segregated and then kept in seawater taken in situ for 24 h to purge them. In the meantime the organisms were identified to a species level based on external morphological features using the taxonomic key by Klekowski and Węsławski (1991). The nomenclature followed the World Register of Marine Species (WoRMS, www.marinespecies.org). In total, five macroalgal species from the class Phaeophyceae and Florideophyceae, and eleven invertebrate species classified into seven classes: Malacostraca, Asteroidea, Ascidiacea, Anthozoa, Echinoidea, Bivalvia and Polyplacophora, were sampled (Table 1). Debris and epibionts present on macroalgal thalli were gently removed with a toothbrush. The samples were then frozen in zip lock plastic bags at −20 °C for further analysis.

Before laboratory analyses, all tools and glassware were washed in warm water with soap, rinsed thoroughly with deionised water and pure methanol (≥ 99.9 % HPLC grade). Stainless-steel scalpels were also cleaned using the same procedure before the samples were handled. Animals with external skeletons, such as bivalves, gastropods and echinoderms, were deshelled while frozen. The hermit crabs, *P.pubescens*, were also entirely removed from shells of host snails. The frozen samples (whole individuals or soft tissue) were freeze-dried for 48 h (air

pressure 3 Pa, temperature 22 °C) and homogenized using a Retsch MM400 mixer mill. In the case of small organisms, entire individuals or soft tissue of the same taxon (i.e., tunicates, cnidarians, sea urchins, bivalves, gastropods and chitons) were grouped into 3 pools containing between 3 and 12 individuals/tissue samples each to provide sufficient material for chemical analyses. Each sample was then divided into two parts intended for (1) SIA and (2) measurements of the concentrations of pharmaceutical.

2.2. Determination of carbon and nitrogen isotopes

All algae, that were presumed to contain carbonate carbon (e.g., epiphytes), were first subjected to acidification in order to remove inorganic carbon (Schlacher and Connolly, 2014). The $\delta^{13}C$ values in carbonates in the tissues of organisms tend to be less negative than the $\delta^{13}C$ values in their organic components and cannot be related to the organism's diet (DeNiro and Epstein, 1978). To this end 50 ± 1 mg of each sample was placed on a glass Petri dish. The samples were then placed in a desiccator with a glass dish filled with fuming HCl (37, *v/v*, AR). The pressure inside the exicator was reduced using an external air pump and the samples were left for 24 h, whereupon a so called *Champagne test* (Jaschinski et al., 2008) was performed by adding a drop of HCl to two random samples in order to ascertain whether all inorganic carbon had been removed. When no bubbles were observed on the surface, the acidification was considered complete. After acidification the samples were air-dried for 24 h. Each sample (acidified and non-acidified algae, and invertebrates) was then packed individually in a tin cap (3.00 ± 0.05 mg). The carbon ($^{13}C/^{12}C$) and nitrogen ($^{15}N/^{14}N$) isotopic composition of benthic organisms was determined using an elemental analyser (Vario MICRO Cube, Elementar) coupled with a continuous-flow isotope-ratio mass spectrometer (PrecisION, Elementar) that provided simultaneous data on organic carbon and

Table 1
Macrobenthic species collected for stable isotope and pharmaceutical analyses in Isfjorden, Spitsbergen in August 2021.

Taxonomic group	Common name	n[a]	Trophic position/feeding type	C/N, RTL	C content (%)	Isotope ratio (‰)		Source of feeding type
						$\delta^{13}C$	$\delta^{15}N$	
Phylum HETEROKONTOPHYTA								
Class Phaeophyceae								
Alaria esculenta	Winged kelp	3 (nd)	Primary producer	26.5 ± 2.6	37.4 ± 9.2	−21.6 ± 0.2	3.5 ± 0.4	
Laminaria digitata	Oarweed	3 (nd)	Primary producer	30.1 ± 2.1	27.1 ± 5.7	−17.8 ± 0.2	5.1 ± 0.1	
Saccharina latissima	Sugar kelp	3 (nd)	Primary producer	31.8 ± 3.6	31.7 ± 0.6	−19.7 ± 0.8	4.7 ± 1.1	
Desmarestia aculeata	Acid weed	3 (nd)	Primary producer	14.6 ± 0.3	31.5 ± 0.4	−27.7 ± 0.2	4.0 ± 0.0	
Phylum RODOPHYTA								
Class Florideophyceae								
Phycodrys rubens	Sea oak	3 (nd)	Primary producer	10.4 ± 0.5	24 ± 10.1	−36.2 ± 0.3	3.6 ± 0.2	
Phylum ARTHROPODA								
Class Malacostraca								
Hyas araneus	Great spider crab	1(7)	Omnivore	2.3	32.3 ± 2.0	−18.7 ± 0.2	8.9 ± 0.4	1
Pagurus pubescens	*Downy hermit crab*	1 (10)	Omnivore	2.2	34.4 ± 0.9	−19.1 ± 0.1	8.4 ± 0.1	1
Phylum ECHINODERMATA								
Class Asteroidea								
Henricia sanguinolenta	Blood star	1(3)	Predator	2.5	34.2 ± 3.7	−21.4 ± 0.9	9.4 ± 0.8	2
Class Echinoidea								
Strongylocentrotus droebachiensis	Green sea urchin	3 (16)	Grazer	1.0	38.1 ± 3.3	−23.3 ± 0.3	4.2 ± 0.2	3
Phylum CNIDARIA								
Class Anthozoa								
Hormathia nodosa	Rugose anemone	1 (16)	Predator	3.1	35.5 ± 2.3	−22.0 ± 0.5	11.3 ± 0.2	4
Phylum MOLLUSCA								
Class Bivalvia								
Chlamys islandica	Iceland scallop	3(8)	Suspension feeder	1.5	41.9 ± 0.2	−22.1 ± 0.1	6.1 ± 0.0	5
Hiatella arctica	Wrinkled rock borer	3 (12)	Suspension feeder	1.4	41.8 ± 0.2	−21.1 ± 0.1	5.8 ± 0.1	6
Class Gastropoda								
Buccinum glaciale	Glacial whelk	1(6)	Predator/Scavenger	2.8	40.1 ± 0.5	−18.5 ± 0.0	10.5 ± 0.0	7
Buccinum undatum	Common whelk	1 (13)	Predator/Scavenger	2.8	39.2 ± 0.2	−19.2 ± 0.0	10.3 ± 0.0	8
Class Polyplacophora								
Tonicella marmorea	Northern red chiton	3 (11)	Grazer	2.0	38.1 ± 0.2	−20.0 ± 0.0	7.7 ± 0.0	9
Phylum CHORDATA								
Class Ascidiacea								
Halocynthia pyriformis	Sea peach	1 (10)	Suspension feeder	1.9	35.5 ± 0.6	−22.6 ± 0.1	7.3 ± 0.1	6

[1]Berge et al. (2009); [2]Sheild and Witman (1993); [3]Brown et al. (2012); [4] Macdonald et al. (2010); [5]Renaud et al. (2011); [6]Petersen (2007); [7]Włodarska et al. (1996); [8]Himmelman and Hamel (1993); [9]Latyshev et al. (2004).

