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Presence of Pharmaceutical Residues in the Seawater of Arctic Archipelago: Assessing the Potential Routes of the Pharmaceutical Pollution

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Abstract

The occurrence of seven commonly used pharmaceuticals, including diclofenac, fenoprofen, ketoprofen, ibuprofen, naproxen, carbamazepine, clofibric acid, gemfibrozil, estrone, 17β-estradiol, and 17α-ethynylestradiol, was investigated in the seawater of the Arctic during the summer of 2022. Seawater samples were subject to liquid-liquid extraction and solid-phase extraction (SPE). The concentrations of pharmaceuticals in the seawater samples were quantified with high-performance liquid chromatography (HPLC) and a DAD detector. The most abundant pharmaceuticals in the seawater were ibuprofen, with a range of 130-220 ng/L, and the highest concentration was obtained for 17α-ethynylestradiol with a level of 350 ng/L. We discussed possible reasons for pharmaceutical pollution, including the impact on marine species, the role of wastewater treatment technologies, and the potential long-range transportation of pharmaceutical residues via sea surface currents.

Introduction

Pharmaceutical pollution is becoming an outstanding topic, especially among the persistent polluters in ecosystems because of anthropogenic activities. The continuous pollution from domestic and industrial activities and the persistent nature of pharmaceuticals mean they are present in almost every water source. The main route for these pharmaceuticals is the wastewater treatment effluent of domestic and industrial plants. However, the lack of effective treatment technologies and policy awareness poses a significant challenge to controlling this pollution in water sources. This underscores the urgent need for effective treatment technologies and policy awareness to control pharmaceutical pollution (Beausse, 2004; Winker et al., 2008).

Especially for the remote ecosystems such as the Arctic Archipelago, which is considered a pristine environment. However, the Arctic's unique environment, characterized by extreme climatic and hydrological conditions, has made it vulnerable to various ecological disturbances like low temperatures, increased UV radiation, marine circulation patterns that may transport pollution from multiple places, and increasing anthropogenic pressures. The issue about anthropogenic polluters in such remote areas is different from any part of the earth's ecosystem because such cold conditions may influence the persistence of the contaminants, and their long-term effects on marine life and the environment are unpredictable with that knowledge (Kozak et al., 2013).

Unfortunately, the number of pollutants investigated in Arctic is increasing year by year,

threatening both marine biota and human health which are polybrominated diphenyl ethers (PBDEs), polychlorinated biphenlys (PCBs), perfluorinated compounds (PFCs), persistent organic pollutants (POPs) and pharmaceuticals (Butt et al., 2010; Kallenborn et al., 2018; Weigel et al., 2004). The presence of organic pollutants is mainly routed to wastewater treatment plants (WWTPs) or direct sources without any treatment or transportation via either ocean currents or the atmosphere (AMAP, 2017; Dube et al., 2024). Researchers reported that throughout the Canadian Arctic and the water column of Fram Strait, organochlorine pesticides and PCBs were investigated in recent years (Ma et al., 2018). Comparable results with model predictions and a quantitative analysis of these compounds' net import from the Atlantic to the Arctic Ocean were observed (Ma et al., 2018). Also, according to the studies, the occurrence of mercury and methylmercury in the Arctic is caused by atmospheric transportation (Steffen et al., 2015).

From that point of view, pharmaceuticals are classified as emerging contaminants. Therefore, it is essential to underline that pharmaceutical compounds can be detected even in remote areas for various reasons. This study discussed the occurrence of selected pharmaceuticals in the Arctic Archipelago and potential transport mechanism routes.

Materials and Methods

HPLC-grade, dichloromethane (99.8%), methanol (99.5%), chloroform (99.4%), sulfuric acid (98%) and acetonitrile (≥99.9%) were obtained from Merck (Darmstadt, Germany). The standards for diclofenac, ketoprofen, clofibric acid, gemfibrozil, carbamazepine, estrone, 17β-estradiol, fenoprofen, ibuprofen, naproxen and 17α-ethynylestradiol were purchased from Sigma-Aldrich (purity >95% or higher) (Athens, Greece). Potassium dihydrogen phosphate was obtained from Fluka (Steinheim, Germany). The SPE cartridges [Cleanert PEP (500 mg/6 mL)] were obtained from Agela Technologies (Torrance, USA).

