Ecological risk assessment of the impacts of pharmaceutical and personal care product contamination in the Alaksen National Wildlife Area watershed

by

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Abstract

Twenty-six pharmaceuticals and personal care products (PPCPs) were detected within sediments or surface waters of the Alaksen National Wildlife Area (ANWA), British Columbia, Canada. This is the most comprehensive study measuring PPCPs (a total of 141) in a watershed along the South Arm of the Fraser River. It is predicted that these PPCPs mainly originate from upstream municipal wastewater treatment plants. Thirteen classes of PPCPs were detected including NSAIDs, beta-blockers, anti-depressants, stimulants, illicit drugs, and more. An ecological risk assessment of these PPCPs present in surface waters and sediments in the ANWA was conducted using a deterministic risk assessment approach. This assessment shows that surface water concentrations of PPCPs are not likely to pose a risk to aquatic wildlife. However, PPCP sediments concentrations may be of ecological concern and sediments are a significant sink for PPCPs. Bioaccumulation data indicates potential acute toxicity in avian predators from azole antifungal accumulation.

Keywords: Ecological risk assessment; pharmaceuticals and personal care products; terrestrial; aquatic; Polar organic chemical integrative sampler; bioaccumulation food web modelling

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List of Acronyms

ß	Bile solubility enhancement, the estimated increase in solubility of chemicals in bile fluids
µg/L	Micrograms per litre
AF	Assessment factor
ANWA	Alaksen National Wildlife Area
ASTM	American Society for Testing Materials
BC	British Columbia
BMF	Biomagnification factor
BPA	Bisphenol A
CAS	Chemical abstract number
CCME	Canadian Council of the Ministers of the Environment
CNS	Central nervous system
COPC	Contaminants of potential concern
COSEWIC	Committee on the Status of Endangered Wildlife in Canada
$C_{aq.invert}$	Concentration of a chemical contaminant in the tissue of an aquatic invertebrate
C_{biota}	Concentration of a chemical contaminant in the tissue of biota consuming a diet item
C_{diet}	Concentration of a chemical contaminant in the tissue of a diet item
C_s	Concentration of the analyte accumulate in a sorbent
C_{shrew}	Concentration of a chemical contaminant in the tissue of a shrew
C_{twa}	Time-weighted water concentration of a specific analyte in water
C_w	Porewater concentration in sediment
CWS	Canadian Wildlife Service
D	Day
DEET	N,N-diethyl-meta-toluamide
ECCC	Environmental Climate Change Canada
ECOSAR	Ecological structural activity relationships
E_A	Efficiency of chemical uptake from the air
E_D	Efficiency of chemical uptake from the diet

EQG	Environmental quality guideline
ERA	Ecological risk assessment
FCSAP	Federal Contaminated Sites Action Plan
FDA	Federal Drug Agency
FEQG	Federal Environmental Quality Guideline
F_{oc}	Fraction of organic carbon in sediment/soil
G	Gram
G_A	Respiration rate
G_B	Bile excretion rate
G_D	Volume of food ingested per day
G_F	Fecal excretion rate
G_U	Urinary excretion rate
HI	Hazard index
HQ	Hazard quotient
HLB	Hydrophilic-lipophilic balance
ICE	Interspecies correlation estimation
K_{air}	Elimination rate constant of a chemical from respiring air
K_{BF}	Biota-feces partitioning coefficient
K_{bile}	Elimination rate constant of a chemical from excreting bile
K_{diet}	Uptake rate constant of a chemical from diet
K_{feces}	E limination rate constant of a chemical from excreting feces
Kg	Kilogram
K_{OA}	Octanol-air partitioning coefficient
K_{OB}	Octanol-bile partitioning coefficient
K_{oc}	Octanol-carbon partitioning coefficient
K_{ow}	Octanol-water partitioning coefficient
K_{urine}	Elimination rate constant of a chemical from excreting urine
L	Litre
L_B	Lipid content of a shrew by percentage of body weight
L/d	Litres per day

LC(D)50	Lethal concentration or dose causing mortality in 50% of a test population
KABAM	K_{ow}-based aquatic bioaccumulation model
Mm	Millimeter
M_s	Mass of the sorbent
MSDS	Material safety data sheets
Ng	Nanogram
NOAEL	No observed adverse effect level
NR	Not reported
NSAID	Non-steroidal anti-inflammatory drug
NWA	National Wildlife Area
OECD	Organisation for Economic Co-operation and Development
PEC	Predicted environmental concentration
PNEC	Predicted no effects concentration
PES	Polyethersulfone
Pka	Acid dissociation constant
POCIS	Polar organic chemical integrative sampler
PPCP	Pharmaceuticals and personal care products
PRC	Performance reference compounds
QSAR	Quantitative-Structure Activity Relationships
RL	Reporting limit
ROC	Receptors of concern
R_s	Sampling rate
SARA	Species At Risk Act
SVHC	Substance of very high concern
T	Time
TRV	Toxicity reference value
US EPA	United States Environmental Protection Agency
US EPA OPP	United States Environmental Protection Agency Office of Pesticide Programs
UV	Ultra-violet
V_B	Volume of the biota of interest

WWTP	Wastewater treatment plants

Chapter 1. Introduction

1.1. Chemicals of emerging concern: pharmaceuticals and personal care products

Pharmaceuticals and personal care products (PPCP) have been discharged into waterbodies extensively from wastewater treatment plants (WWTPs) over the last century, thus are ubiquitous contaminants downstream of urban and rural areas worldwide (Ternes et al., 2004). Indeed, PPCPs are commonly detected in environmental matrices near anthropogenic influences such as WWTPs and industrial areas, and are comprised of a wide array of contaminants typically used as disinfectants (i.e. triclosan and triclocarban), fragrances (i.e. musk's), flame retardants (i.e. polybrominated diphenyl ethers), plasticizers and packaging (i.e. phthalates and bisphenol A), insect deterrents (i.e. N,N-diethyl-meta-toluamide; DEET), preservatives (i.e. parabens) and as UV filters (i.e. methylbenzylidene camphor) in commercial products, as well as in human therapeutics (i.e. hormones, pharmaceuticals, etc.; reviewed by Brausch and Rand, 2011). Pharmaceuticals have been designed to be biologically active in humans, and with high conservation of numerous biological systems and processes across vertebrate taxa (Ebele et al., 2017). Numerous studies have demonstrated biological activity and adverse effects in wildlife exposed to low levels of these contaminants (Ebele et al., 2017). In addition, several personal care products derived from a variety of consumer products that make their way into WWTPs have also been deemed toxic, such as Bisphenol A (BPA), phthalates, brominated flame retardants (Marlatt et al., 2022), yet few environmental quality guidelines exist for this group of contaminants. Ultimately, PPCPs have been labelled contaminants of emerging concern because they are continuously released into the environment due to inadequate removal in wastewater treatment systems, can be persistent in the

environment, are ubiquitously found in aquatic environments and because many induce biological effects in non-target organisms at low concentrations (Alvarino et al., 2018; Ebele et al., 2017; Hayden et al., 2022). As such, WWTP are major point sources of PPCPs as well as onsite septic fields that can leach into the surrounding environment (Kim and Homan, 2020). Indeed, ongoing studies are warranted for most watersheds to determine if PPCPs are present at concentrations that are of concern to wildlife in terms of direct and/or secondary toxic effects (i.e. poisoning scenarios via feeding on animal carcasses has been reported for pharmaceuticals such as diclofenac; Corcoran et al., 2010).

Both pharmaceutical consumption and the development of novel therapeutic compounds are expected to grow each year, outpacing regulatory monitoring of these new substances in the environment as human populations increase (OECD, 2019). Furthermore, the occurrence of PPCPs are proportional to the level of urbanization, where regions with higher numbers of urban centers were proportional to the mass loading of PPCPs in WWTP effluent (Sun et al., 2016). With human populations worldwide projected to reach an estimate of 9.8 billion, changes in land-use from rural landscape to urban landscapes and densification of housing is inevitable, contributing to the growing use and detection of PPCPs in aquatic and terrestrial environments (United Nations, 2017). In Canada, public drug program spending reached $13 billion, accounting for 44% of total drug spending in Canada, resulting in a growth rate of 7.4% from the previous year demonstrating the continual increase in pharmaceutical usage over time (Canadian Institute for Health Information, 2023). Moreover, pharmaceuticals active ingredients are also intensely used in the animal products industry and in aquaculture to treat animals for diseases and increase yields through the application of growth promoting additives such as antimicrobials and hormones (Qaid and Abdoun,

2022). Thus, future contamination of aquatic and terrestrial ecosystems of these pseudo-persistent compounds will only increase.

1.2. Environmental sources, transport and fate

Wastewater treatment plants have been identified as the greatest and most significant contributor of human PPCPs as they are continually collecting and concentrating these substances which are subsequently directly discharged into aquatic environments as a metabolites, parent or conjugated forms (Daughton and Ternes, 1999; Kreuzinger, 2008). Traditionally wastewater management have primarily focused on enhancing water quality by reducing nutrient loads and biological oxygen demand (BOD) in wastewater effluents to lower the risk of oxygen depletion and eutrophication in receiving waters (Kreuzinger, 2008). As such, traditional WWTPs were not designed specifically to deal with the wide range of micropollutants including pharmaceutical active ingredients, personal care products and other commercial chemicals used in industry and agriculture (Kreuzinger, 2008). Thus contributing to the global widespread detection of PPCPs in the various compartments in urbanized regions as these substances are recalcitrant to wastewater treatment and are released within finished effluent (Kim and Homan, 2020; Kreuzinger, 2008; Lin et al., 2009). Indeed, within Canada, PPCPs have been detected in surface waters in raw sewage (Lajeunesse et al., 2008), primary-treated effluents (Lajeunesse et al., 2008), finished WWTP effluents (Miao et al., 2004), lakes (Li et al., 2010), river water (Metcalfe et al., 2010), fish tissues (Metcalfe et al., 2010). Factors that influence the frequency of detection of PPCPs in WWTP effluent and septic field leachates include population, seasonality, and wastewater treatment technologies (Kim and Homan, 2020). In municipalities with centralized WWTP, these wastewaters containing PPCPs are concentrated into the wastewater influent where the removal of PPCPs is dependent on the wastewater

treatment technology utilized and dependent on the physicochemical and structural properties of the PPCPs (Alvarino et al., 2018). The removal efficiencies of PPCPs in WWTPs can range from <10% (i.e. carbamazepine) to >90% (i.e. ibuprofen) where this variation in removal efficiencies are likely due to the differences in WWTP processes employed, operational parameters and the inherent chemical properties of the PPCP (Joss et al., 2005). The PPCPs that enter WWTPs may be eliminated by adsorption to sludge, stripping, abiotic transformations, and biodegradation or are simply recalcitrant to wastewater treatment efforts and are released into receiving waters unabated (Kreuzinger, 2008). To date, the most promising strategy for the removal of PPCPs in domestic wastewater occur in tertiary wastewater treatment systems which include: advanced oxidation, ultraviolet (UV) treatment, ozonation, chlorination or membrane filtration (Loganathan et al., 2023).

In Ontario, surface waters sampled near WWTP outfalls contained carbamazepine, clofibric acid, ketoprofen, fenoprofen, caffeine, cotinine, fluoxetine and trimethoprim, thus demonstrating WWTP effluents being an important contributor to PPCPs found in Canadian aquatic environments (Metcalfe et al., 2003b). In Victoria, BC, effluent samples from two primary wastewater treatment outfalls (where solids are only screened to 6 mm) were collected where seven out of seven pharmaceuticals were measured between 2004 to 2006 sampling years (Saunders et al., 2016). In rural agricultural landscapes, these substance can occur through on-site septic systems, application of biosolid amendments (separated solid sewage waste) collected from sewage treatment or from livestock excreta that may run off and contaminate downstream watersheds including surface waters and potentially groundwater (Metcalfe et al., 2003b). Recently, the BC Ministry of the Environment released a technical report summarizing the findings of monitoring studies of PPCPs in various environmental

compartments in the Burrard Inlet (Braig et al., 2019). These monitoring studies were conducted by various organizations including consulting firms, industry and academia, detecting 13 PPCPs in seawater, 11 in marine sediments, and in biota such as mussel (Braig et al., 2019). Although environmental monitoring of WWTP outfalls have demonstrated that PPCPs are present in marine environments in British Columbia, Canada, the occurrences of PPCPs in freshwater systems impacted by upstream WWTPs is not well characterized in the Fraser River Basin.

1.3. Study Area

The Alaksen National Wildlife Area (ANWA) is a protected wildlife area that is situated on the northern tip of Westham Island, Delta, British Columbia, Canada and is located at the end of the main arm of the Fraser River and is currently managed by the Canadian Wildlife Service (CWS) branch of Environment Climate Change Canada (ECCC), (Harrison et al., 1999). The ANWA encompasses an area of 349 hectares and contains a variety of habitats including estuarine habitats, intertidal mudflats, vegetated marshes, active agriculture fields, old agricultural field grasslands, urbanized zones, riparian forests, remnant wetlands, sloughs and ponds (Environment and Climate Change, 2020). The perimeter of ANWA has been dyked with walking trails running along their crest. Units of irrigation ditches can be found along interior ditches and around the perimeter of agricultural fields, which are all interconnected by a series of culverts and water control structures with access to the Fraser River depending on the ebb and flow of the tide. The perimeter of each agricultural field is surrounded by hedgerows, wooded lots or grass margins, which provides an important refuge for beneficial arthropods that can support pest management efforts (Augustinowicz et al., 2019). Waters from the lower Fraser River are able to invade the dykes on the perimeter of Westham Island and pose a potential source of anthropogenic contaminant inputs

associated with urbanization such as industrial and municipal effluents carried in the waters. The ANWA has a long history of agricultural usage even before its establishment as the National Wildlife Area (NWA) and there is concern about the potential impact of agricultural contaminants (i.e. pesticides, nutrients and metals) on wildlife and aquatic life in the ANWA. Moreover, due to being situated at the end of the Fraser River, it is subject to upstream point sources of contamination such as WWTP effluents, paper and pulp mill effluents, lumber industries and non-point sources such as urban storm water and agricultural runoff (Nener and Wernick, 1997).

The ANWA is an ecologically important wildlife habitat found along the Pacific Flyway and supports hundred of thousands to a million migratory birds annually as a stopover and overwintering ground (Environment and Climate Change Canada, 2011). There are a total of 210 species that are native, introduced (invasive) or have been observed at this site (i.e. migratory birds) (Table S5). These species consist of mammals (18), amphibians (2), reptiles (4), fish (6), plants (89) and birds (91). In addition, there are 15 species observed in the ANWA that are either threatened or endangered under the Species At Risk Act (SARA) or the Committee on the Status of Endangered Wildlife in Canada (COSEWIC) (Table S6). Agricultural activities are the primary ecological management tool utilized to produce quality habitats and sufficient foraging opportunities for wildlife and migratory birds. Presently, these agricultural practices include the use of a five-year crop/livestock rotation where there are 2 years of intensive cultivation of cash crops followed by three years of grassland (forage) recovery to reduce the negative impact of agriculture on soil quality and to sustain suitable habitats for wildlife populations (Augustinowicz et al., 2019). Livestock production also takes place in agricultural fields in ANWA and are an integral component to maintain the soil structure and improved water infiltration, increased soil fertility, and higher yields of subsequent

crops and are pastured on some fields during the three years of forage grass cultivation (Augustinowicz et al., 2019). However, livestock excreta may serve as a potential source of veterinary pharmaceuticals if these animals have received recent treatments prior to being placed on the agricultural fields where field runoff could introduce these PPCPs into the surrounding aquatic environment. Due to the remote location of the ANWA, public bathrooms in this site include the use of two septic systems whose septic fields discharge in adjacent soils. Thus, sources of PPCPS within the ANWA could occur from WWTPs, septic field leachate and livestock excreta.

1.4. Polar organic chemical integrative samplers (POCIS)

Typical concentrations of PPCPs in surface waters are detected in the nanogram to microgram per litre levels or may be undetectable by current chemical analytical techniques. Thus, traditional grab sampling of water may not be able to sufficiently characterize surface water concentrations and may result in poor analytical recoveries of PPCPs. In recent years, the development of passive samplers has allowed for the detection of chemical contaminants over longer term durations and are capable of providing semi-quantitative analysis of chemicals. In particular, polar organic chemical integrative samplers (POCIS) have been used in the detection and quantification of PPCPs and are a type of passive sampler that can capture and detect polar and semi-polar compounds. The pharmaceutical-configured POCIS sampler consists of an HLB (a universal polymeric reversed-phase sorbent that binds to acidic, basic and neutral compounds) sorbent sandwiched between two polyethersulfone (PES) microporous membranes and are flattened together by steel rings (Harman et al., 2011). The uptake of compounds into the sorbent is governed by first order kinetics and the porous nature of the PES slows the uptake of lipophilic compounds, whereas hydrophilic compounds can easily pass through the aqueous micropores of the PES and adsorb to the sorbent

(Harman et al., 2011). After deployment, the sorbents with the accumulated contaminants can be analyzed and the time-weighted water concentration can be estimated if an experimental sampling rate (R_s) is available (Bartelt-Hunt et al., 2011; Harman et al., 2011). These concentrations of analytes in water can be modeled using Equation 1 below as described by Alvarez et al. (2004).

Equation 1. Time-weighted concentration of the contaminant of interest from a POCIS passive sampler

$C_{twa} = \frac{C_S \cdot M_S}{R_S \cdot t}$ (Alvarez et al., 2004)

Where C_{twa} is the time-weighted water concentration of a specific analyte in water (ng/L), C_s is the concentration of the analyte accumulated in the sorbent (ng analyte/g sorbent), M_s is the mass of the sorbent in the POCIS (g sorbent), R_s is the sampling uptake rate of a specific analyte (L/d), and t is the amount of time the POCIS was deployed (d).

Passive sampling offers considerable advantages over traditional grab sampling, especially for microcontaminants such as PPCPs. For example, passive samplers are deployed for weeks to months at a time allowing for analytes to accumulate and concentrate to levels that can be detected by current analytical methods. Additionally, POCIS can provide a time-weighted concentration of microcontaminants in water. Together, these characteristics of POCIS allows for the detection of nano-level (ng/L) concentrations of contaminants and episodic contamination events (Alvarez et al., 2004). In contrast, traditional grab sampling can only provide information on an instantaneous point of reference, thus providing insight only on the current chemistry of the environment sampled.