[a] Number of replicates (number of individuals); nd – not determined.

nitrogen content. Data were expressed in the standard δ notation (‰) relative to the Vienna Pee Dee Belemnite (PDB) for carbon and relative to N_2 in atmospheric air for nitrogen. Certified reference materials from the International Atomic Energy Agency (IAEA), IAEA N-1 (ammonium sulphate; $\delta^{15}N = 0.4 \pm 0.2$ ‰; mean ± SD) and IAEA C-6 (sucrose; $\delta^{13}C = -10.8 \pm 0.5$ ‰), were used as primary standards. Secondary standards included sulfanilic acid (Sigma-Aldrich; $\delta^{13}C = -28.5 \pm 0.3$ ‰; $\delta^{15}N = -0.4 \pm 0.3$ ‰) and were used as quality control. Replicated measurements of different batches of the sea bass pool provided standard deviations of ±0.3 ‰ and ± 0.3 ‰ for $\delta^{13}C$ and $\delta^{15}N$, respectively. Because of a relatively small difference in carbon stable isotope composition between the consumer and its food source, animal $\delta^{13}C$ is indicative of the dietary carbon sources of organisms but is less indicative of its trophic position. Nitrogen stable isotope ($\delta^{15}N$) values are by contrast known to increase with the increasing trophic position of a consumer in the food web so, the relative trophic level (RTL) for each faunal species was estimated using a model developed by Hobson and Welch (1992):

$$RTL = \left(\delta^{15}N_{consumer} - \delta^{15}N_{baseline}\right)/3.4 + 1,$$

where $\delta^{15}N_{consumer}$ is the nitrogen isotope ratio of a consumer, $\delta^{15}N_{baseline}$ is the nitrogen isotope baseline and 3.4 is the ^{15}N trophic enrichment factor, TEF (Olive et al., 2003). In the Arctic marine ecosystems, a TEF in the range 3.4 ‰–3.8 ‰ has been commonly applied to most ecological groups (Pedersen, 2022). A large-scale comprehensive study on TEF for four Arctic regions (a total 107 species including 78 benthic taxa) showed that in benthic food webs, $\Delta^{15}N$ did not differ significantly between the Arctic regions with an average fractionation factor of 3.4 % (Hoondert et al., 2021). The nitrogen isotope baseline was calculated as the mean $\delta^{15}N$ of all primary producers (macroalgae). The formula is a simplified modification of the Post's (2002) food web model and was successfully employed to define trophic levels of different species or trophic guilds in Arctic marine and coastal systems e.g., the Chuckchi Sea (Iken et al., 2010), Hornsund, Spitsbergen (Sokołowski et al., 2014) and Kongsfjorden, Spitsbergen (Kędra et al., 2012).

2.3. Measurement of pharmaceutical concentrations

100 ± 1 mg of each sample was homogenized in a microcentrifuge tube that contained three brand new 2.8 mm ceramic beads and about 10 mg of 0.1 mm brand new ceramic beads, 750 μL of mid-polar solvent (a mixture of 250 μL of Milli-Q water and 500 μL of acetonitrile and a methanol mixture in a 1:1 ratio, *v/v*) and 30 μL of internal standard working solution (isotopically labelled standards of selected analytes at a concentration of about 1 μg mL^{-1}). The solid-liquid extraction (SLE) was performed using homogeniser Bead Ruptor Elite (Omni Corporation). The bead homogenization was performed using two cycles, 30 s each at speed of 8 m s^{-1}. The samples were then sonicated for 15 min at 25 °C and centrifuged for 3 min at 15000 rpm. 375 μL of supernatant from each sample was then transferred into a new Eppendorf tube. The solvent was evaporated under N_2 to a volume of about 200 μL and then diluted twice with 200 μL of 0.1 % formic acid (*v/v*). Blanks containing internal standard working solution were prepared at the same time according to the same protocol. Detection and measurement of pharmaceutical concentrations in extracts were performed with LC-MS/MS. Target analytes were separated on a 50 × 2.1 mm, 1.9 μm Poroshell HPH-C18 column from Agilent using an Infinity 1260 II liquid chromatography unit, also from Agilent. The mobile phases were water and methanol, both containing 5 mM ammonium formate. To elute the analytes a linear gradient elution was employed: 0 min 99%A, 1 min 99%A, 9 min 1%A, 12 min 1%A, 12.1 min 99%B. A flow rate was maintained at 0.6 mL min^{-1} with column temperature at 40 °C. Mass spectrometry was performed on an Agilent 6470 triple quadrupole mass analyser with capillary voltage of 4.00 kV, gas/sheath gas flow of 8/10 L m^{-1} and temperatures of 250/300 °C and the nebuliser operating pressure of 241 kPa. Dwell time for all compounds was set to 500 ms, dEMV (+ and -) and 400 AU, and call accelerator voltage was 4 V. The method included 35 analytes each monitoring two transitions with the exception of aspirin. The HPLC–MS/MS system was controlled by MassHunter acquisition software B09.0, while the data were processed using Mass Hunter QQQ for quantitative analysis B10.0 (both from Agilent). The analytes were quantified against matrix matched (blank, in-house cultivated *Calanus*) calibration curves in a range of 500–0.25 ng g dw^{-1} (a minimum of 6 points including zero, each point conforming to ±15 % accuracy and LOQ ±20 %). Where available, responses were corrected by internal standards. Recovery and precision, which were calculated on the basis of the coefficient of variation ($n = 3$), varied among analytes and were > 93.6 % and < 10.7 %, respectively. The limit of detection (LOD) was defined as S/N of 3, while the limit of quantification (LOQ) was S/N of 10 with an additional requirement of accuracy as mentioned above. In cases where LOD was not assessed by on-column injection LOQ was calculated as three times the standard deviation of the blank. If the concentrations of analytes obtained were below the LOD or the LOQ of the method, they were excluded from the data set for a given sample. The concentration of pharmaceuticals and stimulants in biota was expressed on the basis of dry weight (dw), which reduces methodological bias due to differences in water content among samples. The use of freeze-dried material for drug extraction is a routine preprocessing step in pharmaceutical analytics of biological samples (e.g., Miller et al., 2018; Gómez-Regalado et al., 2023).