Seawater samples were collected from the Arctic during the summer of 2022 and analyzed in the laboratories as soon as possible. First, 1L surface water samples were fixed with 0.1% nitric acid after sampling to prevent microbial activities and kept in dark and cold conditions till analysis. Then, the filtration step is done to eliminate the total suspended solid that may interact with analytes and result in degradation. Liquid-liquid extraction is essential when dealing with large volumes of samples, so dichloromethane/chloroform (1/1, v/v) solution was used, and sample volumes decreased to approximately 10 mL. Then, it evaporated until dry and collected with 3 mL methanol in two steps. In this study, selected target analytes are different from each other in chemical properties, which have acidic, neutral, and steroidal properties that affect solid phase extraction performance. Sosnowka-Nosek et al. (2014) investigated the SPE performance of basic, neutral, acidic, and steroidal pharmaceuticals on a combined method; therefore, the solid phase extraction method was modified from (Sosnowska-Nosek et al., 2014). Then, analytes were analyzed in HPLC-DAD with a range of 220- 330 nm wavelength (Korkmaz et al., 2023). C18 column (250 × 4.6 mm, 5 µm) were used in separations.Ten microliters of each sample were analyzed with HPLC (DAD detector). 25 mM potassium dihydrogen phosphate and acetonitrile were used as the mobile phases. The flow rate was set to 1.2 mL/min. (Camacho-Muñoz et al., 2009; Debska et al., 2005). Several steps were performed to validate the method. First, the main stock solutions were prepared by 10 mg of each target compound which is dissolved in 100 mL of methanol. Working solutions prepared by dilution of main stock solutions with concentrations of 50, 100, 200, 400, and 500 ppb with methanol. Linearity was assessed by plotting the concentration of each compound against the peak area obtained from HPLC-DAD analysis. The limit of detection (LOD) and limit of quantification (LOQ) of the instrument were calculated by multiplying the signal-to-noise ratio (S/N) of ten blank samples by 3 and 10, respectively. Additionally, method detection limit (MDL) and method quantification limit (MQL) were determined with dividing the LOD and LOQ by the SPE enrichment factor (1000) of the water samples. Validation results are shown in Table 1.

Table 1. Chemical properties, method detection limit, method quantification limit, and recoveries of the target pharmaceuticals in seawater of the Artric.

Therapeutic group	Pharmaceutical	Molecular formula	Log K_{ow}	Solubility (mg/L)	MDL (µg/L)	MQL (µg/L)	R ±RSD (%)
Nonsteroidal anti-inflammatory (NSAIDs)	Diclofenac	$C_{14}H_{11}C_{l2}NO_2$	4.51	2.37	0.021	0.069	81±3.70
	Ibuprofen	$C_{13}H_{18}O_2$	4	21	0.014	0.047	98±3.06
	Fenoprofen	$C_{15}H_{14}O_3$	3.1	slightly	0.017	0.057	94±3.83
	Naproxen	$C_{14}H_{14}O_3$	3.18	15.9	0.017	0.057	68±3.89
	Ketoprofen	$C_{16}H_{14}O_3$	3.12	51	0.029	0.096	69±4.40
Lipid regulators	Clofibric acid	$C_{10}H_{11}C_lO_3$	2.84	582.5	0.051	0.169	66± 4.00
	Gemfibrozil	$C_{15}H_{22}O_3$	4.77	11	0.014	0.047	69± .22
Hormones	Estrone	$C_{16}H_{22}O_2$	3.13	12.42	0.045	0.15	96±1.04
	17β-estradiol	$C_{18}H_{24}O_2$	4.01	3.9	0.031	0.101	97±2.06
	17α-ethynylestradiol	$C_{20}H_{24}O_2$	3.67	11.3	0.008	0.026	100±4.35
Antiepileptic	Carbamazepine	$C_{15}H_{12}N_2O$	2.77	17.6	0.034	0.113	92±2.88