1.5. Ecological risk assessment framework

Ecological risk assessment (ERA) is the process of evaluating both the likelihood and magnitude of ecological impacts in non-human organisms, populations or communities that may occur from the exposure to human-induced stressors

(Environment and Climate Change Canada, 2012). The purpose of an ERA is to determine the extent of ecological risks as a result of the exposure to stressors which subsequently guide remedial decisions made by environmental risk managers for contaminated sites (Environment and Climate Change Canada, 2012). Risk assessments are an iterative process and involves multiple tiered approaches to prioritize the investigation of contaminants or sites (Environment and Climate Change Canada, 2012). In the Canadian Council of the Ministers of the Environment (CCME) Framework for Ecological Risk Assessment, a three-tier framework is recommended which includes a screening assessment, preliminary quantitative ERA, and detailed quantitative ERA, with each tier increasing in complexity (CCME, 1996). A more recent ERA guidance document for the Federal Contaminated Sites Action Plan also mentions the iterative process of a ERAs but doesn't distinguish discrete tiers of ERAs as in the CCME guidance (Environment and Climate Change Canada, 2012). In contrast to the CCME ERA guidance, the FCSAP ERA guidance document recommends further risk assessments only if the future ERA can significantly advance the understanding of the risks and reduce the uncertainty from using simplified conservative assumptions in the event unacceptable risks are suspected (Environment and Climate Change Canada, 2012). In the early phases of an ERA, screening-level assessments are conducted using simplified and conservative assumptions to determine if current exposure of a stressor to an ecological receptor could have the potential to cause adverse effects or health risks. The advantage of screening-level approaches in an ERA is that it allows for the swift elimination of many contaminants that may be present at a site at negligible levels and provides the risk assessor means to prioritize chemicals of potential concern (COPC) that may be of ecological significance. However, because of the conservative assumptions and simplicity of models that may be used, there is high uncertainty associated with screening-level assessments. Thus, further iterations of increasingly

complex ERA are conducted to minimize uncertainty and can be used as predictive tools for determining whether contaminants can have potential for ecological impacts (CCME, 1996).

Regardless of the tier of the ERA, each risk assessment will include four major phases which are: problem formulation, exposure assessment, effects assessment and risk characterization. Problem formulation is the first step of any ERA where an overview of the nature of the contamination in the context of the site is qualitatively framed, temporal and spatial boundaries of the ERA are defined, and site management goals are established (Environment and Climate Change Canada, 2012). The objective of problem formulation is to identify foundational elements of the ERA including: COPCs to be evaluated, their sources and transport pathways, receptors of potential concerns (ROPC) that may be sensitive to these COPCs, exposure pathways to ROPCs (i.e. inhalation, oral, dermal exposure, etc.) and identifying valuable ecological components (i.e. critical migratory waterfowl habitat and benthic community structure) to be protected (Environment and Climate Change Canada, 2012). Within this phase, available data pertaining to the site is compiled from literature, historical data, monitoring studies, previous preliminary studies and site investigations, which are summarized by a conceptual site model (CCME, 1996).

Exposure assessment and effects assessment are considered the analytical phases of an ERA and can be conducted concurrently. In exposure assessment, the extent of the contamination and route of exposure to receptors within the site are characterized. This can be determined by directly measuring environmental media (i.e. surface water, sediments, porewater, soils or dietary items) a receptor may be exposed to, internal measures of receptor tissue concentrations of contaminants, or even modelled exposure data using known emission parameters (Environment and Climate

Change Canada, 2012). Effects assessment characterizes the potential effects of a contaminant on receptors at environmentally relevant concentrations. These effects can be predicted using various types of measures including site-specific toxicity tests (i.e. *in situ* tests, toxicity testing using site-collected media), toxicity data from peer-reviewed literature, site-specific biological studies (i.e. community structure analysis), or indirect biological information (i.e. comparison between the site of interest and a reference site) (Environment and Climate Change Canada, 2012).

Risk characterization combines all aspects of the ERA together to provide an estimate of the probability and extent of ecological impacts that may occur from each phase of the ERA. Frequently, hazard quotients (HQ) are used in risk characterization to evaluate risk (particularly in screening assessments) and are computed by taking the ratio of point estimate of an exposure term (i.e. abiotic media concentration) by a point estimate of an adverse effect term (i.e. LD50, lethal dose to 50% of a test population; NOAEL, no observed adverse effect concentration) (Environment and Climate Change Canada, 2012). The advantage of characterizing risk using the HQ approach is that it allows for efficient screening of contaminants with low or negligible ecological impacts and provides a means for the risk assessor to allocate resources into other priority substances that have higher potential for ecological risk (CCME, 1996; Environment and Climate Change Canada, 2012). Though HQs are useful in determining whether exposure scenarios will have negligible adverse outcomes to receptors, in many cases HQs are erroneously used to infer the magnitude ecological impact when they are computed above a value of one and may only reflect worst-case scenarios (i.e. an HQ of 2 does not equal twice the risk of an HQ of 1) (Allard et al., 2010; Environment and Climate Change Canada, 2012; Tannenbaum, 2005). Therefore, HQs remain useful as a preliminary screening step in the ERA process but should be used as a mechanism for

prioritization for proceeding contaminants into more detailed ERAs or to be used as acceptable environmental standards (i.e. environmental quality guidelines) that should not be exceeded without further evaluation of ecological risks (CCME, 1996; Environment and Climate Change Canada, 2012).

1.6. Research objectives

The objective of this study was to conduct a screening-level ERA to determine whether presently measured concentrations of PPCPs would cause unacceptable ecological impacts on aquatic and terrestrial receptors in the ANWA. To achieve the aims of this research, environmental exposure was characterized by taking environmental measurements of PPCPs in the sediment, surface waters and modelled food-web transfer of PPCPs to receptors in the ANWA. In addition, to characterize the potential hazards that may pose on ecological components, available toxicological data from environmental quality guidelines, peer-review literature and quantitative structure activity relationships (QSAR) were utilized.

Chapter 2. Materials and methods

2.1. Exposure assessment

2.1.1. Environmental sampling and chemical analysis

Various environmental matrices were sampled in 2020 within the ANWA by CWS and several pesticides, heavy metals and PPCPs were measured as part of a larger study to assess the risks these contaminants pose to wildlife at this site. Specifically, the present study focuses on PPCPs measured in sediment grab samples and water samples collected via polar organic chemical integrative samplers (POCIS; Figure 1). The sediment samples were collected in February and September of 2020 in the sampling sites listed in Figure 1 and were collected at depths of up to 0.1 m within sediments of irrigation ditches, sloughs, or ponds. The POCIS in the pharmaceutical configuration were deployed during the spring and summer (January and August 2020) to detect trace levels of PPCPs in the surface waters of ANWA (Figure 1). January and August POCIS units were deployed for 44 (2 sites, 1 field blank) and 56 days (4 sites, 1 field blank), respectively. POCIS were pre-assembled and stored in air-tight containers prior to transport to sampling sites. Field blanks were included whereby POCIS membranes and their respective POCIS sampling units were transported to the field and handled in the field in the same manner as non-blank POCIS units, except these units were not deployed into the water but returned to the lab for analysis. These POCIS field blanks were utilized as a field control to account for any potential contamination that may occur during the transport and handling of the samplers prior to their deployment into the water. Sediment and POCIS samples were sent to SGS AXYS Analytical Services (Sidney, BC, Canada) for chemical extraction and quantification using high performance liquid chromatography combined with tandem mass spectrometry (LC-MS/MS)

according to SGS AXYS PPCP Method MLA-075 (revised EPA 1694 method), and were analyzed for 141 PPCP analytes, including parent compounds or their metabolites (Table S1 and Table S2). Detection limits for each analyte are reported as “reporting limits” and were defined as the lower method calibration limit (LMCL) or as a sample specific detection limit (SDL). The LMCL is determined by prorating the analyte concentration using the lowest calibration limit for a surrogate multiplied by the extract volume used in the analysis divided by the sample size (SGS AXYS Analytical Services Ltd., unpublished). The SDL was calculated by SGS AXYS using the QuanLynx software individually for each sample analyses by converting the area equivalent of 3.0 times the estimated chromatographic noise height to a concentration in the same manner that analyte peaks responses are calculated as analyte concentrations (SGS AXYS Analytical Services Ltd., unpublished),

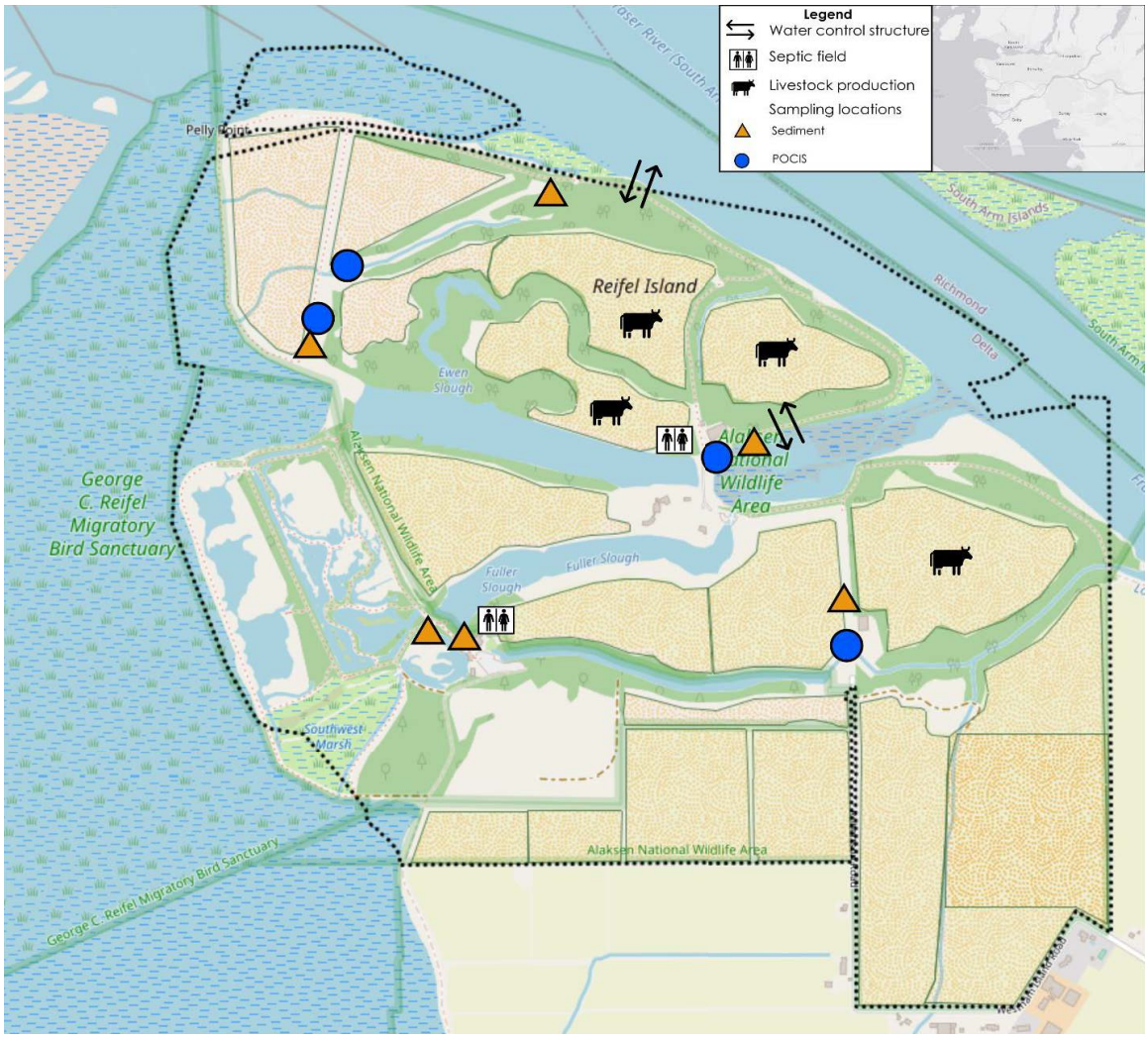

Figure 1. Map of Alaksen National Wildlfie Area with sediment and polar organic integrative sampler deployment sites.

Orange-filled polygons represent agricultural fields, blue circles represent sediment sample sites (n=6), and orange triangles represent POCIS deployment sites (n=6). Fields where cattle grazing takes place during forage years of the five-year crop/livestock rotation are indicated by the cattle silhouettes. Septic fields which service public washrooms are listed, along with water control structures (i.e. screw gates) directly connecting the irrigation ditches of the ANWA with the Fraser River.

2.1.2. Sediment porewater and surface water PPCP estimations

In addition to characterizing the sediment as an environmental matrix, porewater concentrations were also estimated. Porewater concentrations were calculated using the equilibrium partitioning approach (Burgess et al., 2012), which assumes that non-ionic chemicals in sediments partition between organic carbon and porewater. By using

the partitioning coefficient for organic carbon and water (K_{oc}) predicted from EPISuite v4.1 (US EPA, 2012) and fraction of organic content in sediments (f_{oc}), it is possible to predict the contaminant concentration within the porewater for non-ionic chemicals with log K_{ow} > 2 (Burgess et al., 2012; Equation 2). Given that many PPCPs are ionized in most environmental conditions, K_{oc} was obtained using the molecular connectivity index (MCI) method within EPISuite v4.1 (US EPA, 2012) rather than predicting K_{oc} with log K_{ow}. The f_{oc} of the sediments of the ANWA was approximated by using the organic content of agricultural soils within the site based on a previous soil chemistry study (Augustinowicz, 2021). Thus, porewater concentrations (C_w) can be calculated by dividing sediment concentrations by the product of K_{oc} and f_{oc} (Equation 2).

Equation 2. Equilibrium partitioning and freely dissolved porewater concentrations (Burgess et al., 2012).

$$C_w = \frac{C_s}{Kk_{oc} * f_{oc}}$$

C_w = Porewater concentration of an analyte (µg/L)

K_{oc} = Organic-carbon partitioning coefficient for an analyte

f_{oc} = fraction of organic content in sediments, f_{oc} = 0.0169 for agricultural soils in ANWA (Augustinowicz, 2021).

The concentrations of PPCPs measured via POCIS were also used to estimate surface water concentrations. Following chemical analysis of each of the POCIS unit extracts for PPCPs whereby measurement units are reported as mass (ng) per sampler, this value can then be used as an input parameter in Equation 1 to calculate the time-weight average surface water concentration of PPCPs in ANWA. Sampling rates (R_s) were compiled from 12 laboratory or *in situ* calibration studies previously published for each of the 21 PPCPs detected in the samplers (Table S3). If multiple R_s values were available for a specific analyte, the lowest R_s for that analyte was selected to calculate the surface water concentrations to establish a conservative estimate for the predicted

environmental concentrations (PEC) in surface waters. Additionally, if there were no R_s values available in literature for an analyte detected in POCIS in the present study, it was estimated using the linear relationship between log K_{ow} and the R_s values of various PPCPs (n=30) derived from a static POCIS laboratory calibration experiment which included R_s data for basic PPCPs, neutral PPCPs, and endocrine disrupting compounds ($R_s = 0.171 \times \text{Log } K_{ow} + 0.19$, $R^2 = 0.84$; Li et al., 2010). In the Li et al., 2010 POCIS laboratory calibration study, acidic compounds, triclosan, 4-nonylphenol, and sertraline were excluded from the dataset to achieve a better fit of the linear regression. Among the PPCPs detected in POCIS in this study, cloxacillin and cotinine are poorly represented by the Li et al. (2010) regression since both have pka values that were less than 7 (2.78 and 4.79, respectively); thus, there would be high uncertainty when estimating the R_s of these compounds using this linear relationship at typical environmental pH ranges.

2.1.3. Bioaccumulation and food web modelling

To understand the impact of potentially bioaccumulative PPCPs to the terrestrial food web in ANWA, PPCPs with log K_{ow} greater than 5 were analyzed using the K_{ow}-based aquatic bioaccumulation model (KABAM) published by the US EPA to predict whether dietary uptake of contaminants in terrestrial biota such as birds and mammals would reach concentrations that are toxic. KABAM is a generalized bioaccumulation and food web model designed by the US Environmental Protection Agency Office of Pesticide Programs' Environmental Fate and Effects Division that represents a freshwater aquatic ecosystem and can quantitatively describe the trophic transfer of a pesticide from the abiotic environment to seven trophic components within the food web (US EPA, 2015). Furthermore, this model can determine the total terrestrial dietary consumption of contaminated aquatic prey within an aquatic ecosystem at steady state

thus, approximating the potential dose an animal is exposed to via dietary sources (US EPA, 2015). The KABAM model is based on an aquatic bioaccumulation model proposed by Arnot and Gobas in which kinetic parameters such as uptake (i.e. through diet) and elimination (i.e. bile, urine, feces and respiration) rate constants from various biological compartments are used to predict tissue residue concentrations of hydrophobic chemicals in aquatic organisms using only physicochemical properties of the substance such as log K_{ow} and log K_{oc} (Arnot and Gobas, 2004). However, it is important to note that KABAM does not account for metabolic biotransformation and assumes that no metabolism is taking place. This may overestimate chemical accumulation for chemicals that are metabolized into non-toxic metabolites or excreted rapidly or may underestimate if more toxic and/or persistent metabolites are created. Ultimately, KABAM is used to predict tissue residues of contaminants in aquatic guilds such as zooplankton, phytoplankton, benthic invertebrates, filter feeders, small-sized fish, medium-sized fish, and large-sized fish (see conceptual model in Figure 2) using only a minimal amount of chemical input parameters.

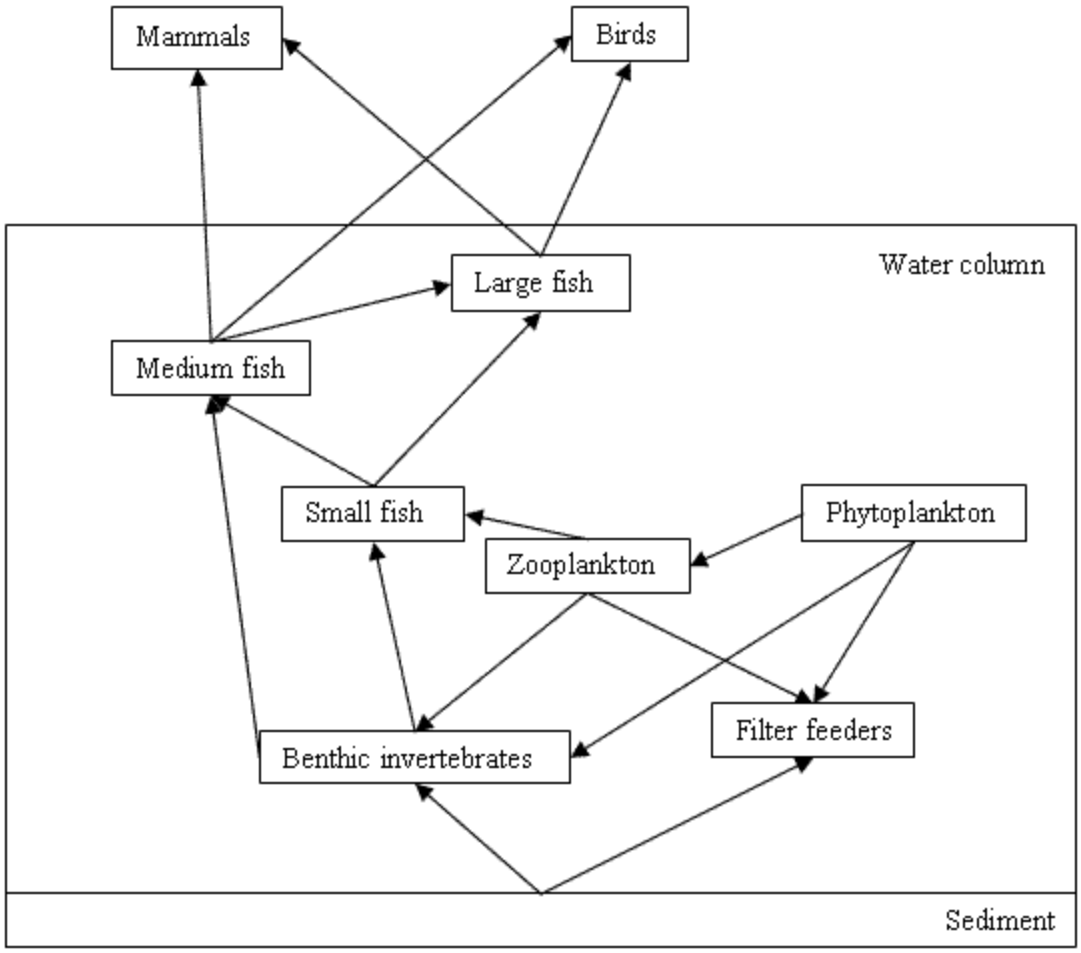

Figure 2. Conceptual model of the freshwater ecosystem described in the K_{ow}-based aquatic bioaccumulation model (KABAM) originally published in KABAM Version 1.0 User's Guide and Technical Documentation.