2.4. Calculation of trophic transfer

Data on pharmaceutical concentrations and RTLs for all macrobenthic species (algae and invertebrates) were included in the assessment of trophic transfer. Biomagnification potential of pharmaceuticals and stimulants was estimated using the trophic magnification factor (TMF) that was calculated in two steps based on the modified model of Broman et al. (1992) for trophic transfer of organic contaminants:

Step 1 (Eq. 1):

$$log\ C_{compartment} = B\ RTL + A,$$

where $C_{compartment}$ is the concentration of a pharmaceutical in macrobenthic organisms, A and B are the function parameters and RTL is the relative trophic level. The constant A is a scaling factor that depends on concentration at the base of the food web (Rolff et al., 1993) and the parameter B estimates the biomagnification potential of the compound. If $B > 0$, the pharmaceutical is biomagnified in the food web while $B < 0$ is an indication of biodilution or trophic dilution.

Step 2 The TMF was computed after antilogarithmic back-transformation (Eq. 2):

$$TMF = 10^{B}.$$

For $TMF < 1.0$ the pharmaceutical decreases in concentration with each relative trophic level (also called trophic dilution) and $TMF > 1.0$ indicates an increase in drug concentration with increasing trophic position (biomagnification through food webs). This theoretical model has been employed successfully to track, for example, changes in concentration of pharmaceuticals with successive trophic levels of invertebrates and fish of the North Bosque River, Texas (Du et al., 2014) and in the benthic food web of the Lake Baiyangdian, North China (Zhang et al., 2020). The 95 % confidence of a TMF was calculated based on the 95 % confidence interval (CI) of the slope (Kosfeld et al., 2021), using Eq. 2.

2.5. Data analysis

In order to reduce data dispersion resulting from the high inter-replicate variability of pharmaceutical concentrations in different species univariate variance test (based on the mean and the standard

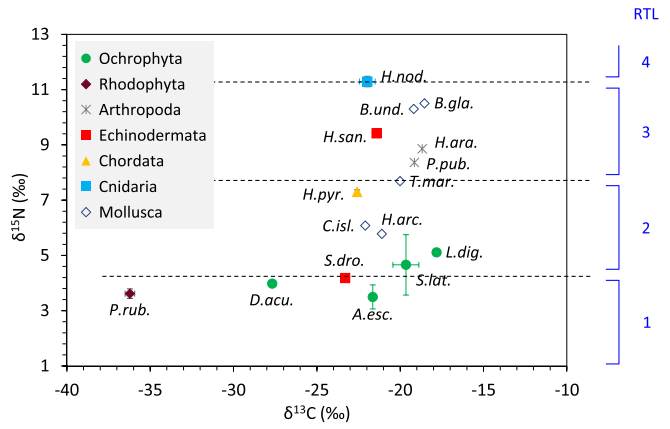

Fig. 1. $\delta^{13}C$ and $\delta^{15}N$ of producers (macrobenthic algae) and consumers (macrobenthic invertebrates) of coastal rocky-bottom in Isfjorden, Spitsbergen. Data are presented as mean ± SD (n = 3) for each taxon. RTL – relative trophic level, dashed lines separate trophic levels at 3.4 ‰ $\delta^{15}N$; *P.rub. - Phycodrys rubens*, *D.acu. - Desmarestia aculeata*, *A.esc. - Alaria esculenta*, *S.lat. - Saccharina latissima*, *L.dia. - Laminaria digitata*, *P.pub. - Pagurus pubescens*, *H.ara. - Hyas araneus*, *S.dro. - Strongylocentrotus droebachiensis*, *H.san. - Henricia sanguinolenta*, *H.pyr. - Halocynthia pyriformis*, *H.nod. - Hormathia nodosa*, *C.isl. – Chlamys islandica*, *H.arc. - Hiatella arctica*, *T.mar. - Tonicella marmorea*, *B.und. - Buccinum undatum*, *B.gla. - Buccinum glaciale*.

deviation multiplied by two) was used to detect outlying data. The defined outliers were then removed from a dataset and further calculations. Non-transformed data were included in all statistical models followed by analyses of normality with the Kolmogorov-Smirnov test and a test of goodness of fit as prerequisites. Due to the non-normal distribution (Shapiro–Wilk test for goodness of fit) and non-homogenous variances (Bartlett's test) in most data, a non-parametric approach was used in the statistical analysis. The significance of individual differences between two data groups was examined using the Mann–Whitney *U* test and among > two groups with Kruskal-Wallis test. The functional relationships between pairs of variables were described using Spearman's correlation analysis using Eq. 1. The level of significance was set at $p < 0.05$. Analyses were performed using STATISTICA version 13.1 (Statsoft Inc., USA).

3. Results

3.1. Structure of the macrobenthic food web

Since no significant differences between acidified and non-acidified algal material (data not shown) were found for any variable ($\delta^{13}C$, $\delta^{15}N$, the contents of organic N and C, and C/N) (Mann–Whitney *U* test, $n = 25$ pair cases), only data from the non-acidified samples were included in further analyses. The mean $\delta^{13}C$ of individual taxon in Isfjorden ranged from −36.2 ± 0.3 ‰ for the sea oak *Phycodrys rubens* to −17.8 ± 0.2 ‰ for the oarweed *Laminaria digitata* and no differences were noted between producers and consumers i.e., all invertebrate species grouped into one data set (Mann-Whitney *U* test) (Table 1, Fig. 1.). The mean $\delta^{15}N$ of macrobenthic taxa spanned a much smaller range of 7.8 ‰ (from 3.5 ± 0.4 ‰ for the winged kelp *Alaria esculenta* to 11.3 ± 0.2 ‰ for the rugose anemone *Hormathia nodosa*) with higher values in consumers than in producers (Mann-Whitney *U* test, $Z = -5.07$, $n = 48$, $p < 0.001$). Significant variations were also observed among taxonomical classes within the consumer group for carbon (Kruskal-Wallis test; $H = 29.023$, $df = 6$, $p < 0.001$) and nitrogen isotope ratios (Kruskal-Wallis test; $H = 30.979$, $df = 6$, $p < 0.001$) with the highest values in gastropods and anthozoans, respectively. The RTL calculated ranged between 1.0 for the green sea urchin *Strongylocentrotus droebachiensis* and 3.1 for *H.nodosa*. Despite some overlap among macroinvertebrates belonging to different taxa and trophic groups, either bivalves, ascidian and echinoid with filter feeding or grazing strategies occupied the first trophic level (RTL < 2). Most faunal taxa, including omnivorous crustaceans, predatory asteroid, predatory/scavenging gastropods and a grazing chiton, had an intermediate trophic position (2 < RTL < 3).