Six stations around the Arctic Pole are investigated in this study; three are offshore in the Svalbard Archipelago, and others are in the Barents Sea, the shoreline of Norway. The station map is shown in Figure 1. Svalbard archipelago is in the Atlantic Arctic, where the Arctic Ocean connects to the North Atlantic Ocean via the Barents Sea and the Fram Strait (Jones et al., 2021). Most Arctic waters originate from the North Atlantic, the primary source of the Arctic's mid and deep waters. Arctic inflows occur from the Pacific Ocean and Atlantic Ocean, but outflow occurs only from the Arctic to the Atlantic Ocean. Inflows from the Atlantic occur via two pathways: one is from the eastern Fram Strait via the West Spitsbergen Current and the Barents Sea Overflow (Carroll & Carroll, 2003). Arctic hydrographic and oceanographic elements depend on two oceans, which have also suffered from anthropogenic pressure in recent years. The first report on pharmaceutical occurrence at the Arctic Pole was done by Weigel et al. in 2004. Since then, various pharmaceutical groups such as antibiotics, NSAIDs, antiepileptics, antidepressants, hormones, lipid regulators, beta-blockers, and their metabolites were investigated. According to the 2016 AMAP (Arctic Monitoring and Assessment Programme) report, 112 compounds from 26 PPCP groups were studied in several mediums across the Arctic such as atmospheric, terrestrial, freshwater, and marine samples (AMAP, 2017). The main route for emerging contaminants entering the Arctic is linked to untreated or insufficiently treated wastewater. In such cold and remote environments, installation of sufficient WWTPs is usually not feasible and affordable for less populated areas (Gunnarsdóttir et al., 2013). Removal rates of the pharmaceuticals depend on the treatment technology and the compound's physicochemical properties. In the Arctic, removal rates in WWTPs range between 10%-100%. The study revealed that the pollution level in decentralized wastewater treatment systems was two to three times higher than the centralized sewage systems in other regions (Kallenborn et al., 2018). Key challenges in developing efficient WWTPs in such areas include harsh climatic conditions, lack of infrastructure, shortage of qualified personnel and resources, and an unsteady, varied flow of wastewater (Vialkova & Glushchenko, 2021). Therefore, there are many direct discharges over the Arctic Pole. Norway Statistics showed that the fraction of the direct discharges from small WWTPs (for <50 pe) in North counties exhibited a decreasing trend from 1.4% to 0.7% between 2005-2022 (Norway Statistics, n.d.). In addition, no production facilities of PPCPs have been reported from Western Arctic environments. Therefore, potential release from industrial areas must be excluded when determining the potential sources of the pharmaceutical pollution (Kallenborn et al., 2018). Station coordinates and sea-surface temperatures are given in Table 2.