Seven trophic components are depicted and are the feeding guilds that represent the simulated freshwater ecosystem. Arrows show the direction of trophic transfer of a bioaccumulated chemical. https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/kabam-version-10-users-guide-and-technical

The second component of the KABAM model calculates the food ingestion rate and water consumption rate of piscivorous terrestrial birds and mammals to estimate the potential dietary exposure of bioaccumulated chemicals from an aquatic prey diet. However, key wildlife species of ecological importance within the ANWA (such as owls) do not solely consume fish reducing the applicability of the use of the current KABAM model. Thus, based on the current ecological setting of the ANWA, it would not sufficiently represent groups such as birds of prey or other higher trophic predators that

may incorporate higher proportions of small mammals in their diet. Therefore, this model was modified to include a terrestrial earthworm-shrew bioaccumulation model published by Gobas et al. and was parameterized using shrew-specific data reported in Armitage and Gobas to characterize the bioaccumulation of chemicals in mammalian prey. This shrew bioaccumulation model predicts the bioaccumulation of dietary contaminants by modelling the biomagnification factor (BMF) of a contaminant using the log K_{ow} of the contaminant and by modelling the kinetic parameters (Table 1) of both the shrew and earthworm at steady state described in Equation 3 (Armitage and Gobas, 2007; Gobas et al., 2003). However, instead of using earthworms as the representative prey species in the bioaccumulation equation for the shrew, the present study used the aquatic invertebrates tissue concentration as the prey biota rather than earthworm tissue residue since soils were not collected in this study for the chemical quantification of PPCPs. Furthermore, given the known presence of aquatic shrew in the ANWA (i.e. the pacific water shrew, *Sorex bendirii*) in which aquatic and terrestrial insects are dietary constituents, it is plausible that shrew native to the ANWA watershed may primarily utilize aquatic invertebrates as a food source. This further supports the substitution of earthworms with aquatic invertebrates in Equation 3 for the present risk assessment. Additionally, this modified food-web model does not represent other lower trophic mammalian prey such as voles (which are primarily herbivorous and are the primary prey species for some birds), thus this feeding relationship provides a conservative approximation of the expected dose in terrestrial predators.

Equation 3. Biomagnification factor equation at steady state for shrew whose diet is composed of only aquatic invertebrates (Gobas et al., 2003).

$$BMF = \frac{C_{biota}}{C_{diet}} = \frac{C_{shrew}}{C_{aq.invert}} = \frac{k_{diet}}{k_{air}+k_{urine}+k_{bile}+k_{feces}} \quad at\ steady\ state$$

BMF = biomagnification factor

C_{biota} = concentration of chemical contaminant in the tissue of the biota consuming a diet item

C_{diet} = concentration of chemical contaminant in the tissue of diet item

C_{shrew} = concentration of chemical contaminant in the tissue of the shrew

$C_{aq.invert}$ = concentration of chemical contaminant in the tissue of the aquatic invertebrate

K_{diet} = uptake rate constant of a chemical from diet

K_{air} = elimination rate constant of a chemical from respiring air

K_{urine} = elimination rate constant of a chemical from excreting urine

K_{bile} = elimination rate constant of a chemical from excreting bile

K_{feces} = elimination rate constant of a chemical from excreting feces

Table 1. Kinetic parameters and values for the terrestrial shrew bioaccumulation model to predict the tissue residue of PPCPs in small insectivorous mammals accumulated from sediment and the water column of Alaksen National Wildlife Area.

Model Parameter	Value or Equation	Reference
Dietary uptake constant (K_{Diet})	$K_{Diet} = \frac{E_D \times G_D}{V_B}$	Gobas et al. 2003
Respiratory elimination constant (K_{Air})	$K_{Air} = \frac{E_A \times G_A}{V_B \times L_B \times K_{OA}}$	Gobas et al. 2003
Urinary elimination constant (K_{Urine})	$K_{Urine} = \frac{G_U}{V_B \times L_B \times K_{OW}}$	Gobas et al. 2003
Fecal elimination constant (K_{Fecal})	$K_{Fecal} = \frac{G_F}{V_B \times K_{BF}}$	Gobas et al. 2003
Bile elimination constant (K_{Bile})	$K_{Bile} = \frac{G_B}{V_B \times L_B \times K_{OB}}$	Gobas et al. 2003
Octanol-bile partitioning coefficient (K_{OB})	$K_{OB} = \frac{kK_{OW}}{ß}$, where ß = 10	Gobas et al. 2003
Volume of a shrew (V_B)	10^{-5} m^3	US EPA, 1993; Wildlife Handbook
Efficiency of chemical uptake from diet (E_D)	90 %	Armitage et al. 2007
Efficiency of chemical uptake from air (E_A)	70 %	Gobas et al. 2003
Volume of food ingested (G_D)	9.1 x 10^{-6} m^3/d	US EPA, 1993; Wildlife Handbook
Respiration rate (G_A)	0.034 m^3/d	US EPA, 1993; Wildlife Handbook
Urine excretion rate (G_U)	5 x 10^{-6} m^3/d	Armitage et al. 2007
Fecal excretion rate (G_F)	1.7 x 10^{-6} m^3/d	Armitage et al. 2007
Bile excretion rate (G_B)	4 x 10^{-7} m^3/d	Armitage et al. 2007

K_{diet} = uptake rate constant of a chemical from diet

K_{air} = elimination rate constant of a chemical from respiring air

K_{urine} = elimination rate constant of a chemical from excreting urine

K_{bile} = elimination rate constant of a chemical from excreting bile

K_{feces} = elimination rate constant of a chemical from excreting feces

ß = bile solubility enhancement, the estimated increase in solubility of chemicals in bile fluids (Armitage and Gobas, 2007)

K_{OB} = partitioning coefficient between octanol and bile

In addition to the freshwater aquatic food-web parameterized by KABAM, a terrestrial food-web representing important terrestrial feeding guilds in the ANWA was constructed for birds and mammals (Figure 3). The feeding guilds represented in this model for birds include insectivores, piscivores, and carnivores whose diet consist of small mammals only and generalist carnivores whose diet consists of both fish and small mammals (Table 2). Representative feeding guilds for mammals include insectivores, piscivores, carnivores whose diet consist of small mammals. Dietary preferences were nominally assigned assuming the feeding guild solely fed on their primary prey species (i.e. insectivores only consumed invertebrates), except in the case for avian carnivores with a dual diet between fish and small mammals where 50% was assigned to each prey item, respectively. Due to a number of SARA and COSEWIC listed species (15 species) observed in the ANWA, an additional food-web model was constructed using SARA species-specific characteristics and dietary preferences (Table 3).

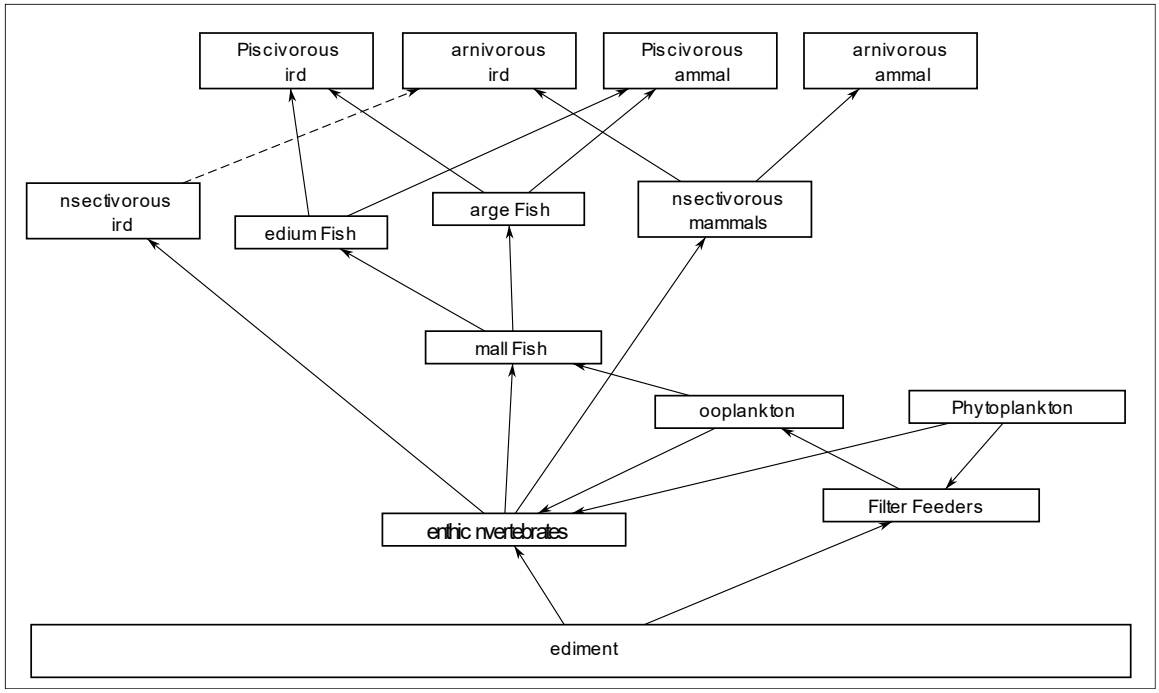

Figure 3. Representative food web of the freshwater ecosystem of Alaksen National Wildlife Area including aquatic and terrestrial components. Arrows depict a prey to predator feeding relationship.

Table 2. Terrestrial food web and dietary preferences of representative feeding guilds of birds and mammals of Alaksen National Wildlife Area.

Feeding Guild	Surrogate Species	Dietary Preference (%)				
		Aquatic Invertebrate	Small Fish	Medium Fish	Large fish	Small Mammal
Mammals						
Insectivore	Vagrant shrew	100	0	0	0	0
Carnivore - small mammals	Mink	0	0	0	0	100
Piscivore	River otters	0	0	0	100	0
Birds						
Insectivore	American Robin	100	0	0	0	0
Piscivore	Great Blue Heron	0	0	0	100	0
Carnivore - small mammals	Barn Owl	0	0	0	0	100
Carnivore - fish and mammals	Bald Eagle	0	0	0	50	50

Table 3. Terrestrial food web and dietary preferences of Species At Risk Act listed animals observed in Alaksen National Wildlife Area.

Common Name	Species Name	Dietary Preference (%)				
		Aquatic Invertebrates	Small Fish	Medium Fish	Large Fish	Small Mammal
Barn owl western population[1]	*Tyto alba*	0	0	0	0	100
Barn swallow[2]	*Hiundo rustica*	100	0	0	0	0
Great Blue Heron[2]	*Ardea herodias fannini*	0	0	0	65	35
Horned grebe[3]	*Podiceps auratus*	50	50	0	0	0
Western grebe[4]	*Aechmophorus occidentalis*	0	100	0	0	0
Olive-sided flycatcher[5]	*Contopus cooperi*	100	0	0	0	0
Short-eared owl[6]	*Asio flammeus*	0	0	0	0	100
Peregrine falcon[2]	*Falco peregrinus pealei*	0	0	0	0	100
Black swift[7]	*Cypseloides niger*	100	0	0	0	0
Pacific water shrew[8]	*Sorex bendirii*	1	0	0	0	0
Little brown myotis[9]	*Myotis lucifugus*	1	0	0	0	0
Western painted turtle Pacific coast population[10]	*Chrysemys picta bellii*	1	0	0	0	0

[1]Campbell et al., 1987

[2]Environment and Climate Change Canada, 2012: FCSAP Ecological Risk Assessment Guidance Module 3

[3]COSEWIC, 2009, dietary preferences were assigned using the author's professional judgement based on this reference.

[4]COSEWIC, 2014

[5]Environment and Climate Change Canada, 2016

[6]British Columbia, 1996

[7]Marin, 1999

[8]Lindgren, 2004
[9]Environment Climate Change Canada, 2015
[10]US EPA, 1993; Wildlife Handbook

2.1.4. Surrogate receptor characteristics and oral dose calculation

Receptor characteristics for each guild such as body weight, feeding rate, drinking rate and incidental soil ingestion for adult animals were compiled from the FCSAP Ecological Risk Assessment Guidance Module 3, US EPA Wildlife Exposure Factors Handbook Volume I, peer-reviewed literature, government websites or other organizational sources (Table 4). Each feeding guild was represented by a surrogate receptor, preferentially native species or species with a known presence in the area. Otherwise, closely related species (i.e. from the same genus) that also occupy similar ecological niches and habitats were selected. In most cases, empirically measured feeding rates and drinking rates were not available and were estimated using allometric equations as described by Nagy, (1987) and Calder and Braun, (1983), respectively. Soil ingestion rates were set at a default rate 2% unless otherwise stated in FCSAP Ecological Guidance Module 3 or in US EPA Wildlife Factors Handbook Volume I. Similarly, receptor characteristics for SARA or COSEWIC listed species were individually compiled using species-specific data when possible (Table 5).

Table 4. Biological characteristics of surrogate receptors of the Alaksen National Wildlife Area.

Surrogate Receptor	Feeding Guild	Body Weight Lower Limit (kg)	Body Weight Upper Limit (kg)	Feeding rate (kg/d)	Drinking rate (L/d)	Incidental soil ingestion (%)
Vagrant shrew	Insectivore	-	0.009	0.00306[a]	0.002[c]	2
American mink	Carnivore	0.570	1.06	0.148	0.032	2
Northern river otter	Piscivores	7.30	7.70	0.231	0.616	2
American robin	Insectivore	0.0774	0.0806	0.0975	0.011	4
Great blue heron	Piscivore	2.10	2.50	0.300	0.100	2
Barn owl	Carnivore	0.312	0.362	0.335[b]	0.030[c]	2
Bald eagle	Carnivore	3.70	6.40	1.15	0.256	2

Receptor characteristics were obtained from FCSAP Ecological Risk Assessment Guidance Document Module 3 unless otherwise noted. Feeding rates obtained from FCSAP Ecological Risk Assessment Guidance Document Module 3 report feeding and drinking rates at kg and L per kg body weight basis. Final rates calculated using the upper body weight limit.

[a]Feeding (kg/kg-bw) and drinking rates (L/kg-bw) were based on the receptor characteristics of the common shrew reported in the FCSAP Ecological Risk Assessment Guidance Document Module 3 and were calculated using the body weight of a vagrant shrew (9 g).

[b]Calculated using the food metabolic rate equation for all birds described by Nagy 1987
Where:

$$food\ ingestion\ rate\ \left(\frac{kg}{d}\right) = 10^{-0.188+0.651\times\log(kg\ body\ weight)}$$

[c]Calculated using the allometric equation described by Calder and Braun 1983
Where:

$$drinking\ rate\ \left(\frac{L}{d}\right) = 0.059 \times kg\ body\ weight^{0.67}$$

Table 5. Biological characteristics of Species At Risk Act or Committee on the Status of Endangered Wildlife in Canada listed species that are known to occur in the Alaksen National Wildlife Area.

Common Name	Species Name	Body weight male (kg)	Body weight female (kg)	Feeding Rate (kg/d)	Drinking Rate (L/d)	Incidental soil ingestion (%)
Barn owl western population	*Tyto alba*	0.312[a]	0.362[a]	0.335[b]	0.0300[c]	2
Barn swallow	*Hiundo rustica*	0.0181	0.0192	0.00499	0.00422	2
Great Blue Heron	*Ardea herodias fannini*	2.50	2.1	0.450	0.100	2
Horned grebe	*Podiceps auritus*	0.300-0.570[d]		0.0285[e]	0.0342[e]	2
Western grebe	*Aechmophorus occidentalis*	1.43[f]	1.199[f]	0.0715[e]	0.0857[e]	2
Olive-sided flycatcher	*Contopus cooperi*	0.0340[g]	0.031[g]	0.00884[h]	0.00748[h]	2
Short-eared owl	*Asio flammeus*	0.315[i]	0.380[i]	0.345[b]	0.0310[c]	2
Peregrine falcon	*Falco peregrinus pealei*	0.652	0.977	0.0586	0.0586	2
Black swift	*Cypseloides niger*	0.0450[j]		0.0117[h]	0.0099[h]	2
Pacific water shrew	*Sorex bendirii*	0.0132[k]		0.00449[l]	0.0020[l]	2
Little brown myotis	*Myotis lucifugus*	0.005-0.009[m]		0.00450[n]	0.001[n]	2
Western Painted Turtle	*Chrysemys picta bellii*	0.177[o]	0.327[o]	0.0003[p]	NR	6

Values in the body weight column depicted as a range are body weights for both sexes.

[a]The Barn Owl Trust 2021; https://www.barnowltrust.org.uk/

[b]Calculated using the food metabolic rate regression equation for all birds described by Nagy 1987

Where:

$$food\ ingestion\ rate\ \left(\frac{kg}{d}\right) = 10^{-0.188+0.651\times\log(kg\ body\ weight)}$$

[c]Calculated using the allometric regression equation described by Calder and Braun 1983

Where:

$$drinking\ rate\ \left(\frac{L}{d}\right) = 0.059 \times kg\ body\ weight^{0.67}$$

[d]COSEWIC, 2009

[e]Feeding and drinking rates were calculated using body weight adjusted mallard rates from FCSAP Ecological Risk Assessment Guidance Document Module 3.

[f]COSEWIC, 2014

[g]Environment and Climate Change Canada, 2016

[h]Feeding and drinking rates were calculated using body weight adjusted barn swallow rates from FCSAP Ecological Risk Assessment Guidance Document Module 3.