3.2. Concentration of pharmaceuticals and stimulants in macrobenthic organisms

Matrix interferences prevented detection and quantification of certain spiked drugs from the biota samples. Thirteen target compounds (of 35 analysed) were detected (> LOD) in various components of the Arctic food web collected from the hard bottom in Isfjorden (Table 2). Two stimulants CAF and NIC, an analgesic and antipyretic drug PCT and an antibiotic CIP were target drugs ubiquitously detected (> LOD) in all macrobenthic algae and invertebrate species. The quantification frequencies (> LOQ) across all samples (16 species) of CAF and NIC, an antiepileptic CBZ, a non-steroidal anti-inflammatory drug DIC, PCT and two antibiotics CIP and TC were > 50.0 %, while the frequencies of other pharmaceuticals CIT, ENF, OXO, OTC, SMZ and TMP were below 25.0 %

Table 2
Analytes quantified at frequency > 0.0 % in hard-bottom macrobenthic organisms from Isfjorden, Spitsbergen. LOD (ng g^{-1} dry weight) – limit of detection, LOQ (ng g^{-1} dry weight) – limit of quantification. Analytes detected but not quantified in biological samples due to matrix interferences: Allethrin, Altenolol, Amoxicillin, Aspirin, Atrazine, Azamethiphos, Benzocaine, Cypermethrin, Deltamethrin, Clotrimazole, Desmethylvenlafaxine, Diflubenzuron, Emamectic (benzonate), Florfenicol, Fluconazole, Fluoxetine, Ibuprofen, Miconazole, Norfluoxetine, Praziquantel, Propranolol, Simvastatin.

Analyte	Therapeutic class	LOD	LOQ	Quantification frequency in biological samples (%)[a]
Caffeine (CAF)	Stimulant	0.17	0.50	81.3
Nicotine (NIC)	Stimulant	2.00[b]		100.0
Carbamazepine (CBM)	Antiepileptic	0.04	0.13	56.3
Citalopram (CIT)	Antidepressant	0.04	0.13	25.0
Diclofenac (DIC)	Non-steroidal anti-inflammatory drug (NSAID)	0.04	0.13	93.8
Paracetamol (PCT)	Analgesic and antipyretic	0.17	0.50	87.5
Enrofloxacin (ENF)	Antibiotic	0.17	0.50	6.3
Ciprofloxacin (CIP)	Antibiotic	0.17	0.50	87.5
Oxolinic acid (OXO)	Antibiotic	0.04	0.13	18.8
Oxytetracycline (OTC)	Antibiotic	0.08	0.25	18.8
Sulfamethoxazole (SMZ)	Antibiotic	0.17	0.50	12.5
Tetracycline (TC)	Antibiotic	0.08	0.25	56.3
Trimethoprim (TMP)	Antibiotic	0.04	0.13	18.8

[a] Calculated for mean data (total number of samples = 16).
[b] Nicotine was measured in the blank samples at concentrations between LOD and LOQ. The blank concentration was <2.0 ng g^{-1} dry weight.

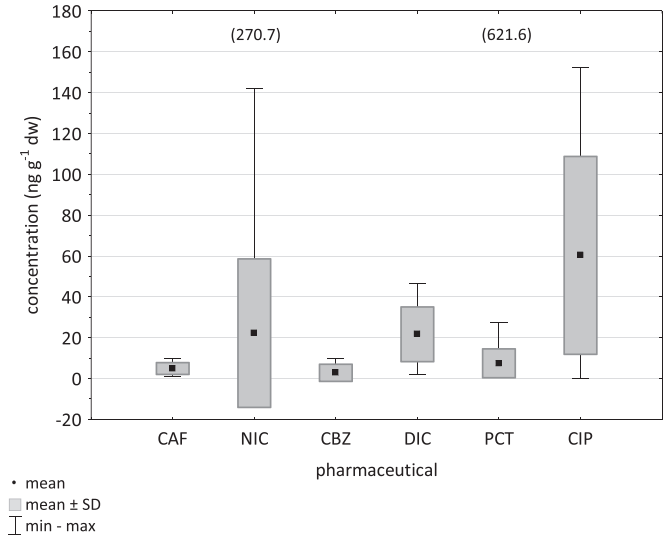

Fig. 2. Concentration of pharmaceuticals in hard-bottom macrobenthic organisms from Isfjorden, Spitsbergen. Data are presented as mean for all algal and invertebrate species ± SD and max-min range. To reduce data dispersion resulting from high inter-replicate variability of pharmaceutical concentrations in different species outlying data for NIC and PCT were detected and removed from dataset using univariate variance test (based on the mean and the standard deviation multiplied by two). The outlining data are showed in brackets inside the graph.

(Table 2). It is noteworthy that nicotine was measured in the blank samples at concentrations between LOD and LOQ and its quantification was therefore connected with lower accuracy and precision than other analytes. When all samples are considered, the highest average concentration was measured for CIP (mean ± SD; 60.3 ± 48.4 ng g^{-1} dw, n = 14) followed by PCT (51.3 ± 164.3 ng g^{-1} dw, n = 14) and NIC (37.8 ± 71.4 ng g^{-1} dw, n = 16). A lower level was detected for DIC (21.6 ± 13.4 ng g^{-1} dw, n = 15) and the average concentration of other pharmaceuticals fell below 6.0 ng g^{-1} dw (Fig. 2). Among all pharmaceuticals PCT was measured at the highest level (621.6 ± 67.6 ng g^{-1} dw, n = 3) in the sea peach *Halocynthia pyriformis*, while NIC in the acid weed *Desmarestia aculeata* and the winged kelp *Alaria esculenta* (270.7 ± 220.7 ng g^{-1} dw, n = 3 and 142.1 ± 17.6 ng g^{-1} dw, n = 3, respectively). Thallus of the oarweed *Laminaria digitata*, another benthic macrophyte, contained the maximum level of CAF (17.6 ± 5.4 ng g^{-1} dw, n = 3). The concentration of CIP was highest in the soft tissue of the blood star *Henricia sanguinolenta* (152.3 ± 0.0 ng g^{-1} dw, n = 3) and of the rugose anemone *H.nodosa* (143.1 ± 40.5 ng g^{-1} dw, n = 3), and that of CBZ in the downy hermit crab *Pagurus pubescens* (20.8 ± 0.0 ng g^{-1} dw, n = 3). The predatory cnidarian *H.nodosa* also showed elevated concentrations of DIC and TC (46.4 ± 65.4 ng g^{-1} dw, n = 3, and 0.9 ± 0.0 ng g^{-1} dw, n = 3, respectively). Significant variation in drug concentrations among trophic groups (Table 1) was generally observed only for CAF (Kruskal-Wallis test; H = 14.057, df = 5, $p < 0.05$) and NIC (Kruskal-Wallis test; H = 18.680, df = 5, $p < 0.01$) while other pharmaceuticals did not differ among trophic guilds.