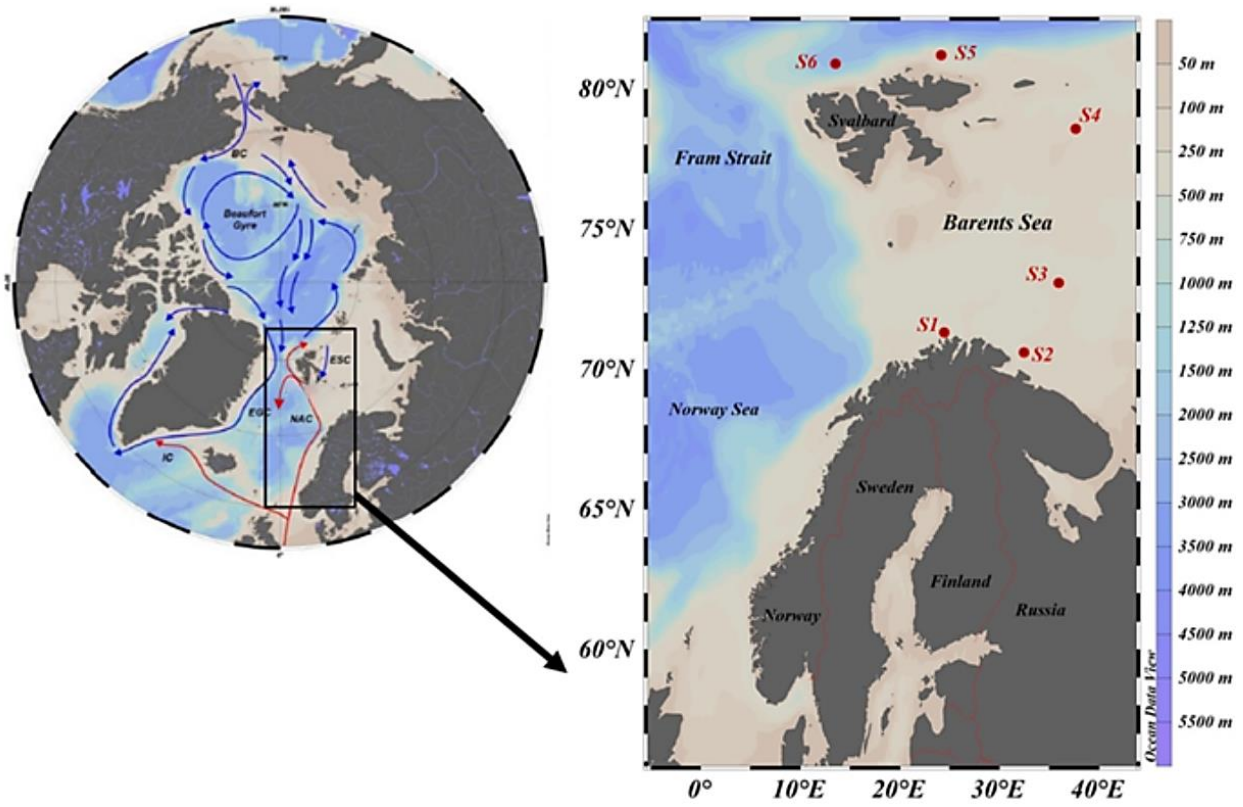

Figure 1. Station map (On the left, surface water circulation of the Arctic Pole is demonstrated (blue lines are cold currents, red lines are warm currents) NAC North Atlantic Current, ESC East Spitsbergen Current, EGC East Greenland Current, IC Irminger Current, BC Bering Current modified from (Łącka et al., 2020), on the right, station map (from Ocean Data View version ODV 5.2.1, https://odv.awi.de/)).

Results and Discussion

Figure 2 and Table 3 show the concentrations of the target analytes in this study. Among the NSAID's (ibuprofen, ketoprofen, naproxen, diclofenac, fenoprofen) only fenoprofen and ibuprofen were detected with the range of 210-230 ng/L in 3 out of 6 stations, 130-220 ng/L in all stations, respectively. Other NSAID analytes were not detected or below the method detection limit. Diclofenac was expected at all stations due to its rapid degradation by photodegradation and biodegradation (Andreozzi et al., 2003; Yamamoto et al., 2005) and widespread global use. However, the research group also expected that the cold environment of the Arctic could potentially slow down the biodegradation of diclofenac (Kallenborn et al., 2008; Weigel et al., 2004). Since this did not occur, it could be inferred that photodegradation might have taken place during the transportation of the samples. Fenoprofen is a highly persistent compound in the aquatic environment because of the low treatment level in wastewater treatment plants (Kramer et al., 2018). As mentioned earlier, fenoprofen was detected at three out of six stations- two located along the shoreline of Norway and one offshore of the Svalbard Archipelago. The detection of fenoprofen may be attributed to the

Table 2. Station coordinates and sea surface temperature (SST)

Station	Latitude	Longitude	SST (°C)
S1	71˚ 19' 13.20"	24˚ 25' 28.85"	10.1
S2	70˚ 36' 05.38"	32˚ 27' 38.43"	10.6
S3	73˚ 05' 09.53"	35˚ 55' 31.56"	7.5
S4	73˚ 42' 34.43"	36˚ 47' 01.29"	3.1
S5	75˚ 32' 59.43"	31˚ 43' 15.53"	1.1
S6	75˚ 50' 25.20"	37˚ 34' 46.43"	0.9