[i]British Columbia, 1996

[j]Marin, 1999

[k]Lindgren, 2004

[l]Feeding and drinking rates were calculated using body weight adjusted common shrew rates from FCSAP Ecological Risk Assessment Guidance Document Module 3.

[m]Environment Climate Change Canada, 2015

[n]Feeding rate was described as eating "half its body weight per day", thus taking the upper body weight limit of 9 g and dividing by two results in 4.5 g/d.

[o]US EPA Wildlfe Factors Handbook Volume I, specifically the painted turtle (*Chrysemys picta*) entry

[p]Weber, 2019

Equation 4. Total bioaccumulated dietary dose based on food preferences.

Total dietary dose (µg/kg) =

$$\frac{p_{invert} \times C_{invert} + p_{small\ fish} \times C_{small\ fish} + p_{large\ fish} \times C_{large\ fish} + p_{small\ mammal} \times C_{small\ mammal}}{body\ weight\ (kg)}$$

Where:

P_i = proportional weight of the prey item indicated by the subscript (unitless).
C_i = prey tissue concentration of the prey item indicated by the subscript (µg/kg).

The total PPCP oral exposure to terrestrial animals was calculated by coupling the KABAM modelled aquatic and terrestrial prey tissue data with a site-specific food-web model (Equation 4 and 5).

Equation 5. Total oral dose from dietary and drinking water sources.

Total oral dose (µg/kg) =

$$Total\ dietary\ dose\ (\frac{\mu g}{kg}) + \frac{drinking\ rate\ \left(\frac{L}{d}\right) \times C_{water}\left(\frac{\mu g}{L}\right)}{body\ weight\ (kg)}$$

Where:

C_{water} = concentration of PPCP in water (µg/L)

2.2. Effects assessment

2.2.1. Toxicity reference value derivation

To characterize the potential ecological hazards posed by PPCPs in this risk assessment, numerical benchmarks for each PPCP were compiled or derived to predict a concentration or dose at which no or negligible adverse health effects would occur. Numerical toxicological benchmarks selected in this risk assessment included environmental quality guidelines (EQG) from the federal government of Canada (Canada FEQG or CCME) or provincial EQGs (BC). If no EQG were available for a PPCP, ecotoxicity studies from peer-reviewed literature, government or industry reports were reviewed to derive a toxicity reference value (TRV). Toxicological studies were compiled from databases such as the ECOTOX Knowledgebase (Olker et al., 2022), Web of Science, US EPA OPP, and US Federal Drug Agency (FDA) pharmaceutical reports.

The quality of the studies compiled was deemed acceptable without restrictions if the following parameters were included in each study: chemical analysis of exposure media during the exposure experiment; standardized laboratory methods (i.e. OECD, ASTM, US EPA standardized testing, or followed good laboratory practices); three or more replicates per concentration tested; three or more different concentrations tested; and inclusion of the measurement of ecologically relevant endpoints at the apical level. If no quality studies could be identified, quantitative structure activity relationships (QSAR) were used to determine the compound's toxicity based on the relationship between chemical class and known toxicity to reference taxa. Specifically, the Ecological Structural Activity Relationships (ECOSAR) computational program by the US EPA was used when QSAR was relied upon for some PPCPs to estimate chronic toxicity for fish, Daphnid, mysid and green algae, whereby the most sensitive toxicity value of these species was selected. After finding the most sensitive applicable TRV, an assessment factor based on the European Chemical Agency assessment factor framework was applied in order to derive a predicted no effects concentration (PNEC) for each PPCP (European Chemicals Agency, 2008; see Table 6). For instances where an EQG was available for a PPCP, the derived EQG value was used as the PNEC with no assessment factor applied.

2.2.2. Interspecies correlation estimation

Terrestrial TRVs were compiled from EQGs (e.g. CCME tissue residue guidelines), peer-reviewed literature, material safety data sheets (MSDS), and FDA pharmacological reviews. However, in circumstances where only rodent acute toxicity data was available, interspecies correlation estimation (ICE) models published by the US EPA (Web-ICE) were used to predict avian acute toxicity (Raimondo et al., 2010). ICE models use least-squares regression of the sensitivity relationship between two species

using a large dataset of chemicals including a varied range of chemical classes. To reduce model error, interspecies models were selected if they had a mean square error (MSE) < 0.95, R^2 > 6, slope > 0.6, and close taxonomic distance (< 5) (Raimondo et al., 2010). The model conforming to most of these criteria was the *Rattus norvegicus* (Norway rat) to the family Passeridae (MSE = 0.300, R^2 = 0.703, slope = 0.955, taxonomic distance = 5) and was chosen to model avian acute toxicity from acute rodent toxicity studies.

Table 6. Assessment factor framework from ECHA 2008.

Available Data	Assessment Factor
At least one short-term L(E)C50 from each of three trophic levels (fish, invertebrates (preferred Daphnia) and algae)	1000
One long-term EC10 or NOEC (either fish or Daphnia)	100
ECOSAR modelling using chronic toxicity[a]	100
Two long-term results (e.g. EC10 or NOECs) from species representing two trophic levels (fish and/or Daphnia and/or algae)	50
Long-term results (e.g. EC10 or NOECs) from at least three species (normally fish, Daphnia and algae) representing three trophic levels	10
Species sensitivity distribution (SSD) method	5-1
Field data or model ecosystems	Reviewed on case by case basis

https://echa.europa.eu/documents/10162/17224/information_requirements_r10_en.pdf/

[a]This criterion was not part of the ECHA assessment factor framework and was selected by the risk assessor to address the uncertainty of using a modelled toxicity value.

2.3. Risk characterization

To assess the ecological risks of PPCP examined via water (January and August of 2020) and sediment (February and September of 2020) sampling collections chemical analyses at the ANWA, a deterministic approach was used to compare toxicity to environmental exposure. This method essentially calculates a hazard quotient for each PPCP by dividing a point estimate of exposure (i.e. the maximum porewater concentration, surface water concentration or total oral dose) by a point estimate of

effects (i.e., PNEC at the organismal level for growth, reproduction or survival for the most sensitive species reported to date). A hazard quotient greater than one indicates a potential for adverse effects to occur in species exposed to the contaminant at current environmental concentrations, while a hazard quotient lower than one indicates that there is negligible potential for an adverse effect to occur in species exposed to the contaminant at current environmental concentrations. In addition to assessing the risk of individual PPCPs on ecological receptors of the ANWA, the effects of mixtures of PPCPs were also evaluated. Multi-chemical exposures at the ANWA on wildlife were evaluated using the hazard index approach (HI). The sum of the hazard quotients for PPCPs sharing the same mode of action were computed, deriving the hazard quotient for a pharmaceutical class (i.e. central nervous system (CNS) stimulants, anti-depressants, etc.) or personal care product category (i.e. antibacterial agent, sunscreen, mosquito repellants, etc.). Values of HI greater than one indicate potential ecotoxicological risk while HI values lower than one indicates no risk.

Chapter 3. Results

3.1. Pharmaceutials and personal care products as contaminants of potential concern at the Alaksen National Wildlife Area

A total of 26 different PPCPs were detected and quantified above their respective reporting limits (RL) in either sediment and POCIS including, anti-hyperglycemics, anti-fungals, insect repellent, chemotherapeutics, non-steroidal anti-inflammatories (NSAID), anti-convulsants, beta-blockers, bronchodilators, anti-depressants, illicit drugs (cocaine and opioids), plastics, and five different classes of antibiotics (Table 7 and 8). At least one PPCPs was measured in each sediment sampling site, whereas the 44 and 56-day POCIS deployments yielded a minimum of five PPCPs detected in surface waters. However, the quinolone antibiotic sarafloxacin and the insect repellent DEET were detected in at least one POCIS field blank, possibly due to field contamination or laboratory error. Using the sediment and POCIS chemistry data, the porewater and time-weighted surface water concentrations were determined for each detected PPCP analyte, respectively. Chemical identifiers and physicochemical properties of each PPCP measured above a RL were compiled including CAS number, compound class, molecular weight, log K_{ow}, log K_{oc}, log K_{oa}, boiling point, melting point, vapour pressure, water solubility and Henry's a w onstant (Table 4).

In the present study a total of seven out of 141 different PPCPs were quantified above LOQ in sediment samples (Table 7). Concentrations of PPCPs varied and ranged from 0.49 (metformin) to 1400 µg/kg (DEET). The insect repellent DEET was ubiquitously found in all six PPCP sediment samples and within the field and lab blank controls. At this time, it is unclear whether the detection of DEET was due to contamination during chemical analysis since the lab blank sample exhibited DEET at

similar concentrations to three of the sediment samples (PPCP 1-PPCP 5) or due to field contamination during sediment sampling. However, DEET was detected at sediment concentrations much higher at PPCP 6 site (1400 µg/kg) than those detected in the lab blank samples at PPCP 2, 3 and 5 (ranged from 1.1 to 47.2 µg/kg). Furthermore, PPCP 6 is the closest in proximity to the Fraser River, thus measured sediment concentrations of DEET may be due to upstream anthropogenic inputs such as WWTP effluents. Pharmaceutical active ingredients such as metformin (anti-diabetic drug, 0.49 – 0.516 µg/kg), daunorubicin (chemotherapeutic drug, 3.27 µg/kg), erythromycin-H_2O (antibiotic, 3.44 µg/kg) and anti-fungal drugs including clotrimazole (1.39 µg/kg) and miconazole (2.40 – 25.8 µg/kg) were also detected in sediments (Table 7). Bisphenol A (BPA) was detected at a single site at 7.61 µg/kg, which was found in the site closest to the George Reifel Bird Sanctuary. Porewater concentrations were determined for each PPCP detected in sediments and ranged from 0.0304 (clotrimazole) to 1.76 x 10^6 ng/L (DEET).

Table 7. Pharmaceuticals and personal care products detected in sediments (µg/kg) at the Alaksen National Wildlife Area.

	Therapeutic Class	PPCP 1	PPCP 2	PPCP 3	PPCP 4	PPCP 5	PPCP 6
Metformin	Anti-hyperglycemic	0.516 (1.14)	-	-	0.49 (1.08)	-	-
Erythromycin-H_2O	Macrolide antibiotic	3.44 (2.00)	-	-	-	-	-
Miconazole	Anti-fungal	3.36 (0.000358)	-	-	-	2.4 (0.000256)	25.8 (0.00275)
DEET	Insect repellent	47.2 (59.4)	1.3 (1.64)	1.42 (1.79)	39.1 (49.2)	1.1 (1.39)	1400 (1763)
Daunorubicin	Anti-neoplastic	3.27 (1.70)	-	-	-	-	-
Bisphenol A	Plasticizer	-	7.61 (30.4)	-	-	-	-
Clotrimazole	Anti-fungal	-	-	-	-	1.39 (0.0000304)	-

Using sediment samples concentrations and equilibrium partitioning as described in Burgess et al. (2012) porewater concentrations were estimated and are shown in parentheses (µg/L).

In addition, eleven classes of PPCPs were detected in surface waters at the ANWA in POCIS extracts including non-steroidal anti-inflammatories (NSAID), CNS stimulants, antibiotics, beta-blockers, insect repellent, anti-fungals, opioids, anti-convulsants and anti-diabetics (Table 8). A total of 22 PPCPs were detected across all

POCIS deployed in ANWA. Upon preliminary temporal analysis of PPCPs detected in POCIS, the frequency of PPCP detection showed seasonal variation, with samplers deployed in January-March 2020 detecting a greater number of analytes (average of 15 PPCPs detected per site) than those deployed from August-October 2020 (average of 6.5 detects per site). Conversely, when POCIS 1 and POCIS 2 were sampled again in the same location from August to October, the number of PPCPs detected in the samplers were reduced and averaged 7 detects per site. Furthermore, the relative abundances of the classes of PPCPs detected in POCIS 1 and 2 changed depending on the sampling period. The relative proportions of antifungals decreased from 45 and 58% (spring sampling) to 15.7 and 12.1% (summer) for POCIS 1 and 2, respectively (Figure 4). Interestingly, the relative proportions of DEET were lower in the spring compared to the summer deployment despite being measured at higher concentrations in the spring at 78.2 and 55 ng/POCIS in the spring compared to 44.3 and 46.3 ng/POCIS for POCIS 1 and 2, respectively. In addition, and coinciding with the sediment chemistry data, DEET was detected in all POCIS extracts as well as cotinine (nicotine metabolite), which was also detected in all POCIS extracts. Moreover, both DEET and sarafloxacin were detected in the field blank at 10.3 and 17.8 ng/POCIS, respectively. The Log K_{ow} of POCIS detects ranged from -2.64 to 3.79 indicating that POCIS was preferentially sequestering polar and semi-polar compounds. Cocaine and its metabolite benzoylecgonine were only detected in sites near septic fields and in ditches between Fields 14E and 3. Multiple classes of antibiotics used in both human health and veterinary care were detected in POCIS and sediments including sulfonamides, beta-lactams, macrolides, and fluoroquinolones.

Table 8. Pharmaceuticals and personal care products detected at the Alaksen National Wildlife Area using POCIS water samplers (ng/POCIS) deployed from January to March and August to October (2020) at four sites. All values are in ng/POCIS.

Chemical	Compound Class	January 2020 Sampling Sites			August 2020 Sampling Sites					Lab Blank
		Field Blank	POCIS 1	POCIS 2	Field Blank	POCIS 1	POCIS 2	POCIS 3	POCIS 4	
Ibuprofen	NSAID	-	6.15	4.28	-	-	-	-	-	-
Naproxen	NSAID	-	10.8	10.3	-	-	-	-	-	-
Caffeine	CNS stimulant	-	19	36.2	-	-	-	-	-	-
Cocaine	CNS stimulant	-	0.796	0.918	-	-	-	0.214	-	-
Benzoylecgonine	Cocaine metabolite	-	1.08	2.22	-	0.369	0.245	-	-	-
Amphetamine	CNS stimulant	-	-	-	-	-	-	16.1	16.2	-
Cotinine	Nicotine metabolite	-	2.04	2.26	-	1.95	0.92	1.67	1.73	-
Sulfamethoxazole	Antibiotic	-	-	2.69	-	-	-	-	-	-
Cloxacillin	Antibiotic	-	-	-	-	3.84	-	-	-	-
Tylosin	Antibiotic	-	-	-	-	-	-	7.13	-	-
Moxifloxacin	Antibiotic	-	-	-	-	-	-	11.7	4.94	-
Atenolol	Beta-blocker	-	0.423	0.987	-	0.474	-	-	-	-
Metoprolol	Beta-blocker	-	0.596	0.823	-	0.532	-	-	-	-
Citalopram	Anti-depressant	-	-	0.731	-	-	-	-	0.602	-
Venlafaxine	Anti-depressant	-	1.28	2.25	-	1.87	1	-	-	-
DEET	Insect repellent	10.3	78.2	55	22.1	44.3	46.3	56.1	57	0.486
Thiabendazole	Anti-fungal	-	2.04	-	-	-	-	-	-	-
Theophylline	Anti-asthma	-	7.97	12.2	-	8.19	-	19.1	-	-
Codeine	Opioid	-	-	2.61	-	1.79	2.46	-	-	-
Carbamazepine	Anti-convulsant	-	2.5	2.52	-	4.25	2.12	-	-	-
Metformin	Anti-diabetic	-	0.717	2.22	-	-	-	-	-	-
Sarafloxacin	Antibiotic	17.8	-	-	-	-	-	-	-	-

3.1.1. Surface water and sediment porewater pharmaceutical and personal care product estimations

To predict the surface water exposure concentrations of PPCPs in the ANWA, estimates were calculated using POCIS concentrations and the lowest R_s value found in literature for a specific analyte, resulting in a conservative estimate of the time-weighted average PPCP surface water concentrations which ranged from 0.052 (cocaine) to 18.7 ng/L (caffeine) (Table 9; Equation 1). Moxifloxacin, theophylline and cloxacillin were detected in surface waters using POCIS at several sites, but did not have an experimentally derived R_s value, thus, the R_s was predicted using the linear relationship between R_s and log K_{ow} of each of the three analytes (Li et al., 2010).

Table 9. Time-weighted surface water concentrations (ng/L) of pharmaceuticals and personal care products in Alaksen National Wildlife Area calculated from total analytes detected in POCIS sorbents according to Alvarez et al., 2004.

Chemical	R_s (L/d)	R_s Reference	January 2020 Sampling Sites		August 2020 Sampling Sites			
			POCIS 1	POCIS 2	POCIS 1	POCIS 2	POCIS 3	POCIS 4
Ibuprofen	0.197	Li et al., 2010	0.71	0.494	-	-	-	-
Naproxen	0.072	Mathon et al., 2014	3.41	3.25	-	-	-	-
Caffeine	0.044	Barlett-Hunt et al., 2011	9.81	18.7	-	-	-	-
Carbamazepine	0.065	Baz-Lomba et al., 2017	0.874	0.881	1.17	0.582	-	-
Thiabendazole	0.182	Mathon et al., 2014	0.255	-	-	-	-	-
Sulfamethoxazole	0.050	Mathon et al., 2014	-	1.22	-	-	-	-
Benzoylecgonine	0.027	Baz-Lomba et al., 2017	0.909	1.87	0.244	0.162	-	-
Cloxacillin	0.620	Predicted value[a]	-	-	0.111	-	-	-
Cocaine	0.074	Baz-Lomba et al., 2017	0.244	0.282	-	-	0.0516	-
DEET	0.240	Barlett-Hunt et al., 2011	7.41	5.21	3.30	3.45	4.17	4.24
Metoprolol	0.069	Guibal et al., 2020	0.196	0.271	0.138	-	-	-
Theophylline	0.129	Predicted value[b]	1.40	2.14	1.13	-	2.64	-
Citalopram	0.109	Baz-Lomba et al., 2017	-	0.152	-	-	-	0.0986
Venlafaxine	0.104	Li et al., 2010	0.280	0.492	0.321	0.172	-	-
Atenolol	0.027	Baz-Lomba et al., 2017	0.356	0.831	0.313	-	-	-
Codeine	0.090	MacLeod et al. 2007	-	0.659	0.355	0.488	-	-
Cotinine	0.034	Barlett-Hunt et al., 2011	1.36	1.51	1.02	0.483	0.877	0.909
Metformin	0.086	Kim and Homan 2020	0.189	0.587	-	-	-	-
Tylosin	1.330	Bartelt-Hunt et al., 2011	-	-	-	-	0.0957	-
Moxifloxacin	0.358	Predicted value[a]	-	-	-	-	0.583	0.246
Amphetamine	0.041	Hahn et al., 2022	-	-	-	-	7.01	7.06

[a] Compounds with no sampling rate (R_s) values available from literature were modelled using the linear relationship between log K_{ow} and R_s.