3.3. Trophic transfer of pharmaceuticals and stimulants

In order to avoid the uncertainty associated with calculating trophic magnification factors, the TMF was computed only for drugs with a quantification frequency > 50 % i.e., CAF, NIC, CBZ, DIC, PCT and CIP. Although the quantification frequency for TC was also >50 % the antibiotic was excluded from the calculation of TMF due to the pharmaceutical concentration < LOQ for all species of algae which are a carbon source in the food web (Table 3). Of six linear regressions between log-transformed pharmaceutical concentrations (without lipid normalization) in macrobenthic algal and invertebrate species, and RTLs of different food web components slopes were significant only for NIC (negative; trophic dilution) and CIP (positive; biomagnification). The concentration of CBZ tended to decrease from producers to predators; that of PCT tended to increase, while concentrations of CAF and DIC remained at a fairly similar level across subsequent trophic levels. The estimated TMFs and the 95 % confidence intervals were: 0.3 (0.1–0.5) for NIC, 0.4 (0.1–2.1) for CBZ, 0.9 (0.5–1.7) for DIC, 0.9 (0.5–1.9) for CAF, 1.3 (0.7–2.7) for PCT and 2.8 (1.2–6.4) for CIP (Fig. 3).

4. Discussion

4.1. Trophic structure of hard-bottom macrobenthic community

Stable carbon ($\delta^{13}C$) and nitrogen ($\delta^{15}N$) isotopes have been used with increasing frequency to examine the structure of food webs and the trophic status of organisms in marine systems (e.g., Silberberger et al., 2018; Zhao et al., 2022) including the Arctic regions (McMeans et al., 2013; Kortsch et al., 2015; Paar et al., 2019; Włodarska-Kowalczuk et al., 2019; Calizza et al., 2022). The natural abundance of isotopes, $\delta^{15}N$ in particular, in organic compounds and biota also provides a convenient tool for quantifying the transfer of pollutants across trophic levels (Coat et al., 2011; Corsolini and Sarà, 2017; Han et al., 2022). Stepwise enrichment between food and consumer (so-called trophic enrichment or shift) means the increase of the nitrogen isotope ratio allows an estimation of the trophic level of an organism (RTL) within the food web. This was possible in this study because all primary producers displayed non-different $\delta^{15}N$ values allowing determination on a unique isotopic baseline for the benthic consumers. Biplot of $\delta^{15}N$ by $\delta^{13}C$ of the dominant algal and invertebrate species (Fig. 1) shows that most consumers rely on similar basal carbon sources. The carbon isotope ratio was not used to the define trophic position of animals and the energy pathway in this food web so, all species were included in further food web analyses. This study did not analyse suspended particulate organic matter (SPOM), a carbon source of hard-bottom suspension feeders in the coastal zone i.e., bivalves and ascidians, for stable isotopes. In Isfjorden concentrations of particulate organic carbon (POC) in the surface water of areas distant from direct river runoffs and glaciers typically fall into a very low range 19–22 μg L^{-1} in August (Delpech et al., 2021) reducing markedly food availability for filter-feeding benthic invertebrates. Renaud et al. (2015) reported that most suspension feeding bivalves from deeper areas in Isfjorden had isotopic signals consistent with more than a 50 % contribution from kelps and rock weeds. Żmudczyńska-Skarbek and Balazy (2017) demonstrated moreover that stable isotope ratios of carbon (−23.5 ‰) and nitrogen (4.49 ‰) of SPOM, collected in August 2014 in surface water from an area of dense kelp forest (water depth 5–10 m) i.e., close to this study's sampling site, were similar to those measured for macroalgae.

The defined food web structure in Isfjorden, with four trophic levels and linear pattern of the main energy pathway (Fig. 1), reflected the trophic organisation of shallow-water communities inhabiting the hard bottom in fjords of the western Spitsbergen well. Paar et al. (2019) reported similar carbon and nitrogen isotopic ratios and trophic links within benthic organisms inhabiting the Arctic kelp belts in Kongsfjorden. Based on combined fatty acid and stable isotope analyses the authors have shown that erect Phaeophyta and Rhodophyta were poorly used by macrozoobenthos as a food source, either fresh or as detritus highlighting the dietary importance of pelagic and benthic microalgae (diatoms and flagellates). Renaud et al. (2015) on the other hand documented via the dual stable isotope approach that macroalgal detritus contributes significantly to food-webs near the shore in Isfjorden. The trophic position of consumers reflected species-specific dietary preferences and feeding mode of animals with predatory cnidarian and gastropods occupying the highest level well (Table 1, Fig. 1). It is noteworthy that markedly low $\delta^{15}N$ of the green sea urchin (4.2 ‰) that, fell within a range typical for macrophytes (3.5 ‰ – 5.1 ‰) and was

Table 3
Concentration of pharmaceuticals (ng g^{-1} dw) in various components of the Arctic hard-bottom food web from Isfjorden, Spitsbergen. Data are presented as mean ± SD. Values for LOD and LOQ are given in Table 2.