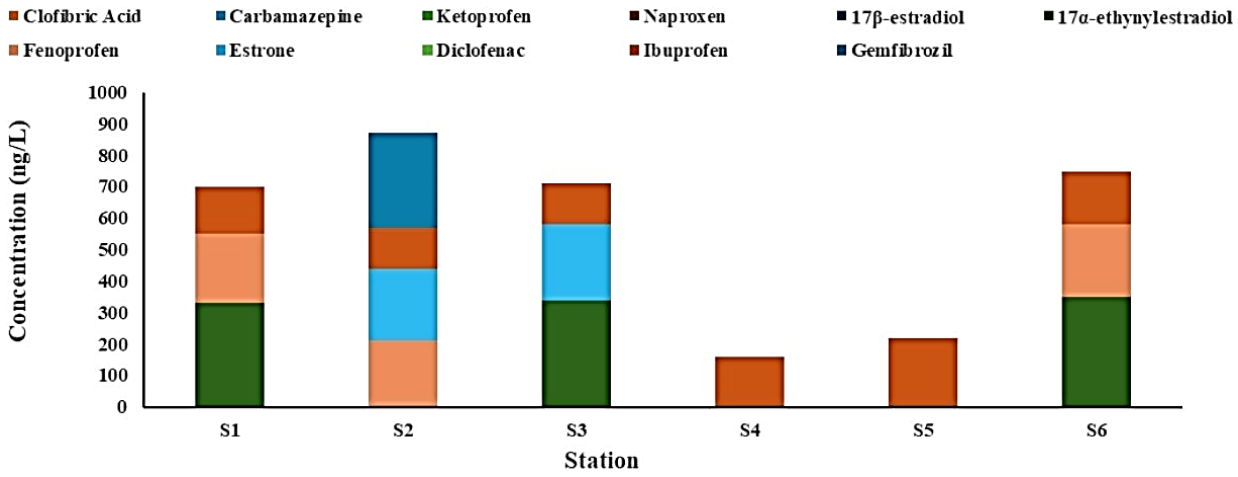

Figure 2. Station map (On the left, surface water circulation of the Arctic Pole is demonstrated (blue lines are cold currents, red lines are warm currents) NAC North Atlantic Current, ESC East Spitsbergen Current, EGC East Greenland Current, IC Irminger Current, BC Bering Current modified from (Łącka et al., 2020), on the right, station map (from Ocean Data View version ODV 5.2.1, https://odv.awi.de/)).

Table 3. Detected concentrations (ng/L) of pharmaceuticals in Arctic seawater samples

Compounds	Stations					
	S1	**S2**	**S3**	**S4**	**S5**	**S6**
Carbamazepine	<MQL	n.d	n.d	n.d	n.d	n.d
Ketoprofen	n.d	n.d	n.d	n.d	n.d	n.d
Naproxen	n.d	n.d	n.d	n.d	n.d	n.d
Fenoprofen	220	210	n.d	n.d	n.d	230
Diclofenac	n.d	n.d	n.d	n.d	n.d	n.d
Ibuprofen	150	130	130	160	220	170
Estrone	n.d	230	240	n.d	n.d	n.d
17β-estradiol	n.d	n.d	n.d	n.d	n.d	n.d
17α-ethynylestradiol	330	n.d	340	n.d	n.d	350
Clofibric Acid	n.d	n.d	n.d	n.d	n.d	n.d
Gemfibrozil	<MDL	300	n.d	n.d	n.d	n.d

low efficiency and limited number of wastewater treatment plants (WWTPs) in these areas. Ibuprofen is the most detected analyte in this study; it is detected at all stations. Ibuprofen has a half-life value of 50 days (Buser et al., 1999). Low annual average ambient temperature and daylight conditions, which change seasonally in northern regions, resulted in long-term depositions and prolonged environmental stability of the pollutants. Both prolonged stability and the long half-life of the ibuprofen may result in high detection frequency of the analytes in this study.