Where:

$$R_s = 0.171 \cdot \log k_{ow} + 0.196 \text{ (Li et al., 2010)}$$

Log K_{ow} was replaced with log D at pH 7 to account for proportion of neutral species present at circum-neutral pH.

[b] This value was calculated using log K_{ow} in the Li et al. 2010 equation.

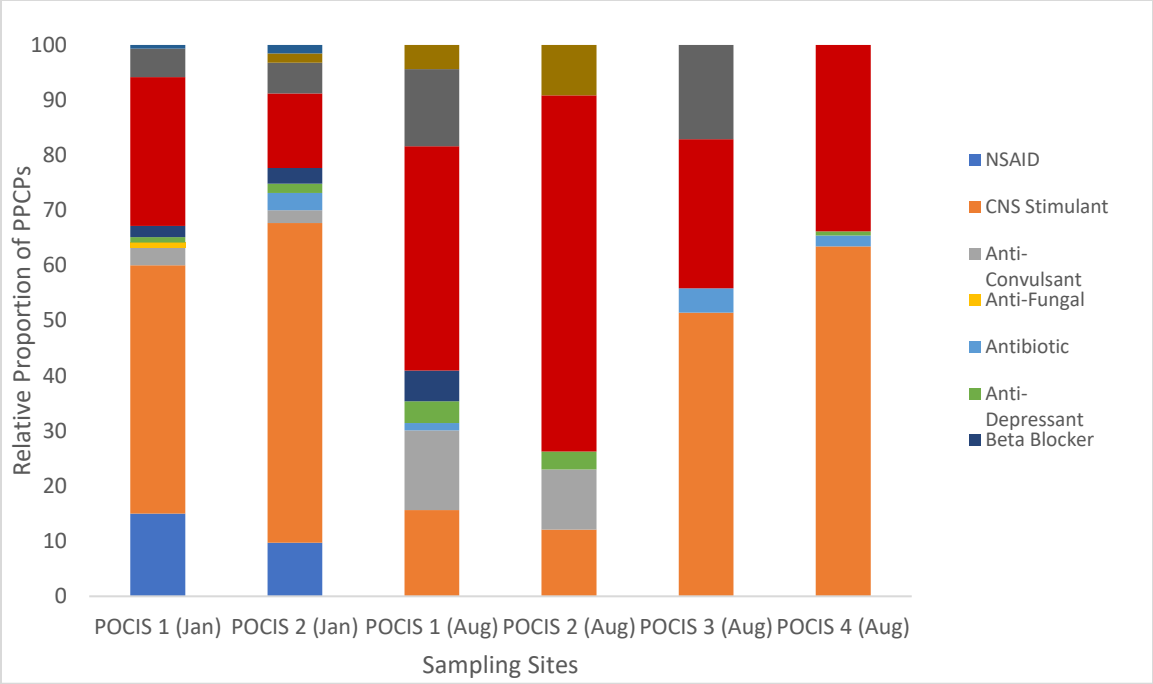

Figure 4. The occurrences of pharmaceuticals and personal care product (PPCPs) classes and their respective proportions at each sampling site after deployment in surface waters at the Alaksen National Wildlife Area.

January and August (2020) POCIS samplers were deployed for 44 and 56 days, respectively, at four sites POCIS 1, POCIS 2, POCIS 3 AND POCIS 4).

3.1.2. Aquatic ecological risk assessment of pharmaceuticals and personal care products

The results of the aquatic ecological risk assessment are presented in Tables 10 and 11. All HQs values for PPCPs detected in the surface waters at the ANWA via POCIS were below one, indicating no risk of acute or chronic toxicity to aquatic receptors. Within the water column, ibuprofen, sulfamethoxazole, and cocaine almost exceeded the PNEC threshold with HQ values of 0.710, 0.779 and 0.705, respectively (Table 10). In addition, PPCPs were grouped by therapeutic class in their respective sampling locations to evaluate mixture effects and this analysis revealed that the highest combined exposure to NSAIDs (HI = 0.711), beta-blockers (HI = 0.00271), and anti-depressants (HI = 0.0938) did not present a risk to aquatic biota of ANWA (Table 11). However, mixtures of CNS stimulants, which include caffeine, cocaine, benzoylecgonine,

amphetamine and cotinine, resulted in HI values of 0.956 and 1.39 for POCIS 1 and POCIS 2, respectively, during the January to March sampling period. In subsequent sampling in August to October, no exceedances were observed in any POCIS samples via individual or mixtures of PPCPs. At POCIS sampling sites (POCIS 1 and POCIS 2) in August, HI values were below one at 0.0489 and 0.0324 at POCIS 1 and POCIS 2, respectively. In sediments, the maximal detected concentrations of metformin, miconazole, daunorubicin, and clotrimazole resulted in HQ values less than one. Conversely, erythromycin-H_2O, DEET and BPA concentrations in sediments exceeded PNEC values resulting is HQ values of 2.00, 33.9, and 21.7, respectively (Table 12). Notably, HQs for DEET exceeded PNEC values in multiple sites (PPCP 1 and PPCP 6) indicating potential widespread ecological harm at environmentally relevant concentrations. PPCP 1, 2, and 6 were the only sediment sampling locations where HQ values exceed one.

Table 10. Aquatic ecological risk assessment of pharmaceuticals and personal care products detected in the Alaksen watershed.

Chemical	Drug Class	PEC (µg/L)	Biota	Endpoint	Duration	TRV (µg/L)	Reference	AF	PNEC (µg/L)	HQ
Surface Water										
Ibuprofen	NSAID	0.00071	Invertebrate	LOEC – Behaviour	2 h	0.01	De Lange et al., 2006	10	0.001	0.71
Naproxen	NSAID	0.00341	Green algae	IC25 – Growth	72 h	32	Brun et al., 2006	10	3.2	0.00107
Tylosin	Antibiotic	0.0000957	Aquatic plant	NOEC – Growth	7 d	100	Brain et al., 2004	100	1	9.57E-05
Moxifloxacin	Antibiotic	0.000583	Green algae	LOEC – Growth	96 h	5	Wan et al., 2021	100	0.05	0.0117
Sulfamethoxazole	Antibiotic	0.00122	Invertebrate	EC10 – Growth	96 h	0.0157	Yu et al., 2011	10	0.00157	0.779
Cloxacillin	Antibiotic	0.000111	Fish	NOEC – NR	Chronic	3040	ECOSAR 2.2	100	30.4	3.64E-06
Thiabendazole	Anti-Fungal	0.000255	Fish	NOEC – NR	21 d	12	US EPA 1992	10	1.2	0.000212
Caffeine	CNS Stimulant	0.0187	Amphibian	NOEC – Growth	28 d	0.6	Fraker et al., 2004	10	0.06	0.312
Cocaine	CNS Stimulant	0.000282	Fish	LOEC – Histology	50 d	0.02	Capaldo et al., 2019	50	0.0004	0.705
Benzoylecgonine	Cocaine Met.	0.00187	Invertebrate	LOEC – Oxidative stress	11 d	0.5	Parolini et al., 2013	100	0.005	0.374
Amphetamine	CNS Stimulant	0.00706	Fish	NOEC – NR	Chronic	348	ECOSAR 2.2	100	3.48	0.00203
Cotinine	Nicotine Met.	0.00151	Aquatic plant	NOEC – Growth	7 d	1000	Brain et al., 2004	100	10	0.000151
Citalopram	Anti-Depressant	0.000152	Fish	NOEC – Behaviour	21 d	0.2	Olsén et al., 2014	100	0.002	0.0762
Venlafaxine	Anti-Depressant	0.000492	Fish	NOEC – Glucose reduction	3 h	2.774	Ings et al., 2012	100	0.0277	0.0177
Atenolol	Beta Blocker	0.000831	Fish	NOEC – Growth	32 d	3200	Winter et al., 2008	10	320	2.60E-06
Metoprolol	Beta Blocker	0.000271	Fish	LOEC – Histology	28 d	1	Triebskorn et al., 2007	10	0.1	0.00271
Metformin	Anti-diabetic	0.000587	Fish	NOEC – NR	32 d	780	Moermond et al., 2016	-	780	7.52E-07
DEET	Insect Deterrent	0.00741	Green algae	NOEC – Growth	96 h	521	Harada et al., 2008	10	52.1	0.000142
Carbamazepine	Anti-Convulsant	0.00117	EQG	-	-	10	CCME 2018	-	10	0.000117
Theophylline	Anti-Asthma	0.00264	Fish	EC10 - Development	48 h	90983	Pruvot et al., 2012	1000	91	2.90E-05
Sediments										
Metformin	Anti-diabetic	1.14	Fish	NOEC – NR	32 d	780	Moermond et al., 2016	-	780	0.00146
Erythromycin- H_2O	Erythromycin Met..	2.00	Aquatic plant	NOEC – Growth	7 d	10	Pomati et al., 2004	10	1.00	2.00
Miconazole	Anti-fungal	0.00275	Invertebrate	LOEC – Reproduction	21 d	22	Furuhagen et al., 2014	100	0.22	0.0125
DEET	Insect repellent	1763	Green algae	NOEC – Growth	96 h	521	Harada et al., 2008	10	52.1	33.9
Daunorubicin	Anti-neoplastic	1.70	Invertebrate	NOEC – NR	Chronic	782	ECOSAR 2.2	100	7.82	0.218
Bisphenol A	Plasticizer	30.4	EQG	-	Chronic	1.4	ECCC 2017	-	1.4	21.7
Clotrimazole	Anti-fungal	0.0000304	Amphibian	LOEC - Development	14 d	0.1	Shi et al., 2012	10	0.01	0.00304

Point estimates in the form of the maximum concentration of PPCP detected in surface water or sediments and toxicity reference values (TRV) were selected in the derivation of hazard quotients. Selection of TRVs depended on the availability of environmental quality guidelines for the PPCPs, derived using the most sensitive indirect acute and chronic laboratory studies, or modelled by quantitative structure activity relationships. Assessment factors were assigned based on the quality and availability of the toxicity database for a PPCP.

EQG – Environmental quality guideline
PEC – Predicted environmental concentration
TRV – Toxicity reference value
AF – Assessment factor
PNEC – Predicted no effects concentration
HQ – Hazard quotient
Met. – Metabolite
NR – not reported

Table 11. Site-specific aquatic risk assessment of individual (HQ) and mixture (HI) effects of pharmaceuticals and personal care products in surface waters of the Alaksen National Wildlife Area.

Chemical	Compound Class	January 2020 Sampling Sites		August 2020 Sampling Sites			
		POCIS 1	POCIS 2	POCIS 1	POCIS 2	POCIS 3	POCIS 4
		HQ					
Ibuprofen	NSAID	0.710	0.494	-	-	-	-
Naproxen	NSAID	0.00107	0.00102	-	-	-	-
	HI_{NSAID}	0.711	0.495	-	-	-	-
Tylosin	Antibiotic	-	-	-	-	0.0000957	-
Moxifloxacin	Antibiotic	-	-	-	-	0.0117	0.00492
Sulfamethoxazole	Antibiotic	-	0.777	-	-	-	-
Cloxacillin	Antibiotic	-	-	0.00000365	-	-	-
Thiabendazole	Anti-Fungal	0.000213	-	-	-	-	-
Caffeine	CNS Stimulant	0.164	0.312	-	-	-	-
Cocaine	CNS Stimulant	0.610	0.705	-	-	0.129	-
Benzoylecgonine	Cocaine Metabolite	0.182	0.374	0.0488	0.0324	-	-
Amphetamine	CNS Stimulant	-	-	-	-	0.00201	0.00203
Cotinine	Nicotine Metabolite	0.000136	0.000151	0.000102	-	0.0000877	0.0000909
	$HI_{stimulant}$	0.956	1.39	0.0489	0.0324	0.131	0.00212
Citalopram	Anti-Depressant	-	0.0760	-	-	-	0.0493
Venlafaxine	Anti-Depressant	0.0101	0.0178	0.0116	0.00620	-	-
	$HI_{Anti\text{-}depressant}$		0.0938	-	-		
Atenolol	Beta Blocker	0.00000111	0.00000260	0.000000978	-	-	-
Metoprolol	Beta Blocker	0.00196	0.00271	0.00138	-	-	-
	$HI_{Beta\text{-}blocker}$	0.00196	0.00271	0.00138	-	-	-
Metformin	Anti-diabetic	0.000000242	0.000000753	-	-	-	-
DEET	Insect Deterrent	0.000142	0.000100	0.0000633	0.0000661	0.0000800	0.0000814
Carbamazepine	Anti-Convulsant	0.0000874	0.0000881	0.000117	0.0000582	-	-
Theophylline	Anti-Asthma	0.0000154	0.0000235	0.0000124	-	0.0000290	-
Codeine	Opioid	-	0.659	0.355	-	-	-
	HI_{Total}	1.68	3.42	0.417	0.0387	0.143	0.0560

PPCPs were grouped by therapeutic classes. Mixtures of antibiotics were not evaluated due to the lack of multiple detections of antibiotics in a single site.

HI – Hazard index

HQ – Hazard quotient

Table 12. Aquatic risk assessment of pharmaceuticals and personal care products detected in the sediments of the Alaksen National Wildlife Area.

Chemical	Compound Class	September 2020 Sampling Sites					
		PPCP 1	PPCP 2	PPCP 3	PPCP 4	PPCP 5	PPCP 6
		HQ					
Metformin	Anti-diabetic	0.00146	-	-	0.00139	-	-
Erythromycin-H_2O	Antibiotic	2.00	-	-	-	-	-
Miconazole	Anti-fungal	0.00163	-	-	-	0.00116	0.0125
DEET	Insect repellent	1.14	0.0314	0.0343	0.946	0.0266	33.9
Daunorubicin	Anti-neoplastic	0.218	-	-	-	-	-
Bisphenol A	Plasticizer	-	21.7	-	-	-	-
Clotrimazole	Anti-fungal	-	-	-	-	0.00304	-
HI_{Total}		3.36	21.7	0.0343	0.946945132	0.0308	33.9

Hazard quotients are presented in this table and were calculated by taking estimated porewater concentration calculated using equilibrium partitioning and dividing it by toxicity reference values derived in the effects assessment.

HQ – Hazard quotient
HI – Hazard index

3.1.3. Terrestrial ecological risk assessment of pharmaceuticals and personal care products

Among the PPCPs detected in sediments and POCIS, only clotrimazole and miconazole had physicochemical characteristics that suggested the potential for bioaccumulation based on the Canadian Environmental Protection Act (i.e. log K_{ow} > 5). The HQs obtained by comparing KABAM modelled dietary exposure to PPCPs are summarized in Table 13 and Table 14. In terms of the food web representative of the terrestrial feeding guilds of the ANWA, clotrimazole was the only PPCP that had an HQ value greater than one, with a value of 2.86 observed within the Birds-Carnivore (small mammals) group. The HQ values for clotrimazole in the Alaksen food-web ranged from 2.04 x 10^{-7} to 2.86. However, there was no risk of acute toxicity from bioaccumulated dietary exposure to miconazole with HQ values ranging from 2.04 x 10^{-6} to 0.931. For the SARA or COSEWIC listed species, only clotrimazole presented a potential hazard to barn owls (HQ = 2.85) with HQ values ranging from 0.0601 (barn swallow) to 2.85 (barn

owls). Conversely, miconazole did not pose a risk to any listed species with HQ values between 0.0169 (little brown myotis) to 0.9305 (barn owls).

Table 13. Terrestrial ecological risk characterization of the pharmaceuticals and personal care products in the Alaksen National Wildlife Area to surrogate wildlife receptors.

	Mammals				Birds			
Chemicals	Herbivore	Insectivore	Carnivore (small mammal diet)	Piscivore	Insectivore	Piscivore	Carnivore (small mammal diet)	Carnivore (small mammal and fish diet)
Clotrimazole	0.000000204	0.00176	0.00966	0.00212	0.280	0.379	2.86	0.562
Miconazole	0.00000204	0.000683	0.00375	0.00126	0.091	0.189	0.931	0.232

Values within the table represent hazard quotients calculated by taking the highest estimated sediment and surface water concentration as input parameters in the K_{ow}-based aquatic bioaccumulation model.

Table 14. Terrestrial ecological risk characterization of the pharmaceuticals and personal care products to ecological receptors listed in the Species At Risk Act or the Committee on the Status of Endangered Wildlife in Canada.

Chemicals	Barn owl	Barn swallow	Great Blue Heron	Horned grebe	Western grebe	Olive-sided flycatcher	Short-eared owl	Peregrine falcon	Black swift	Pacific water shrew	Little brown myotis	Western painted turtle
Clotrimazole	2.8562	0.0601	0.5638	0.2098	0.1722	0.1528	2.8083	0.1853	0.1465	0.5114	0.0624	0.0771
Miconazole	0.9305	0.0196	0.2477	0.0808	0.0741	0.0499	0.9149	0.0604	0.0478	0.1387	0.0169	0.0252

Values within the table represent hazard quotients calculated by taking the highest estimated sediment and surface water concentration as input parameters in the K_{ow}-based aquatic bioaccumulation model.

Chapter 4. Discussion

Only two Canadian EQGs for PPCPs were available (i.e., BPA and carbamazepine) to be used as a TRV for this ERA, while 25 detected PPCPs required derivation of a TRV from peer-reviewed ecotoxicological literature (CCME, 2018; Environment Climate Change Canada, 2018). Based on this ERA, the findings of the present aquatic ecological risk assessment demonstrates that BPA, erythromycin and DEET detected in sediments may pose significant risks to ANWA aquatic life due to individual HQs exceeding one at three sites (PPCP 1, PPCP 2 and PPCP 6). Interestingly, current individual surface water concentrations of PPCPs detected in POCIS did not present any risk. However, the complex mixtures of PPCPs present in surfaces waters at two sites within in the ANWA (POCIS 1 and POCIS 2) may induce adverse effects to aquatic wildlife when considering mixture toxicity of these substances additively. In addition, in the terrestrial ecological risk assessment using the KABAM model, clotrimazole posed a potential risk to predators whose primary diet consisted of small mammals, including multiple at-risk species (i.e. various owl species). Collectively, based on the ERA of PPCPs in this study, it is clear that the concentrations of PPCPs at multiple sites within the ANWA are present at levels that that can have negative consequences to wildlife health.

In the context of the study area, the 27 PPCPs detected in the aquatic media of ANWA in the present ERA are likely released via two primary pathways: human wastewater and veterinary treatment of livestock. Since the ANWA is situated downstream from three municipal WWTPs, is serviced by two non-centralized septic systems and contains lands designated for agricultural activities and is actively used for the production of cattle, it is not surprising that a considerable number of detections of

human and veterinary PPCPs were observed in environmental samples collected in this study. Several studies have identified WWTPs as known point sources of a range of PPCPs. For example, Metcalfe et al. surveyed acidic and neutral drugs in WWTP effluents from 14 Canadian cities and detected multiple classes of drugs including analgesics/anti-inflammatories, lipid regulators, and anti-epileptic drugs (Metcalfe et al., 2003a). Currently, no municipal WWTP biosolids are added to agricultural fields of ANWA as soil amendments, thus the origin of the veterinary PPCPs observed above detections limits in this study likely occurs from recently treated livestock.