Analyte	CAF	NIC	CBZ	CIT	DIC	PCT	ENF	CIP	OXO	OTC	SMZ	TC	TMP
Species													
Macrobenthic algae													
Alaria esculenta	7.0 ± 1.1	142.1 ± 17.6	0.7 ± 0.1	< LOD	19.3 ± 1.8	6.6 ± 0.0	< LOQ	2.1 ± 0.7	< LOD	< LOD	2.5 ± 0.0	< LOQ	0.9 ± 0.0
Laminaria digitata	17.6 ± 5.4	24.4 ± 1.0	0.6 ± 0.2	3.0 ± 0.0	22.8 ± 4.0	5.3 ± 5.5	< LOD	3.8 ± 3.4	< LOD	< LOD	< LOD	< LOQ	< LOQ
Saccharina latissima	6.6 ± 0.0	46.8 ± 0.0	< LOQ	< LOD	42.9 ± 20.0	< LOQ	< LOD	42.2 ± 37.2	< LOD	< LOQ	< LOQ	< LOQ	0.5 ± 0.0
Desmarestia aculeata	5.2 ± 2.7	270.7 ± 220.7	9.8 ± 12.9	6.6 ± 0.0	23.3 ± 25.0	< LOQ	< LOD	51.9 ± 70.1	< LOD	< LOQ	< LOQ	< LOD	< LOQ
Phycodrys rubens	8.3 ± 3.9	7.1 ± 0.0	9.2 ± 0.0	< LOD	15.4 ± 9.1	4.6 ± 5.0	< LOQ	18.9 ± 23.8	< LOD	< LOD	< LOD	< LOQ	< LOD
Macrobenthic invertebrates													
Hyas araneus	1.7 ± 0.2	9.5 ± 1.2	0.1 ± 0.0	< LOD	1.8 ± 0.9	6.7 ± 0.7	< LOD	< LOQ	< LOD	< LOD	< LOD	0.3 ± 0.0	< LOD
Pagurus pubescens	< LOQ	9.6 ± 12.7	20.8 ± 0.0	< LOD	22.9 ± 0.0	15.8 ± 2.9	< LOD	79.2 ± 99.9	< LOD	< LOD	< LOD	0.7 ± 0.0	< LOD
Henricia sanguinolenta	3.1 ± 1.1	3.2 ± 2.1	0.1 ± 0.0	6.7 ± 0.0	12.4 ± 20.7	2.0 ± 0.9	< LOQ	152.3 ± 0.0	< LOD	< LOD	< LOD	< LOQ	< LOD
Strongylocentrotus droebachiensis	2.4 ± 2.4	45.3 ± 47.9	< LOD	< LOD	< LOD	8.8 ± 8.7	< LOD	78.7 ± 0.0	0.5 ± 0.0	< LOD	< LOD	< LOD	< LOD
Hormathia nodosa	< LOQ	3.1 ± 1.9	< LOD	< LOD	46.4 ± 65.4	27.5 ± 17.7	< LOQ	143.1 ± 40.5	0.3 ± 0.0	0.5 ± 0.0	< LOD	0.9 ± 0.0	< LOD
Chlamys islandica	1.1 ± 0.0	23.2 ± 37.7	< LOD	2.9 ± 0.0	9.8 ± 0.0	4.0 ± 2.6	< LOD	80.3 ± 100.2	< LOD	< LOD	< LOD	0.4 ± 0.0	< LOD
Hiatella arctica	1.6 ± 0.0	5.4 ± 1.9	< LOQ	< LOD	36.6 ± 0.0	0.8 ± 0.3	0.6 ± 0.0	37.3 ± 0.0	< LOQ	0.3 ± 0.0	< LOD	0.8 ± 0.0	< LOD
Buccinum glaciale	9.8 ± 8.3	2.0 ± 1.4	0.3 ± 0.2	< LOD	36.7 ± 61.6	4.8 ± 4.8	< LOD	88.3 ± 0.0	< LOD	< LOD	< LOD	0.3 ± 0.0	< LOD
Buccinum undatum	6.6 ± 1.0	2.2 ± 0.3	1.2 ± 0.0	< LOD	14.8 ± 20.8	6.2 ± 2.9	< LOD	< LOQ	< LOD	< LOD	1.1 ± 0.0	0.3 ± 0.0	< LOD
Tonicella marmorea	5.1 ± 1.5	8.0 ± 6.8	< LOD	< LOD	10.2 ± 14.3	3.7 ± 0.4	< LOD	25.9 ± 35.9	0.3 ± 0.0	< LOD	< LOD	0.3 ± 0.0	0.7 ± 0.0
Tonicella marmorea	5.1 ± 1.5	8.0 ± 6.8	< LOD	< LOD	10.2 ± 14.3	3.7 ± 0.4	< LOD	25.9 ± 35.9	0.3 ± 0.0	< LOD	< LOD	0.3 ± 0.0	0.7 ± 0.0
Halocynthia pyriformis	< LOD	1.5 ± 1.2	< LOD	< LOD	9.3 ± 15.9	621.6 ± 67.6	< LOQ	100.3 ± 99	< LOD	0.4 ± 0.1	< LOD	0.9 ± 0.2	< LOD

more ^{15}N-depleted than all other consumers, was also observed earlier in Isfjorden (4.5 ‰; Renaud et al., 2015) and Kongsfjorden (3.7 ‰; Paar et al., 2019). Specific diets comprising kelps (Kelly et al., 2008), epiphytic microalgae (Paar et al., 2019) and possibly also microphytobenthos (Sokołowski et al., 2014) may account for such a depleted position of this grazer. The calculated RTLs for consumers varied from 1.0 to 3.1 i.e., within an extent recommended to achieve the objective of quantifying biomagnification potential of a chemical (Borgå et al., 2012).

4.2. Transfer of pharmaceuticals and stimulants in the Arctic food web

In contrast to records of increasing levels of drugs and stimulants in sewage effluent, receiving seawater and sediment (AMAP, 2017; Huber et al., 2016; Kallenborn et al., 2018; Stroski et al., 2020; Xie et al., 2022) field data on concentrations of these compounds in biota, particularly in marine invertebrates, in Arctic locations are scarce. The low number of reports detailing the occurrence in marine biota is most probably due to the limited capabilities required for multi-residue determination of many pharmaceuticals in complex biological matrices (Miller et al., 2018), very low environmental concentrations and sampling restrictions (Gaw et al., 2014). Given the number of drugs so far detected in various concentrations in the Arctic municipal effluent, WWTP and abiotic elements, and the known tendency of some drugs to bioconcentration based on physicochemical properties (Zenker et al., 2014), it is likely that pharmaceuticals show potential for assimilation and accumulation in marine organisms with adverse effects (Gaw et al., 2014). This study therefore contributes to the current knowledge on the presence of drugs and stimulants in polar regions with the first field data on their concentrations in marine benthic organisms in the European part of the Arctic. Concentrations of pharmaceuticals and stimulants quantified in macrobenthic algae and animals in Isfjorden were normalised to biomass content but not to any biochemical factor. According to Haddad et al. (2018) normalising concentrations of ionizable pharmaceutical residues (e.g., amitriptyline AMI, caffeine CAF, diltiazem DIL, diphenhydramine DIP, fluoxetine FLU and sertraline SER) in aquatic tissue to neutral lipids, polar lipids or the total protein fraction proofed useless in bioaccumulation and biomagnifications studies. Due to the potential variation of drug levels in different animal tissues (Tanoue et al., 2015) the whole body concentrations were measured in this study, as is consistent with the diet-based concept of the trophic magnification factor (Borgå et al., 2012; Xie et al., 2017). Of 13 analytes analysed in this study only DIC and CAF had previously been quantified in substantial amounts in seawater off Longyearbyen (Kallenborn et al., 2008), the main settlement in Spitsbergen, located adjacent to the sampling site, that dumps untreated sewage directly into the fjord. Increased levels of these compounds in the coastal zone result undoubtedly from the direct release from Longyearbyen and the nearby international airport, both of which are considered the major sources of pollutants. CAF, DIC and PCT (identified as acetaminophen) were also found in sewage effluent and the receiving seawater close to Ny-Ålesund (Kongsfjorden), a permanent research station in Spitsbergen, in 2017 by Choi et al. (2020) suggesting that the presence of these compounds in the Arctic environment is directly related to human settlements.