Among the hormones, estrone and 17α-ethynylestradiol were detected in the study. The concentration of estrone is ranged from 230-240 ng/L and detected in two stations at the Norway shoreline, and 17α-ethynylestradiol concentration is varied from 330-350 ng/L in three stations, which are located at the Norway shoreline and offshore of Svalbard. 17β-estradiol was not detected, possibly due to its half-life of 2 days or studies showing that 17β-estradiol quickly degrades to estrone (Adeel et al., 2017). In contrast, 17α-ethynylestradiol has a half-life of 81 days (Adeel et al., 2017). Therefore, it is expected that synthetic hormones such as 17α-ethynylestradiol were detected at higher concentrations than natural hormones like estrone.

Lipid regulators such as gemfibrozil and clofibric acid were investigated in the study. Gemfibrozil was detected in two stations located at the shoreline of Norway and ranged between <MDL-300 ng/L. Clofibric acid was detected in any stations. Another study's results in the Arctic region showed that clofibric acid was not detected and suggested that inhabitants do not use clofibric acid regularly in the area. Gemfibrozil is very persistent in surface water ecosystems, with a half-life of 200 days (Araujo et al., 2011; Fang et al., 2019). Temperature has a significant influence on the degradation of pharmaceuticals in water bodies. At lower temperatures, microbial activity slows down, and the degradation rate of compounds in water decreases. Gemfibrozil was detected at one of the highest concentrations in the study, at 300 ng/L, which might be due to its slower degradation rate in colder conditions (Daneshvar et al., 2010). Additionally, its physicochemical properties, such as low biodegradability and resistance to photodegradation, may further contribute to its accumulation in water bodies, especially in colder environments. Few studies have investigated pharmaceuticals in Arctic seawater (Choi et al., 2020; Korkmaz et al., 2022). For example, Korkmaz et al., 2022 reported that the maximum diclofenac concentration in the Svalbard seawater was 440 ng/L, fenoprofen concentration was 600 ng/L, ibuprofen was 1240 ng/L, estrone was 420 ng/L and 17α-ethynylestradiol was 850 ng/L which are significantly higher concentrations than our study. However, several studies examined pharmaceuticals in sewage effluent samples between 2003 and 2013. For example, the maximum detected ibuprofen concentration in Svalbard was reported as 403 ng/L, and in Tromsø, Norway, it was 448 ng/L, which is higher than the concentrations found in our study (AMAP, 2017). A study conducted in Spitsbergen, Svalbard, concludes that the non-target analysis of Arctic seawater identified 17 compounds, including pharmaceuticals and, perfluorinated compounds, PPCPs and their metabolites. The authors emphasized that wastewater discharges are a point source of this pollution. However, the point source of pollution in Arctic region is very limited. Svalbard serves as a scientific base for several countries, and during the summer months, the population in settlements can reach up to 120 people. Additionally, the wastewater treatment technology in the region operates without chemical or microbial treatment; instead, it relies on particulate matter sorption and soil-originated microbial degradation, which is insufficient to eliminate many pollutant compounds. (Choi et al., 2020)

Number of researches about the biological impact of pharmaceuticals on Arctic marine habitant are not sufficient to assess the current situations. However, there are studies on the biological effects of sub-arctic marine species such as rainbow trout (*Oncorhynchus mykiss*) and meager (*Argyrosomus regius*). For example, when diclofenac and ibuprofen were exposed to the dietary rainbow trout, hyalinosis developed in the trout's kidney, and gene expression and along with oxidative stress markers were observed (Hodkovicova et al., 2022). Carbamazepine has an effect of increased plasma ammonia levels in juvenile rainbow trout during blood tests, indicating that the detoxification process of converting harmful ammonia to urea was not functioning correctly (Li et al., 2011). It is also known that zooplankton are the accumulators of pharmaceuticals. For example, ibuprofen was detected in benthic amphipods at concentrations up to 2000 µg/kg and in copepods up to 4000 µg/kg, as well as in nearly every invertebrate species examined in these studies (Sørensen et al., 2023). According to Korkmaz and her colleagues, net plankton suspend solids revealed the presence of ibuprofen, 17α-ethynylestradiol, and 17β-estradiol were detected at concentrations up to 4543 ng/kg (Korkmaz et al., 2022). Therefore, it could be said that pharmaceutical residues in the Arctic threaten the marine life and sustainability of the Arctic waters, which is essential for the population of the Arctic, whose diet relies on aquatic resources.