Twenty-one different PPCPs were detected in surface waters at the ANWA using POCIS samplers across eleven therapeutic classes including NSAIDs, antibiotics, illicit drugs, beta-blockers, and anti-depressants. Based on this deterministic risk assessment, the findings of the present ecological risk assessment demonstrates that the complex mixture of PPCPs present at two sites, POCIS 1 and POCIS 2, could pose a high risk of adverse effects on aquatic wildlife at the ANWA. There are many advantages of POCIS over traditional grab sampling, such as: the ability to accumulate trace environmental levels of contaminants to analytically detectable levels; no need for large sampling volumes required for chemical analysis; and increased similarity to chronic environmental exposure scenarios experienced by aquatic organisms (Alvarez et al., 2004; Harman et al., 2011). However, POCIS are considered semi-quantitative since they only provide time-weighted average contaminant concentrations that are highly dependent on the limited number of experimental calibration derived R_s values for specific chemicals and are highly influenced by environmental factors (Harman et al., 2011; Martínez Bueno et al., 2016). Additionally, R_s values are derived for single chemicals and can vary up to a factor of 100 (Harman et al., 2011). Interestingly, in the twelve POCIS calibration studies compiled in the present risk assessment for the ANWA,

R_s values only varied by a maximum factor of 12 (i.e. citalopram, 0.109 – 1.224 L/d). Furthermore, to account for this variability, the lowest R_s value for individual PPCPs were selected, therefore the most conservative estimates of surface water concentrations of PPCPs were deduced in ANWA.

The uptake of analytes in POCIS deployed in water undergoes three phases, the linear phase (sometimes called the integrative phase), curvilinear phase and the equilibrium phase (Alvarez et al., 2007; Carpinteiro et al., 2016). According to Alvarez et al., the linear phase of analyte uptake in POCIS can last up to 56 days, supporting the duration of the deployments of POCIS in the present study (44 and 56 days) (Alvarez et al., 2007). Use of POCIS within the linear phase allows for the assumption of first-order kinetics and subsequently provides the means to calculate the time-weighted surface water equation. In the current study after comparing the spring (January to March) to the late summer to autumn (August to October) sampling periods, there were a greater number of detected substances in the former period for both POCIS 1 and POCIS 2 sites. In the field, POCIS sampling rates are highly influenced by environmental factors including flow rate, temperature, biofouling, pH and salinity (Harman et al., 2011). In particular, water flow rate is the most significant factor determining if analytes accumulate in POCIS to detectable levels (Harman et al., 2011). During the POCIS deployment times from January 27, 2020 to March 11, 2020, there was an average of 4.55 mm daily precipitation measured at the Vancouver International Airport climate station (Vancouver, BC), whereas during the August 19,2020 to October 14 2020 POCIS deployment, there was a daily average of 2.28 mm (https://climate.weather.gc.ca/climate_data/daily_data_e.html?StationID=51442; accessed November 11, 2023). In terms of hydrological processes, the ANWA is located within the Fraser River Basin and changes in river flow in this region is primarily driven

by snow accumulation and melt processes, resulting in annual winter discharges that peak during the spring and reduces in volume during the summer (Shrestha et al., 2012). Therefore, both snow melt processes affecting the lower Fraser River Basin and elevated precipitation levels during the spring cumulatively increase water flow, likely contributing to some extent to the seasonal distributions of PPCPs observed in the present study. Therefore, seasonal changes such as increased rainfall in the spring in comparison to the late summer will impact the amount of PPCP that is detected using POCIS, which may explain the differences in frequencies of detection in the two sampling periods. To increase the reliability and reduce uncertainty from environmental factors, it is recommended to include performance reference compounds (PRC) in the receiving phase of the samplers (i.e. HLB sorbent) such as isotopically labelled compounds that are not naturally found in the environment prior to use (Godlewska et al., 2021). Assuming that the uptake and release of PPCPs and the PRC are governed by first-order kinetics, the amount of PRC released during deployment due to the external environment can be used to calculate an environmentally adjusted sampling rate within the linear phase of uptake into POCIS (Carpinteiro et al., 2016; Godlewska et al., 2021; Harman et al., 2011). In addition, POCIS in the pharmaceutical configuration (HLB sorbent) preferentially accumulates chemicals with log K_{ow} < 4, which concurs with the log K_{ow} of the PPCPs detected using POCIS in the present study (-2.64 to 3.79) (Alvarez et al., 2004). Consequently, this sampling technique would be not suitable for the detection of hydrophobic PPCPs with higher log K_{ow} values (log K_{ow} > 4) that would be more likely to bioaccumulate in wildlife, and therefore result in increased exposure. This restriction to PPCPs with log K_{ow} values less than four is a major limitation of the present sampling regime and should be expanded to include higher values to capture PPCPs with this increased bioaccumulation and exposure potential, such as coupling

other passive sampling devices (i.e. semi-permeable membrane devices) that could concentrate PPCPs outside this K_{ow} range.

A risk assessment of the effects of mixtures of pharmaceuticals based on therapeutic classes was performed on NSAIDs, CNS stimulants, beta-blockers and anti-depressants as well as total mixtures in surface waters using POCIS; only mixtures of CNS stimulants demonstrated potential risk to receptors in ANWA. Specifically, the HI, which is derived from summing individual HQ values of chemicals with similar modes of actions, of POCIS 2 (Jan) exceeded 1, indicating potential cumulative toxic effects to aquatic biota. Current available ecotoxicological data on CNS stimulants show that these chemicals can cause adverse effects on aquatic receptors such as; acetylcholine esterase (AChE) inhibition, hyperactivity, cytotoxicity, genotoxicity, and oxidative stress (Capaldo et al., 2019; Fraker and Smith, 2004; Parolini et al., 2016). However, to date, there have been little to no toxicological studies on potential population-level effects caused by CNS stimulants.

In addition to deriving HI values based on therapeutic class, the cumulative effects of the mixtures of all PPCPs were considered. In the present study, HI values where all HQs were summed in one sample for all PPCPs, exceeded in POCIS 1 and POCIS 2 during the sampling periods in January, due to higher masses of PPCPs concentrating in POCIS. Though this increased input of PPCPs is most likely due to environmental factors (namely water flow), other seasonal influences from WWTP effluents, septic leachate and livestock production cannot be ruled out at this time. In terms of the main patterns of detections across sites was that DEET and cotinine were detected in all POCIS extracts at consistent concentrations. However, in the case of DEET, it was detected in both field blanks at similar concentrations to the deployed samplers, causing the detection of DEET in surface waters to be inconclusive.

Interestingly, prescription drugs that require daily dosages to maintain steady-state drug plasma concentrations were detected consistently and at relatively constant concentrations (i.e. beta-blockers, anti-depressants and anti-convulsants) in POCIS 1 and 2. Remarkably, metformin was detected in both sediments and POCIS, which is surprising given that metformin is very hydrophilic causing it to be less likely to be sequestered in sediments and is known to have weak sorptive capacity to HLB sorbents in POCIS samplers (Kim and Homan, 2020). Thus, the present ERA demonstrates a need to further characterize the spatial and temporal distribution of PPCPs in ANWA as this study has already shown that within two sampling periods of a year, current concentrations of PPCPs can elicit adverse effects in both aquatic and terrestrial wildlife. Furthermore, given the high conservation of many therapeutic targets among vertebrate species (i.e. Read-Across Hypothesis), environmentally relevant concentrations of PPCPs measured at the ANWA are likely to induce toxicological effects on sensitive vertebrate species such as birds, mammals and fish (Rand-Weaver et al., 2013).

In the present study, BPA was measured at elevated concentrations, exceeding Canadian FEQG for the protection of aquatic life in sediments in a single sampling site (PPCP 2; HQ = 21.7). The plasticizer BPA is of high concern as a toxicant to wildlife at the ANWA since it has been widely studied for its endocrine disrupting effects in wildlife and its ubiquitous, low level continuous prevalence in waters downstream of human activities. Indeed, BPA is a ubiquitous environmental contaminant since it has been widely used since the 1960s as a component of a variety of polymers (i.e., polycarbonate plastics, epoxy resins, or thermal papers) and as such is present in wide range of consumer products, including plastics, receipts, and food packaging (ANSES, 2011; Serra et al., 2019). Due to concerns of reproductive, metabolic, and developmental effects reported in several mammalian and non-mammalian animal

toxicity studies over the last two decades, regulatory bodies worldwide recently banned BPA from baby bottles, and have been implemented restrictions of use in food packaging (European Commission, 2018) and in thermal papers (European Commission, 2016, 2011; Government of Canada, 2010). In 2017, the European Union deemed BPA an endocrine disrupting chemical and a substance of very high concern (SVHC) for both human health (ECHA, 2017a) and for the environment (ECHA, 2017b) and set limits on its importation and use in the European market. In addition, other toxic modes of action eliciting adverse effects in the µg/L to mg/L range have also been reported various species reviewed in Serra et al. (2019; i.e., daphnids (Alexander et al., 1988; Brennan et al., 2006; Hirano et al., 2005); mysids (Alexander et al., 1988; Hirano et al., 2005); lobster (Biggers and Laufer, 2004); and, freshwater (*Pimephales promelas*) and saltwater (*Menidia menidia*) fishes (Alexander et al., 1988)). Although BPA has a short half-life it is considered pseudo-persistent due to its continuous release into the environment which can occur during chemical manufacturing, transport, processing or via post-consumer releases via effluent discharges or land-application of sewage sludge from municipal WWTPs (human excretion or consumer product leachate/wastes), leaching from landfills, combustion of domestic waste and the natural breakdown of plastics in the environment (Crain et al., 2007; Kang et al., 2007; Kinney et al., 2006; Sidhu et al., 2005; US EPA, 2010). Though bioaccumulation potential is considered low to modest for BPA, due to P A's pseudo-persistent nature in the environment this translates into chronic, continuous exposure scenarios and to toxic concentrations. With clearly defined toxicity thresholds for BPA in the form of environmental quality guidelines for water, there is high concern for adverse effects in wildlife at Alaksen due to BPA exposure.

In the present study, DEET was detected in all sediment and water samples collected at all ANWA sites and HQs were 1.14 and 33.9 at PPCP 1 and PPCP 6, respectively. Thus, the present study indicates the concentrations of DEET at these sites exceeds toxicity thresholds, particularly for aquatic plants (*Pseudokirchneriella subcapitata*), but may pose a significant risk to the health of ANWA wildlife (Harada et al., 2008). Most insect deterrents/repellants commercially sold world-wide contain the active ingredient DEET, which has been registered for general use in Canada since 1957 in a variety of veterinary and human use products. As such, with this widespread use as a dermally applied insect repellent, DEET is frequently measured in surface waters, drinking water, ocean waters, wastewater treatment plant effluents as septic tank effluent (reviewed in Aronson et al., 2012; Lawrence et al., 2019). In 2007, DEET was reviewed by Environment Canada and was classified as potentially persistent, not bioaccumulative and not toxic (Government of Canada, 2007). Currently, no environmental quality guideline exists for DEET in Canada. Although there is a paucity of chronic toxicity studies available for risk assessments, there are a number of acute toxicity studies in freshwater fish and invertebrates that allow for HQ derivations. Interestingly, DEET appears to currently be under re-evaluation status by the Canadian Pest Management Regulatory Agency (PMRA), and the previous re-evaluation by this agency was published in 2002 and assessed human health risks with no mention of risk to non-human receptors (PMRA, 2023). The US EPA also purports that DEET is relatively stable, highly hygroscopic, moderately mobile in soil, not persistent, not bioaccumulative and will not result in environmental levels of concern or based on acute risk to fish and invertebrates, but no chronic risks were evaluated (US EPA, 2014). Furthermore, a US EPA final decision on the DEET registration review will be completed after the EPA has completed an Endocrine Disruptor Screening process under FFDCA section 408(p) (US EPA, website accessed March 12, 2023, https://www.epa.gov/insect-

repellents/deet). The present risk assessment also incorporated several acute toxicity studies and reports of acute LD50 values ranging from 8.69 to 235 mg/L for various freshwater fish, 26 to 406 mg/L for various freshwater invertebrates and one amphibian (*Rana nigromaculata*, Dark-spotted frog) acute LD50 value of 53 mg/L (data summarized in Table S1 of Gao et al., (2020)). However, few studies on the sub-lethal or chronic toxicity were available and of those available some do report effective concentrations well below the concentrations observed at the ANWA. For example, Zenobio et al., (2014) reported a LOEC for reduced gonadosomatic index in fathead minnows of 0.0006 mg/L, while a NOEC of 0.521 mg/L for growth inhibition in an aquatic plant (*P. subcapitata*) was reported (Harada et al., 2008), and significant shifts in algal–cyanobacterial community structure with reductions of green algae and some cyanobacterial groups at 0.005 mg/L was demonstrated by Lawrence et al., (2019). Ultimately, toxicity on the mechanism of action of DEET in target and non-target plants and animals is sparse, particularly the longer term sublethal chronic effects. Nonetheless, the HQs greater than one obtained in the present study largely based on acute toxicity data combined with the likely pseudo-persistent, and therefore chronic exposure scenarios at ANWA, may present a high risk to this aquatic system.

Erythromycin (detected as erythromycin-H_2O) was another PPCP observed at elevated environmental concentrations in sediments that may present risk to lower trophic producers (HQ = 2.00). Erythromycin is a macrolide antibiotic commonly used in both human and veterinary care with wide-spectrum activity against gram-positive and some gram-negative bacteria (Schafhauser et al., 2018). In the US, it is estimated that 70% of erythromycin is used for cattle production (Minski et al., 2021). At PPCP 1, where measured sediment concentrations of erythromycin exceeded an HQ of one, multiple fields (fields 3, 14E and 17) used for livestock production were in close proximity

suggesting the source may be from recently treated cattle. In the five-year crop rotation for agriculture in ANWA, three of five years are dedicated to livestock production increasing the likelihood of detecting veterinary related PPCPs such as erythromycin. The half-life of erythromycin in sediments, soils and water are 11.5, 20, and 5.8 – 365 days, respectively, which means that erythromycin may be persistent in water but not sediment or soils (Schafhauser et al., 2018). However, microcosm studies conducted by Jessick et al., (2013) found that erythromycin quickly partitions into sediments from water, but slowly dissipates in water alone, agreeing with the present study where erythromycin was only detected in sediments. The toxic mode of action of erythromycin and other macrolides involve the inhibition of bacterial ribosomes by interfering with the 23S rRNA of the 50S subunit inhibiting protein synthesis (Minski et al., 2021). For non-target receptors, blue-green algae are the most sensitive to erythromycin contamination where *Synechoccus leopoldensis*, *Anabaena cylindrica,* and *Microcystis wesenbergii* had six-day NOEC values of 2, 3.1 and 4.7 µg/L for growth (Ando et al., 2007). Aquatic plants were also quite susceptible with seven-day NOEC values of 10 µg/L for growth (Pomati et al., 2004). Invertebrates (*D. magna*) and fish (*Oryzias latipes*) were comparably more tolerant to erythromycin exposure with chronic NOEC values of 248 (reproduction) and 100 000 (growth) µg/L, respectively (Ji et al., 2012; Meinertz et al., 2010). Due to the high toxicities observed in primary producers, it is recommended to continue to monitor sites nearby active cattle grazing areas to mitigate chronic toxicological effects to wildlife, although one cannot rule out inputs of this antibiotic via septic field leachate or upstream Fraser River WWTP inputs.

The terrestrial compartment was evaluated using the KABAM bioaccumulation and food web model to determine whether dietary concentrations of feeding guilds and individual listed species are at risk. Multiple modifications were made to tailor the model

to ANWA including changing default terrestrial receptors and incorporating empirical or calculated wildlife data based on FCSAP Module 3 and by adding a shrew bioaccumulation model to determine the trophic transfer of contaminants from small mammals to associated predators. KABAM was an attractive option for food web modelling due to its ease of use and ability to model tissue residue concentrations without collecting tissues from prey items in the field. However, future detailed risk assessment should include the sampling of these tissues to accurately portray trophic transfer of contaminants since the results of the KABAM model only provides a prediction of the worst-case scenario. Additional prey tissue sampling would also allow for the assessment of the KA A model's fitness and likelihood of predicting terrestrial exposure to contaminants via diet. Thus, KABAM has shown to be a useful screening tool for analyzing risk to terrestrial receptors in the absence of biota tissue sampling.

Of the PPCPs investigated, based on the KABAM model, detectable levels of clotrimazole via dietary exposure did not present a risk to the aquatic organisms of ANWA (HQ = 0.003), but may be acutely toxic to owl species via the diet (barn owls, HQ = 2.86; short-eared owl, HQ = 2.81). Clotrimazole is an imidazole fungicide whose therapeutic mode of action is through the inhibition of cytochrome P450 51 in fungi, which is responsible for converting lanosterol to ergosterol which is involved in the maintenance of cell membranes (Gyllenhammar et al., 2009). However, CYP inhibition by clotrimazole is not limited to fungal CYP and can act on other CYPs such as CYP 19 (aromatase) in non target organisms (*Xenopus tropicalis,* Gyllenhammar et al., (2009); humans, Trösken et al., (2004)). Indeed, aromatase was found to be upregulated in the gonad/kidney complex and downregulated in the brain in *X. tropicalis* at 14 and 129 µg/L, respectively (Gyllenhammar et al., 2009). Additional endocrine disrupting effects have also been reported such as; steroidogenesis induction and FSH induction in

zebrafish (*Danio rerio*), and, aromatase inhibition in rainbow trout (*Oncorhynchus mykiss*), fathead minnows (*Pimephales promelas*), zebrafish and medaka (*Oryzias melastigma*) (Bhagat et al., 2021). *In vitro* studies using isolated human CYP19 found that anti-fungal azoles such as clotrimazole and miconazole had similar or greater inhibitory concentrations (IC50 = 0.11, 0.064 μM respectively) to azoles used in anti-estrogen therapies (fadrozole IC50 = 0.0076 μM, letrozole IC50 = 0.015 μM) (Trösken et al., 2004). However, its important to note that KABAM does not include elimination via metabolism, which is an important mechanism for the inactivation of clotrimazole. Early rodent studies found that 97% of intravenous or oral clotrimazole was eliminated to inactive metabolites, suggesting that current hazard quotients may overestimate risk to owls (OSPAR Commission, 2013). Therefore, this terrestrial risk assessment provides a conservative estimate of risk from food web effects. In addition, only the acute toxicity of clotrimazole was evaluated and chronic effects such as endocrine disruption may still manifest in terrestrial species.