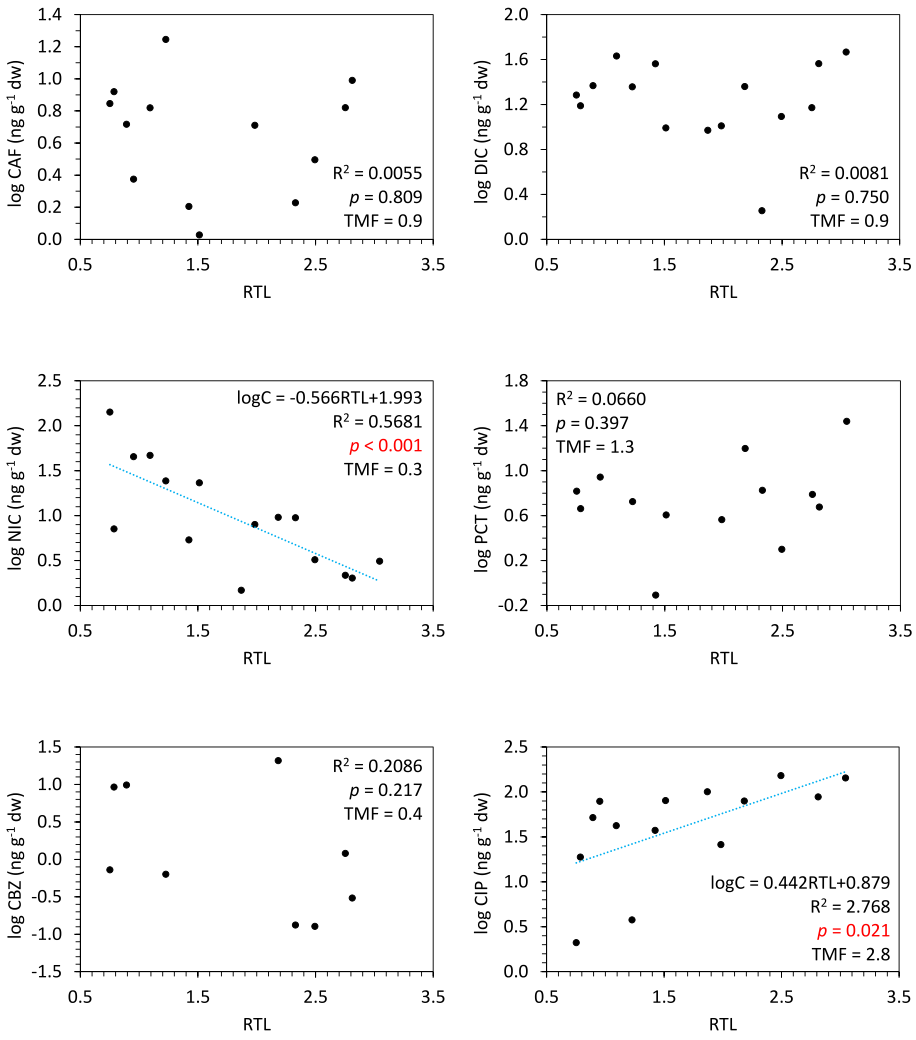

Fig. 3. Log-transformed concentrations of CAF, NIC, CBZ, DIC, PCT and CIP (ng g^{-1} dw) as a function of RTL for selected species (including algae) of the macrobenthic food web in Isfjorden, Spitsbergen. Inserts show coefficient of determination (R^2), probability value (*p*), TMF and equation for significant regressions. Significant effects are marked in red.

Elevated concentrations of some pharmaceuticals (at concentrations of several ng L^{-1} for CBZ, IBU and the lipid-regulating medication gemfibrozil, GEM) in surface seawater at the entrance to Isfjorden were also documented by Korkmaz et al. (2022). Two other target compounds detected herein in elevated concentrations (CIP and NIC) were hitherto not measured in any matrix in this area, indicating potential temporal changes in drug release into the coastal environment. Stroski et al. (2020) reported seven drugs (ATE, CBZ, metoprolol, naproxen, sulphapyridine, sulfamethoxazole and TMP) in wastewater effluent from four Canadian Arctic communities indicative of the importance of local point source discharges.

The relationship between $\delta^{15}N$ or RTL and environmental contaminant concentrations in food web components has been examined in order to estimate trophic transfer of POPs (Morris et al., 2018; Kim et al., 2021) and heavy and trace metals (Zuo et al., 2018) in freshwater and marine basins. For pharmaceuticals and other contaminants of emerging concern (CEC's) the isotopic discrimination approach has been employed to a very limited extent (Du et al., 2014; Xie et al., 2015, 2017; Haddad et al., 2018; Zhang et al., 2020). In the Arctic marine systems no empirical information on trophic transfer of pharmaceuticals and stimulants and their transformation products has yet been published. This study is the first to employ naturally occurring elemental isotopes in order to investigate the bioaccumulation of drugs across trophic positions in the Arctic. When assessing biomagnification potential (TMF) based on environmental samples, care should be taken to use appropriate datasets and analytical methods. Borgå et al. (2012) reported that proper evaluation of TMF for a chemical i.e., sufficient statistical power of regressions, requires an appropriate sample size, independent individual and uncensored data, and pooling of individuals for contaminant and $\delta^{15}N$ analyses. This study includes 16 macrobenthic species (algae and invertebrates) that were collected in triplicate, pooled when necessary and covering a trophic range over at least 3 RTLs. Pharmaceutical and stimulant levels were measured as a whole-body concentration to avoid inter-tissue variations and reduced uncertainty with TMF. Current evidence indicates that pharmaceuticals do not biomagnify in consumers, suggesting that dietary accumulation plays a minor role in accumulation (Du et al., 2014; Lagesson et al., 2016; Xie et al., 2017). Estimates of the TMFs for the macrobenthic food web in Isfjorden demonstrated different bioaccumulation patterns at increasing trophic levels for different compounds. A negative regression slope for NIC and the decreasing tendency for CBZ indicated trophic dilution. Slightly negative slopes of linear regressions (non-significant) between log-transformed CAF and DIC concentrations and RTL resulted in TMFs below 1.0 (Fig. 2) but due to large confidence intervals (95 % confidence) trophic behaviours of these compounds require further evidence. Trophic dilution of CBZ and CAF was recently identified in the food webs of two north-American freshwater systems: effluent-impacted North Bosque River, Texas (Du et al., 2014) and the East Canyon Creek, Utah