Pharmaceuticals can be transformed into metabolites via biological and environmental conditions of the area. The fate and behavior of the pharmaceuticals in marine environments vary in terms of the effects of complexing agents, suspensions, buffer salts, emulsions, and environmental factors such as temperature, dissolved oxygen concentrations, and light intensity (Loftsson, 2014). Because of the Arctic's prolonged periods of low to no solar radiation over the year, the photodegradation rate of the area is very low, especially in winter seasons (Chauhan et al., 2021).

While there is no study about the transportation of pharmaceuticals to the Arctic, several studies about the transport vectors for other chemicals to the Northern Hemisphere can indicate potential pathways other than wastewater effluents for pharmaceutical pollution in the Arctic. Researchers reported that PCBs and organochlorine pesticides were detected throughout the Canadian Arctic and Fram Strait water column (Ma et al., 2018). The measurements showed a net transportation of PCBs from the Atlantic to the Arctic Ocean of 0.04-0.28 tonnes per year (Ma et al., 2018). That might indicate that pharmaceuticals can be transported from one basin to another. Also, the continuous release of pharmaceuticals into the environment affected the receiving and long-distance environments. In the study by Dube et al. (2024), simulations of an ocean transport model showed that diclofenac dispersion from the Baltic region could reach Svalbard along the Norwegian coast via sea-surface currents even without considering the degradation of the compound. In our study, ibuprofen concentrations in seawater samples from offshore Svalbard were slightly higher than those from Norway's coast, which may indicate the influence of sea-surface currents (see Figure 2) on the pharmaceutical pollution already present in the Svalbard region.

Conclusion

This study investigated eleven pharmaceutical compounds in the Arctic region to assess the pollution levels of commonly used pharmaceuticals. Pharmaceutical contamination was detected at all sampling stations, with concentrations ranging from below the method detection limit (MDL) to 350 ng/L. These findings highlight the presence of pharmaceutical residues even in remote Arctic environments, suggesting that long-range transport mechanisms, such as ocean currents and atmospheric deposition, may play a role in the dissemination of contaminants and increase the load of pharmaceuticals in the area. Moreover, the detection of pharmaceuticals at varying concentrations underscores the need for further research into their potential ecological impacts on Arctic marine species and ecosystems, particularly in the context of persistent low temperatures and unique biological processes that may alter the degradation and bioaccumulation of these compounds in such remote and cold environments, the application of advanced treatment technologies to mitigate anthropogenic pressure is highly limited. However, protecting and sustaining the integrity of environmental compartments in these fragile ecosystems is crucial, as the accumulation of pharmaceuticals can have long-term ecological impacts, potentially affecting biodiversity and ecosystem functions. Several wastewater treatment technologies, such as wetlands, moving bed biofilm reactors, and low-temperature-adapted microbial communities, could be used in the Arctic environment for nitrification/denitrification processes. It's important to remember that for micropollutants such as pharmaceuticals, further treatment is needed in the case of biological treatment. Additional chemical treatment is essential to eliminate pharmaceuticals. In this context, input control is another solution to prevent pollution in such remote areas, which would be the most effective way to manage output. Monitoring and screening pharmaceutical pollution in Arctic seawater and the food web are crucial to finding well-suited wastewater treatment technologies.

Ethical Statement

Not applicable.

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Author Contribution

Güldehan Deryal: Conceptualization, Methodology, Validation, analysis, Writing – original draft, Writing – review & editing, Visualization

Nagihan E. Korkmaz: Conceptualization, Methodology, Validation, analysis, Writing – review & editing, Visualization.

Abdullah Aksu: Conceptualization, Methodology, analysis, Writing – review & editing

Ersan Başar: Data collection, Resources.

Cem Gazioğlu: Supervision, Project Administration.

Nuray Çağlar Balkıs: Conceptualization, Writing – review & editing, Supervision.

Burcu Özsoy: Supervision, Project Administration.

Conflict of 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.

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