There are 34 species of waterfowl that are known to occur in the ANWA and depend on this site as migratory stopover or overwintering area. Among these waterfowl, five species are known to be regular visitors of the ANWA including the Lesser Snow Goose (*Chen caerulescens*), resident and migratory Canada Goose (*Branta cadaensis*), Mallard (*Anas platyrhyncos*), Northern Pintail (*Anas acuta*) and American Wigeon (*Anas americana*) (Hatfield, 1991). Based on the wildlife management objective of CWS to protect and conserve migratory birds, the present study did not find any risks of PPCP-related adverse effects to these wildlife species (Environment and Climate Change, 2020). Conversely, birds of prey with diets primarily composed of small mammalian prey items were found to be consuming potentially toxic doses of bioaccumulated clotrimazole. However, the KABAM model assumed these owl species would only

predate on shrews, thus does not account for the variation in their diet. From 1974 to 1975, a study on Barn Owl pellets was conducted in the ANWA which recovered the remains of mammals, birds, insects, fish and crustaceans (Dawe et al., 1978). In the two sampling years of the study by Dawe et al. (1978) found that *Microtus townsendii* (Townsend's vole) comprised 92% of a barn owl's diet in 1974 to 1975, whereas *Sorex vagrans* (vagrant shrew) had an average frequency of occurrence of 20.6% within their diets (Dawe et al., 1978). Thus, the diet presented in the current KABAM model does not accurately reflect the diet of barn owls. However, it provides a conservative estimate of the bioaccumulated exposure of azoles as shrew likely bioaccumulate more of these high log K_{ow} chemicals than voles. Interestingly, the food preferences of barn owls vary based on the habitat types, particularly with rural agricultural and urban landscapes where consumption of *Rattus spp.* and *Mus musculus* by barn owls were proportional to the level of urbanization of their home range (Hindmarch and Elliott, 2015). As land-use in the Lower Fraser Valley change to accommodate the increasing Canadian population, the diets of these city-dwelling owls will be affected and may increase their exposure to bioaccumulated chemical contaminants.

Our present study showed that at environmentally relevant concentrations, PPCPs have the potential to cause deleterious effects across multiple taxa in the ANWA in both aquatic and terrestrial compartments either as single chemicals or in mixtures. Additionally, veterinary drugs were demonstrated to be an important source of PPCP contamination and can accumulate to toxic levels, impacting primary producers in which higher trophic species depend. The present study also detected potentially PPCPs that biomagnify and could reach doses that are potentially acutely toxic to birds of prey. Considering alarming secondary poisoning reports in literature via wildlife feeding on diclofenac (an NSAID) contaminated animal carcasses, environmental monitoring

programs centered on these PPCP are recommended to preserve the critical wildlife habitat of ANWA (Corcoran et al., 2010).

4.1. Future directions

There has been a lack of environmental monitoring data regarding PPCPs in the lower Fraser River, particularly within sensitive wildlife habitats downstream from multiple WWTP outfalls. Monitoring studies pertaining to PPCPs in Canada have been mostly focused on the Great Lakes and Quebec. Thus, further studies characterizing the PPCP loadings in the waters and sediments within the Fraser River would provide a greater understanding of the transport, distribution and fate of these WWTP-related PPCPs. Furthermore, a more robust sampling regime within the ANWA should be performed to understand the spatial and temporal distribution of PPCPs to elucidate a more refined exposure scenario aquatic and wildlife receptors may experience. In addition, assessing the model fitness of the KABAM model using empirically measured prey tissue data would be highly beneficial as it is currently unknown how PPCPs partition within tissues of biota.

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Appendix. Supplementary Data

Table S. 1. List of 141 pharmaceutical and personal care product analytes chemically quantified from sediment samples collected from the Alaksen National Wildlife Area.

PPCP Analyte	Reporting Limit Range (ng/g)
Tetracyclines in positive ionization	
Anhydrochlortetracycline [ACTC]	9.67-37.9
Anhydrotetracycline [ATC]	9.67-37.9
Chlortetracycline [CTC]	3.87-15.2
Demeclocycline	9.67-37.9
Doxycycline	3.87-15.2
4-Epianhydrochlortetracycline [EACTC]	38.7-152
4-Epianhydrotetracycline [EATC]	9.67-37.9
4-Epichlortetracycline [ECTC]	9.67-37.9
4-Epioxytetracycline [EOTC]	3.87-15.2
4-Epitetracycline [ETC]	3.87-15.2
Isochlortetracycline [ICTC]	3.87-15.2
Minocycline	38.7-152
Oxytetracycline [OTC]	3.87-15.2
Tetracycline [TC]	3.87-15.2
Diatrizoic acid	7.73-30.3
Iopamidol	51.6-202
Citalopram	0.305-2.06
Tamoxifen	0.258-1.01
Cyclophosphamide	0.258-1.01
Venlafaxine	0.272-2.06
Acid extraction in positive ionization - Analysis 1	
Amsacrine	0.0306-0.101
Azathioprine	0.644-2.53
Busulfan	1.29-5.06
Clotrimazole	0.272-1.01
Colchicine	0.516-2.02
Daunorubicin	1.36-5.06
Doxorubicin	4.08-15.2
Drospirenone	5.16-20.2
Etoposide	0.644-2.53
Medroxyprogesterone Acetate	2.58-10.1
Metronidazole	1.29-5.06
Moxifloxacin	3.69-10.5 [a]
Oxazepam	2.58-10.1
Rosuvastatin	2.58-10.1
Teniposide	2.58-10.1

Zidovudine	3.87-15.2
Melphalan	16.3-60.7
Acid extraction in positive ionization - Analysis 2	
Alprazolam	0.193-0.758
Amitriptyline	0.204-0.758
Amlodipine	0.648-2.54
Benzoylecgonine	0.0967-0.379
Benztropine	0.477-1.77
Betamethasone	0.967-3.79
Cocaine	0.0967-0.379
DEET	0.193-0.758
Desmethyldiltiazem	0.0967-0.379
Diazepam	0.324-1.27
Fluocinonide	1.3-5.08
Fluticasone propionate	1.3-5.08
Hydrocortisone	3.87-15.2
10-hydroxy-amitriptyline	0.115-0.508 [a]
Meprobamate	0.967-3.79
Methylprednisolone	2.58-10.1
Metoprolol	0.324-1.27
Norfluoxetine	0.324-1.27
Norverapamil	0.0967-0.379
Paroxetine	0.656-2.54
Prednisolone	2.58-10.1
Prednisone	3.87-15.2
Promethazine	0.193-0.758
Propoxyphene	0.204-0.758
Propranolol	0.193-0.758
Sertraline	0.193-0.758
Simvastatin	1.3-5.08
Theophylline	3.87-15.2
Trenbolone	1.3-5.08
Trenbolone acetate	0.193-0.758
Valsartan	2.58-10.1
Verapamil	0.102-0.379 [a]
Acid extraction in positive ionization - Analysis 3	
Acetaminophen	9.67-37.9
Azithromycin	0.967-3.79
Caffeine	9.67-37.9
Carbadox	0.967-3.79
Carbamazepine	0.967-3.79
Cefotaxime	6-45.8
Ciprofloxacin	4.08-212
Clarithromycin	0.967-3.79

Clinafloxacin	6-80.4
Cloxacillin	1.93-7.58
Dehydronifedipine	0.387-1.52
Diphenhydramine	0.387-1.52
Diltiazem	0.193-0.758
Digoxin	3.87-15.2
Digoxigenin	3.87-66.7
Enrofloxacin	3-7.96
Erythromycin-H2O	1.48-5.81
Flumequine	0.967-3.79
Fluoxetine	0.977-3.79
Lincomycin	1.93-7.58
Lomefloxacin	15.1-27.1
Miconazole	0.967-3.79
Norfloxacin	15-53
Norgestimate	3.18-30.4
Ofloxacin	1.5-5.38
Ormetoprim	0.387-1.52
Oxacillin	1.93-7.58
Oxolinic Acid	0.408-1.52
Penicillin G	1.93-7.58
Penicillin V	1.93-7.58[a]
Roxithromycin	0.193-0.758
Sarafloxacin	15-37.9
Sulfachloropyridazine	0.967-3.79
Sulfadiazine	0.967-3.79
Sulfadimethoxine	0.193-1
Sulfamerazine	0.387-1.52
Sulfamethazine	0.387-1.52
Sulfamethizole	0.387-1.52 [a]
Sulfamethoxazole	0.387-1.52
Sulfanilamide	9.67-37.9
Sulfathiazole	0.967-3.79
Thiabendazole	0.967-3.79 [a]
Trimethoprim	0.967-3.79
Tylosin	3.87-15.2
Virginiamycin M1	2.04-18.7 [a]
1,7-Dimethylxanthine	38.7-152
Acid extraction in negative ionization	
Bisphenol A	3.87-15.2
Furosemide	2.58-10.1
Gemfibrozil	0.516-2.02
Glipizide	0.516-2.02
Glyburide	0.516-2.02

Hydrochlorothiazide	5.67-22.2
2-Hydroxy-ibuprofen	2.58-10.1
Ibuprofen	2.58-10.1
Naproxen	1.29-5.06
Triclocarban	0.258-1.01
Triclosan	3.87-15.2
Warfarin	0.258-1.01
Basic extraction in positive ionization	
Albuterol	0.194-0.752
Amphetamine	0.194-0.752
Atenolol	0.194-0.752
Atorvastatin	1.18-1.2
Cimetidine	0.388-0.883
Clonidine	0.776-3.01
Codeine	0.776-3.01
Cotinine	0.194-0.752
Enalapril	0.194-0.752
Hydrocodone	0.776-3.01
Metformin	0.194-0.752
Oxycodone	0.388-1.5
Ranitidine	0.388-1.5
Triamterene	0.194-0.752

Sediment samples were analyzed by SGS AXYS Analytical Services (Sidney, BC, Canada) using the SGS AXYS PPCP Method MLA-075. All reporting limits are reported as lower method calibration limits in all samples, including lab blanks except as noted below.

[a] Reported as sample specific detection limit

Table S. 2. List of 110 pharmaceutical and personal care product analytes chemically quantified from polar organic chemical integrative samplers (POCIS) collected from the Alaksen National Wildlife Area.

PPCP Analyte	Reporting Limit Range
Tetracycline in positive ionization	
Anhydrochlortetracycline [ACTC]	15.1-16.5
Anhydrotetracycline [ATC]	15.1-15.2
Chlortetracycline [CTC]	6.03-6.07
Demeclocycline	15.1-15.2
Doxycycline	6.03-6.07
4-Epianhydrochlortetracycline [EACTC]	60.3-60.7
4-Epianhydrotetracycline [EATC]	15.1-15.2
4-Epichlortetracycline [ECTC]	15.1-15.2
4-Epioxytetracycline [EOTC]	6.03-6.07
4-Epitetracycline [ETC]	6.03-6.07
Isochlortetracycline [ICTC]	6.03-6.07
Minocycline	60.3-60.7
Oxytetracycline [OTC]	6.03-6.07
Tetracycline [TC]	6.03-6.07
Acid extraction in positive ionization - Analysis 1	
Diatrizoic acid	12-36
Iopamidol	80
Citalopram	0.4-1.75
Tamoxifen	0.4
Cyclophosphamide	0.4
Venlafaxine	0.4
Amsacrine	0.04-0.238
Azathioprine	1
Busulfan	2
Clotrimazole	0.4
Colchicine	0.8-3.69
Daunorubicin	2-3.83
Doxorubicin	6
Drospirenone	8
Etoposide	1
Medroxyprogesterone Acetate	4
Metronidazole	2
Moxifloxacin	4-4.36
Oxazepam	4-6.47
Rosuvastatin	4
Teniposide	4
Zidovudine	6
Melphalan	24
Base extraction in positive ionization	

Albuterol	0.299-0.3
Amphetamine	0.299-2.34
Atenolol	0.299-0.3
Atorvastatin	1.2-2.17
Cimetidine	0.598-0.741
Clonidine	1.2-1.2
Codeine	1.2-1.27
Cotinine	0.299-0.3
Enalapril	0.299-0.3
Hydrocodone	1.2-1.2
Metformin	0.299-0.3
Oxycodone	0.598-0.601
Ranitidine	0.598-1.1
Triamterene	0.299-0.3
Acid extraction in positive ionization - Analysis 2	
Acetaminophen	15.1-15.2
Azithromycin	5.02-5.06
Caffeine	15.1-15.2
Carbadox	1.51-2.89
Carbamazepine	1.51-1.52
Cefotaxime	ND
Ciprofloxacin	6.41-15.3[a]
Clarithromycin	1.51-1.52
Clinafloxacin	6.07-9.77
Cloxacillin	3.01-3.54
Dehydronifedipine	2.01-2.02
Diphenhydramine	2.01-2.02
Diltiazem	ND
Digoxin	6.03-6.07
Digoxigenin	6.03-320
Enrofloxacin	3.01-3.6
Erythromycin-H_2O	2.31-2.33
Flumequine	5.02-8.14
Fluoxetine	1.51-1.52
Lincomycin	3.01-3.04
Lomefloxacin	3.01-4.93[a]
Miconazole	1.51-4.01
Norfloxacin	15.1-17.2
Norgestimate	10-10.1
Ofloxacin	1.51-1.66
Ormetoprim	0.603-0.607
Oxacillin	3.01-3.04
Oxolinic Acid	0.603-3.25
Penicillin G	3.01-3.04

Penicillin V	3.01-3.04
Roxithromycin	0.301-0.436
Sarafloxacin	15.1-15.2
Sulfachloropyridazine	1.51-1.52
Sulfadiazine	1.51-1.52
Sulfadimethoxine	0.301-0.474
Sulfamerazine	0.603-0.968
Sulfamethazine	0.603-5.03
Sulfamethizole	0.603-0.607
Sulfamethoxazole	0.603-1.87
Sulfanilamide	15.1-15.2
Sulfathiazole	1.51-1.52
Thiabendazole	1.51-1.52
Trimethoprim	1.51-2.55
Tylosin	6.03-6.07
Virginiamycin M1	ND
1,7-Dimethylxanthine	60.3-60.7
Acid extraction in negative ionization	
Bisphenol A	6.03-31.6
Furosemide	4.02-9.64
Gemfibrozil	0.804-0.809
Glipizide	0.804-0.809
Glyburide	0.804-0.809
Hydrochlorothiazide	8.84-8.9
2-Hydroxy-ibuprofen	4.02-11.8
Ibuprofen	4.02-4.05
Naproxen	2.01-10.4
Triclocarban	0.402-0.405
Triclosan	6.03-6.07
Warfarin	0.402-0.867

POCIS samples were analyzed by SGS AXYS Analytical Services (Sidney, BC, Canada) using the SGS AXYS PPCP Method MLA-075. Reporting limits were reported as lower method calibration limits unless otherwise noted.

[a] Reported as sample specific detection limits

ND – not detected

Table S. 3. List of sampling rates (Rs) compiled for each pharmaceutical and personal care product detected in polar organic chemical integrative samplers for the Alaksen National Wildlife Area ecological risk assessment.

Analyte	R_s ± SD (L/d)	Type of calibration	Reference
Amphetamine	0.041 (± 0.0015)	Laboratory	Hahn et al., 2022
	0.094	Laboratory	Zhang et al., 2008
	0.201 (± 0.038)	Laboratory	Hahn et al., 2022
Atenolol	0.087 (± 0.003)	Laboratory	Li et al. 2010
	0.094 (± 0.015)	Laboratory	Li et al. 2010
	0.073 (± 0.013)	Laboratory	Li et al. 2010
	0.037 (± 0.064)	Laboratory	MacLeod et al. 2007
	0.04 (± 0.07)	Laboratory	MacLeod et al. 2007
	0.107 (± 0.007)	Laboratory	MacLeod et al. 2007
	0.171 (± 0.013)	Laboratory	Bailey et al., 2013
	0.102 (± 0.004)	Laboratory	Bailey et al., 2013
	0.129 (± 0.008)	Laboratory	Bailey et al., 2013
	0.101 (± 0.009)	Laboratory	Bailey et al., 2013
	0.092 (± 0.011)	Laboratory	Bailey et al., 2013
Benzoylecgonine	0.076 (± 0.0008)	Laboratory	Hahn et al., 2022
	0.041	In situ wastewater	Baz-Lomba et al., 2017
	0.027	In situ wastewater	Baz-Lomba et al., 2017
	0.031	In situ wastewater	Baz-Lomba et al., 2017
	0.083	In situ wastewater	Harman et al., 2010
	0.134 (± 0.011)	Laboratory	Yargeau et al., 2014
Bisphenol A	0.531 (± 0.063)	Laboratory	Li et al. 2010
	0.74 (± 0.036)	Laboratory	Li et al. 2010
	0.835 (± 0.058)	Laboratory	Li et al. 2010
	0.482 (± 0.066)	Laboratory	Li et al. 2010
	0.04	Laboratory	Zhang et al., 2008
	0.752 (± 0.043)	Laboratory	Kim and Homan 2020
	0.402 (± 0.117)	Laboratory	Mathon et al., 2014
	0.079 (± 0.026)	Laboratory	Mathon et al., 2014
	0.516 (± 0.036)	Laboratory	Mathon et al., 2014
Caffeine	0.044 (± 0.005)	Laboratory	Bartelt-Hunt et al. 2011
	0.096 (± 0.008)	Laboratory	Li et al. 2010
	0.151 (± 0.018)	Laboratory	Li et al. 2010
	0.127 (± 0.021)	Laboratory	Li et al. 2010
	0.084 (± 0.002)	Laboratory	Hahn et al., 2022
	0.186 (± 0.032)	Laboratory	Kim and Homan 2020
	0.063 (± 0.007)	Artificial stream	Guibal et al., 2020
	0.155 (± 0.017)	Artificial stream	Guibal et al., 2020
	0.17 (± 0.009)	Artificial stream	Guibal et al., 2020
	0.263 (± 0.029)	Artificial stream	Guibal et al., 2020
	0.55 (± 0.108)	Laboratory	Mathon et al., 2014