(Haddad et al., 2018). Subsequent studies in the Tahu Lake, China indicated TMF < 1.0 for several pharmaceuticals including non-steroidal anti-inflammatory drugs: ibuprofen and diclofenac, antibiotics: erythromycin, norfloxacin and tetracycline, steroid estrogens: 17ß-estradiol and 17α-ethynylestradiol and antidepressant sertraline (Xie et al., 2017). In contrast, laboratory experiments using the artificial food chain of algae, crustaceans and cnidarias revealed a bioaccumulation factor > 1.0 for CBZ (Vernouillet et al., 2010). For hydrophobic compounds a decrease in concentration at increasing trophic levels is presumably caused by high biotransformation rates or poor assimilation efficiency and efficient elimination in consumers (Wan et al., 2007). Based on observations of diphenhydramine in freshwater system Du et al. (2014) suggested that the uptake of ionizable pharmaceuticals by aquatic organisms is more likely to occur via the body's surface respiratory organs (inhalation) than assimilation via diet. Inhalation via the gills as the dominating pathway of pharmaceutical uptake in aquatic invertebrates was also proposed by Meredith-Williams et al. (2012). On the other hand, Haddad et al. (2018) documented the importance of diet as an exposure pathway in invertebrates that assimilate food from suspended particulate matter (filter-feeders) and sediments (grazers). Biodilution was also explained by the greater capacity of organisms occupying higher trophic levels to metabolise substances (Gómez-Regalado et al., 2023). It cannot be excluded that a rapid increase in the body mass of higher consumers relative to pharmaceutical accumulation in tissue from food contributes to decreased levels during trophic transfer. This mechanism has been well recognised for several heavy metals such as Fe and Mn (Szteren et al., 2023). Since there is no evidence to support the existence of a general mechanism for the biotransformation of pharmaceutical residues in an organism and its effect on trophic transfer, more studies are required to understand the physiological processes beyond trophic dilution.

The estimated TMF for CIP was >1.0, suggesting increasing concentrations at successive trophic levels in the Arctic food web. Trophic magnification was also suggested for PCT but large confidence interval precluded clear conclusions on its trophic transfer. Biomagnifying behaviour was observed for several antibiotics in Chinese freshwater systems: norfloxacin and enrofloxacin in the Baiyangdian Lake (Zhang et al., 2020), and roxithromycin (Xie et al., 2015), norfloxacin and ciprofloxacin in the Tahu Lake (Xie et al., 2017). Previous studies in trophic-transfer demonstrate that the biomagnification of drugs may be rather an exception in aquatic environments and physiological explanations for the accumulation of pharmaceuticals during trophic transfer are yet to be elucidated. Given the trophic transfer of certain elements (e.g., trace metals; Luoma and Rainbow, 2005) and persistent organic pollutants (e.g., polychlorinated biphenyls and polybrominated diphenyl ethers; Windsor et al., 2019), it may be presumed that the effective assimilation from food combined with a slow efflux out of the body account for drug biomagnification. It is noteworthy that all but one biomagnifying pharmaceuticals are classified as antibiotics that are used to exert bacteriostatic or bactericidal effects in humans. In the case of compounds ionisable in water (e.g., antibiotics) defining factors contributing to bioaccumulation and biomagnification is challenging, while for non-polar compounds a relationship with their hydrophobicity may provide a useful clue (Mueller et al., 2020). The reason for the higher TMF of CIP may thus be its slower biodegradation in the marine environment and bioconcentration at each trophic level. Differing regressions of log-transformed pharmaceuticals and RTLs indicate various behaviours of drugs in the Arctic food web. According to Lagesson et al. (2016) discrepancies in potential of trophic transfer among compounds may be due to short-term variations in pharmaceutical concentrations (and thus exposure of organisms) and taxon-specific differences in diets. Patterns of pharmaceutical concentration within the aquatic food web may also be modified by the chemical properties of these compounds and their transformation in target organisms and in the environment. The bioaccumulation of drugs in subsequent trophic levels is predicted to vary with changes in water temperature and pH i.e., two environmental parameters directly affected by climate change (Bethke et al., 2023).

5. Conclusions

This study provides the first evidence for the Arctic food web that indicates that the behaviour of pharmaceuticals and stimulants varies among target compounds. The trophic transfer of these compounds is thus susceptible to inter-compound variation. Combining nitrogen stable isotope ratios with the direct measurements of drug concentrations in biological samples proved useful in the assessment of biomagnification potential. A trophic magnification factor (TMF) below 1.0 was estimated for NIC, indicating that the compound does not accumulate across the trophic chain. TMF > 1.0 for CIP suggests trophic magnification, a phenomenon observed previously for several antibiotics in freshwater systems. Trophic transfer therefore plays a role in controlling the concentration of CIP in the Arctic benthic communities and should be considered in environmental risk assessment. Behaviours of CBZ, DIC, CBZ and CAF in the food web remained unclear due to the confounding effect of large 95 % confidence of the calculated TMFs.

Ethics statement

No specific permits were required for the study which complied with all relevant regulations. The species collected in this study are not endangered or protected.

CRediT authorship contribution statement

Adam Sokołowski: Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Project administration; Resources; Supervision; Visualization; Writing original draft.

Marlena Mordec: Data curation; Laboratory analysis; Methodology.

Magda Caban: Data curation; Chemical analysis; Investigation; Methodology; Validation; Contribution to writing original draft.

Ida Beathe Øverjordet: Data curation; Chemical analysis; Methodology; Validation.

Ewa Wielogórska: Data curation; Chemical analysis; Methodology; Validation; Contribution to writing original draft.

Maria Włodarska-Kowalczuk: Collection of field samples, Data curation; Taxonomic analysis; Contribution to writing original draft.

Piotr Balazy: Collection of field samples, Data curation; Taxonomic analysis; Contribution to writing original draft.

Maciej Chełchowski: Collection of field samples, Taxonomic analysis.

Gilles Lepoint: Data curation; Stable isotope analysis; Investigation; Methodology; Contribution to writing original draft.

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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