	0.133 (± 0.068)	Laboratory	Mathon et al., 2014
	0.044 (± 0.036)	Laboratory	Mathon et al., 2014
Carbamazepine	0.288 (± 0.009)	Laboratory	Bartelt-Hunt et al. 2011
	0.23 (± 0.016)	Laboratory	Li et al. 2010
	0.397 (± 0.018)	Laboratory	Li et al. 2010
	0.561 (± 0.024)	Laboratory	Li et al. 2010
	0.235 (± 0.046)	Laboratory	Li et al. 2010
	0.112 (± 0.023)	Laboratory	MacLeod et al. 2007
	0.348 (± 0.116)	Laboratory	MacLeod et al. 2007
	0.067	In situ wastewater	Baz-Lomba et al., 2017
	0.065	In situ wastewater	Baz-Lomba et al., 2017
	0.078	In situ wastewater	Baz-Lomba et al., 2017
	0.314 (± 0.063)	Laboratory	Kim and Homan 2020
	0.087 (± 0.011)	Artificial stream	Guibal et al., 2020
	0.29 (± 0.04)	Artificial stream	Guibal et al., 2020
	0.299 (± 0.026)	Artificial stream	Guibal et al., 2020
	0.443 (± 0.08)	Artificial stream	Guibal et al., 2020
	0.6 (± 0.087)	Laboratory	Mathon et al., 2014
	0.157 (± 0.016)	Laboratory	Mathon et al., 2014
	0.497 (± 0.015)	Laboratory	Mathon et al., 2014
Citalopram	0.354 (± 0.02)	Laboratory	Li et al. 2010
	0.735 (± 0.015)	Laboratory	Li et al. 2010
	0.758 (± 0.033)	Laboratory	Li et al. 2010
	0.314 (± 0.086)	Laboratory	Li et al. 2010
	0.242	In situ wastewater	Baz-Lomba et al., 2017
	0.109	In situ wastewater	Baz-Lomba et al., 2017
	0.111	In situ wastewater	Baz-Lomba et al., 2017
	1.224 (± 0.087)	Laboratory	Mathon et al., 2014
	0.175 (± 0.011)	Laboratory	Mathon et al., 2014
Cocaine	0.097	In situ wastewater	Baz-Lomba et al., 2017
	0.074	In situ wastewater	Baz-Lomba et al., 2017
	0.09	In situ wastewater	Baz-Lomba et al., 2017
	0.15	In situ wastewater	Harman et al., 2010
	0.13 (± 0.036)	Laboratory	Yargeau et al., 2014
Codeine	0.09 (± 0.067)	Laboratory	MacLeod et al. 2007
	0.329 (± 0.133)	Laboratory	MacLeod et al. 2007
	0.394 (± 0.049)	Laboratory	Yargeau et al., 2014
Cotinine	0.034 (± 0.011)	Laboratory	Bartelt-Hunt et al. 2011
	0.056 (± 0.0032)	Laboratory	Hahn et al., 2022
DEET	0.24 (± 0.006)	Laboratory	Bartelt-Hunt et al. 2011
Ibuprofen	0.4 (± 0.081)	Laboratory	Bartelt-Hunt et al. 2011
	0.204 (± 0.004)	Laboratory	Li et al. 2010
	0.254 (± 0.019)	Laboratory	Li et al. 2010
	0.348 (± 0.052)	Laboratory	Li et al. 2010

	0.197 (± 0.013)	Laboratory	Li et al. 2010
	0.33 (± 0.052)	Laboratory	Kim and Homan 2020
	0.293 (± 0.064)	Laboratory	Mathon et al., 2014
Metformin	0.086 (± 0.018)	Laboratory	Kim and Homan 2020
Metoprolol	0.309 (± 0.106)	Laboratory	Li et al. 2010
	0.465 (± 0.039)	Laboratory	Li et al. 2010
	0.156 (± 0.034)	Laboratory	Li et al. 2010
	0.097 (± 0.066)	Laboratory	MacLeod et al. 2007
	0.599 (± 0.27)	Laboratory	MacLeod et al. 2007
	0.168	In situ wastewater	Baz-Lomba et al., 2017
	0.143	In situ wastewater	Baz-Lomba et al., 2017
	0.25	In situ wastewater	Baz-Lomba et al., 2017
	0.069 (± 0.009)	Artificial stream	Guibal et al., 2020
	0.228 (± 0.032)	Artificial stream	Guibal et al., 2020
	0.232 (± 0.019)	Artificial stream	Guibal et al., 2020
	0.346 (± 0.062)	Artificial stream	Guibal et al., 2020
Moxifloxacin	N/A		
Naproxen	0.239 (± 0.009)	Laboratory	Li et al. 2010
	0.298 (± 0.016)	Laboratory	Li et al. 2010
	0.392 (± 0.024)	Laboratory	Li et al. 2010
	0.2 (± 0.037)	Laboratory	Li et al. 2010
	0.083 (± 0.055)	Laboratory	MacLeod et al. 2007
	0.116 (± 0.053)	Laboratory	MacLeod et al. 2007
Sulfamethoxazole	0.118 (± 0.012)	Laboratory	Bartelt-Hunt et al. 2011
	0.291 (± 0.004)	Laboratory	Li et al. 2010
	0.348 (± 0.049)	Laboratory	Li et al. 2010
	0.339 (± 0.057)	Laboratory	Li et al. 2010
	0.202 (± 0.019)	Laboratory	Li et al. 2010
	0.092 (± 0.004)	Laboratory	Bailey et al., 2013
	0.113 (± 0.016)	Laboratory	Bailey et al., 2013
	0.093 (± 0.012)	Laboratory	Bailey et al., 2013
	0.085 (± 0.008)	Laboratory	Bailey et al., 2013
	0.094 (± 0.011)	Laboratory	Bailey et al., 2013
	0.08 (± 0.005)	Laboratory	Bailey et al., 2013
	0.253 (± 0.068)	Laboratory	Kim and Homan 2020
	0.053 (± 0.005)	Artificial stream	Guibal et al., 2020
	0.096 (± 0.006)	Artificial stream	Guibal et al., 2020
	0.119 (± 0.007)	Artificial stream	Guibal et al., 2020
	0.154 (± 0.011)	Artificial stream	Guibal et al., 2020
	0.153 (± 0.108)	Laboratory	Mathon et al., 2014
	0.05 (± 0.035)	Laboratory	Mathon et al., 2014
	0.135 (± 0.029)	Laboratory	Mathon et al., 2014
Thiabendazole	0.264 (± 0.004)	Laboratory	Bartelt-Hunt et al. 2011
	0.768 (± 0.081)	Laboratory	Mathon et al., 2014

	0.182 (± 0.017)	Laboratory	Mathon et al., 2014

R_s – Sampling rate (L/d)

SD – Standard deviation

Table S. 4. Physicochemical properties of pharmaceuticals and personal care products detected in the Alaksen National Wildlife Area.

Chemical	Compound Class	CAS Number	Molecular Weight	Log K_{ow}	Log K_{oc}	Log K_{oa}	Boiling Point (°C)	Melting Point (°C)	Vapour Pressure (Pa)	Water Solubility (mg/L)	Henry's Law Constant (atm m^3/mol)
Ibuprofen	NSAID	15687-27-1	206.29	3.79	2.626	9.177	323.11	76	0.0248	41.05	0.000000152
Naproxen	NSAID	22204-53-1	230.27	3.18	2.525	11.038	379.7	153	0.00017	144.9	3.39E-10
Tylosin	Macrolide Antibiotic	1401-69-0	916.12	1.63	2.873	37.257	1046.08	349.84	2.65E-32	0.5065	5.77E-38
Moxifloxacin	Fluoroquinolone Antibiotic	151096-09-2	401.44	0.95	1.49	18.846	623.63	325	1.10524E-06	1146	3.346E-18
Sarafloxacin	Quinolone Antibiotic	98105-99-8	385.37	1.07	2.75	18.175	611.25	243.24	2.16E-12	1139	1.92E-18
Sulfamethoxazole	Sulfonamide Antibiotic	723-46-6	253.28	0.89	2.412	11.298	414.01	167	0.0000174	3942	9.56E-13
Cloxacillin	Penicillin Antibiotic	61-72-3	435.89	2.48	2.81	17.592	667.51	290.85	1.82E-13	13.94	1.89E-17
Erythromycin-H2O	Macrolide Antibiotic	No CAS #	715.93	4.3405	2.008	29.524	778.21	342.56	1.8E-22	0.05497	1.6E-27
Clotrimazole	Anti-Fungal	23593-75-1	344.85	6.1	6.432	12.154	494.52	148	0.000000283	0.02984	3.12E-08
Miconazole	Anti-fungal	22916-47-8	416.14	6.25	5.744	13.249	506.31	349.84	2.36E-08	0.01114	8.7E-09
Thiabendazole	Anti-Fungal/Parasitic	148-79-8	201.25	2	3.617	11.532	443.05	300	0.000000533	335.2	2E-11
Caffeine	CNS Stimulant	58-08-2	194.19	0.16	1	8.765	430.85	238	0.000000977	2632	3.58E-11
Cocaine	CNS Stimulant	50-36-2	303.36	2.17	2.9	11.061	362.63	98	0.0000255	1298	3.28E-11
Benzoylecgonine	Cocaine Metabolite	519-09-5	289.33	-1.32	2.301	10.056	489.11	195	0.000000112	1605	1.03E-13
Amphetamine	CNS Stimulant	300-62-9	135.21	1.76	2.883	6.115	203	11.3	41.4	2803	0.00000108
Cotinine	Nicotine Metabolite	486-56-6	176.22	0.34	2.116	9.936	250	41	0.0509	998600	3.33E-12
Citalopram	Anti-Depressant	59729-33-8	324.4	3.74	4.442	12.699	178	417.85	0.0000151	31.09	2.69E-11
Venlafaxine	Anti-Depressant	93413-69-5	277.41	3.28	2.942	12.359	363.8	98.76	0.0000328	266.7	2.04E-11
Atenolol	Beta Blocker	29122-68-7	266.34	-0.03	1.825	16.412	147	438.63	0.000000103	685.2	1.37E-18
Metoprolol	Beta Blocker	51384-51-1	267.37	1.69	2.057	13.122	362.44	97.97	0.0000384	4777	1.4E-13
Metformin	Anti-diabetic	657-24-9	129.17	-2.64	1.428	10.865	268.97	74.45	0.0101	1000000	7.64E-16
DEET	Insect Deterent	134-62-3	191.28	2.258	2.055	8.25	290	-45	0.267	666	2.08E-08
Daunorubicin	Anti-neoplastic	20830-81-3	527.53	2.19	2.055	25.063	738.98	208	1.27E-18	39.17	1.43E-25
Bisphenol A	Estrogen Agonist	80-05-7	288.31	3.32	1.171	12.747	442.01	144.43	2.96E-08	23470	2.09E-14
Carbamazepine	Anti-Convulsant	298-46-4	236.28	2.25	3.123	10.805	410.02	190.2	0.0000117	17.66	1.08E-10
Theophylline	Anti-Asthma	58-55-9	180.17	-0.39	1	10.123	458.64	273	7.43E-08	2912	1.68E-12
Codeine	Opioid	76-57-3	299.37	1.19	2.845	12.699	405.72	280	2.55E-08	12150	7.58E-14

Physicochemical properties were retrieved from EPISuite v4.1 US EPA 2012

Table S. 5. List of mammals, amphibians, reptiles, fish, plants and birds that are either indigenous, introduced or have been observed in Alaksen National Wildlife Area which total 210 species. Adapted from ECCC 2021, Alaksen National Wildlife Area: Management Plan.

Common name	Genus species
Mammals (18)	
Townsend's Vole	*Microtus townsendii*
Vagrant shrew	*Sorex vagrans*
American Beaver	*Castor canadensis*
Muskrat	*Ondatra zibethicus*
Coyote	*Canis latrans*
Mink	*Neovison vison*
River Otter	*Lontra canadensis*
Racoon	*Procyon lotor*
Douglas' Squirrel	*Tamiasciurus douglasii*
Gray Squirrel	*Sciurus griseus*
Eastern Grey Squirrel	*Scirirus carolinensis*
Roof Rat	*Rattus rattus*
Norway Rat	*Rattus norvegicus*
Deer Mouse	*Peromyscus maniculatus*
Pacific Jumping Mouse	*Zapus trinotatus*
Little Brown Bat	*Myotis lucifugus*
Big Brown Bat	*Eptesicus fuscus*
Yuma Myotis	*Myotis yumanensis*
Amphibians (2)	
Green Frog	*Lithobates clamitans*
Bull Frog	*Rana catesbeiana*
Reptiles (4)	
Red-eared Slider	*Trachemys scripta elegans*
Western Painted Turtle	*Chrysemys picta bellii*
Common Garter Snake	*Thamnophis sirtalis*
Northwestern Garter Snake	*Thamnophis ordinoides*
Fish (6)	
Three-Spined Stickleback	*Gasterosteus aculeatus*
Common Carp	*Cyprinus carpio*
Pumpkin Seed	*Lepomis gibbosus*
Prickly Sculpin	*Cottus asper*
Brown Bullhead Catfish	*Ameiurus nebulosus*
Brassy Minnow	*Hybognathus hankinsoni*
Plants (89)	
American Winter Cress	*Barbarea orthoceras*
Arrowhead	*Sagittaria latifolia*
Bitter Cherry	*Prunus emarginata*
Black Cottonwood	*Populus trichocarpa*

Black Medic	*Medicago lupulina*
Black Twinberry	*Lonicera involucrata*
Bracken Fern	*Pteridium aquilinum*
Broad-leaved Plantain	*Plantago major*
Bull Thistle	*Cirsium vulgare*
Canada Thistle	*Cirsium arvense*
Cascara	*Rhamnus purshiana*
Cleavers	*Galium aparine*
Common Dandelion	*Taraxacum officinale*
Common Hawthorn	*Crataegus monogyna*
Common Horsetail	*Equisetum arvense*
Common Rush	*Juncus effusus*
Common Snowberry	*Symphoricarpos albus*
Common St. John's Wort	*Hypericum perforatum*
Cow Parsnip	*Heracleum lanatum*
Creeping Buttercup	*Ranunculus repens*
Cud Weed	*Gnaphalium uliginosum*
Curled Dock	*Rumex crispus*
Cut Leaf Water Horehound	*Lycopus americanus*
Deer Fern	*Blechnum spicant*
Douglas' Water Hemlock	*Cicuta douglasii*
Douglas-fir	*Pseudotsuga menziesii*
English Holly	*Ilex aquifolium*
English Ivy	*Hedera helix*
European Bittersweet	*Solanum dulcamara*
Evergreen Blackberry	*Rubus laciniatus*
Fireweed	*Epilobium angustifolium*
Fringed Cup	*Tellima grandiflora*
Hairy Cat's-ear	*Hypochaeris radicata*
Henderson's Checker-mallow	*Sidalcea hendersonii*
Herb-Robert	*Geraniun robertianum*
Himalayan Blackberry	*Rubus armeniacus*
Lady Fern	*Athyrium filix-femina*
Lady's Thumb	*Polygonum persicaria*
Lamb's Quarter	*Chenopodium album*
Large-leaved Aven	*Geum macrophyllum*
Lodgepole Pine	*Pinus contorta var. latifolia*
Morning Glory	*Convolvulus arvensis*
Narrow-leaved Plantain	*Plantago lanceolata*
Nodding Beggarticks	*Bidens cernua*
Nootka Rose	*Rosa nutkana*
Oak	*Quercus spp*
Oregon Ash	*Fraxinus latifolia*
Oxeye Daisy	*Leucanthemum vulgare*

Pacific Crabapple	*Malus fusca*
Pacific Dogwood	*Cornus nutttallii*
Pacific Ninebark	*Physocarpus capitatus*
Paper Birch	*Betula papyrifera*
Pearly Everlasting	*Anaphalis margaritacea*
Perennial sow-Thistle	*Sonchus arvensis*
Perennial Sow-thistle	*Sonchus arvensis*
Pineapple Weed	*Matricaria matricarioides*
Purple Leaved Willowherb	*Epilobium ciliatum*
Purple Loosestrife	*Lythrum salicaria*
Red Alder	*Alnus rubra*
Red elderberry	*Sambucus racemosa*
Red-osier Dogwood	*Cornus stolonifera*
Redroot Pigweed	*Amaranthus retroflexus*
Reed Canary Grass	*Phalaris arundinacea*
Salmonberry	*Rubus spectabilis*
Scotch Broom	*Cytisus scoparius*
Sheep Sorrel	*Rumex acetosella*
Shepherd's Purse	*Capsella bursa-pastoris*
Sitka Alder	*Alnus crispa ssp. sinuata*
Sitka Mountain	*Sorbus sitchensis*
Skunk Cabbage	*Lysichiton americanum*
Spiny Sow Thistle	*Sonchus asper*
Stinging Nettle	*Urtica dioica*
Sweet Cherry	*Prunus avium*
Sweet Gale	*Myrica gale*
Sword Fern	*Polystichum munitum*
Thimbleberry	*Rubus parviflorus*
Trailing Blackberry	*Rubus ursinus*
Vetch	*Vicia spp*
Wall Lettuce	*Lactuca muralis*
Water Lily	*Nymphaea odorata*
Western Red Cedar	*Thuja plicata*
White Clover	*Trifolium repens*
White Rein Orchid	*Platanthera dilatata*
White Sweet-clover	*Melilotus alba*
Wild Asparagus	*Asparagus officinalis*
Willow	*Salix spp*
Yarrow	*Achillea millefolium*
Yellow archangel	*Lamiastrum galeobdolon*
Yellow Flag Iris	*Iris pseudoacorus*
Birds (91)	
American Bittern	*Botaurus lentiginosus*
American Coot	*Fulica americana*

American Pipit	*Anthrus rubescens*
American Widgeon	*Mareca americana*
Bald Eagle	*Haliaeetus leucocephalus*
Barn Owl	*Tyto alba*
Barn Swallow	*Hirundo rustica*
Barrowâ€™s Goldeneye	*Bucephala islandica*
Black-bellied Plover	*Pluvialis squatarola*
Black-crowned Night-Heron	*Nycticorax nycticorax*
Black swift	*Cypseloides niger*
Blue-Winged Teal	*Spatula discors*
Bufflehead	*Bucephala albeola*
Cackling Goose	*Branta hutchinsii*
Canada Goose	*Branta canadensis*
Canvasback	*Aythya valisineria*
Cinnamon Teal	*Spatula cyanoptera*
Common Goldeneye	*Bucephala clangula*
Common Loon	*Gavia immer*
Common Merganser	*Mergus merganser*
Cooper's Hawk	*Accipiter cooperii*
Cormorant	*Phalacrocorax*
Double-crested Cormorant	*Phalacrocorax auritus*
Dowicher	*Limnodromus*
Dunlin	*Calidris alpina*
Eurasian Widgeon	*Anas penelope*
Gadwall	*Anas strepera*
Glaucous-winged Gull	*Larus glaucescens*
Golden-crowned Kinglet	*Regulus satrapa*
Goldeneye	*Bucephala*
Gray-bellied Hawk	*Accipiter poliogaster*
Great Blue Heron	*Ardea herodias*
Greater Scaup	*Aythya marila*
Greater White-fronted Goose	*Anser albifrons*
Greater Yellowlegs	*Tringa melanoleuca*
Green-winged Teal	*Anas crecca*
Herring gull	*Larus argentatus*
Hooded Merganser	*Lophodytes cucullatus*
Horned Grebe	*Podiceps auritus*
Killdeer	*Charadrius vociferus*
Lesser Scaup	*Aythya affinis*
Lesser Yellowlegs	*Tringa flavipes*
Long-billed Dowitcher	*Limnodromus scolopaceus*
Long-tailed Duck	*Clangula hyemalis*
Mallard	*Anas strepera*
Mallard	*Anas platyrhynchos*

Marsh Wren	*Cistothorus palustris*
Merlin	*Falco columbarius*
Mew Gull	*Larus canus*
Mute Swan	*Cygnus olor*
Northern Flicker	*Colaptes auratus*
Northern Goshawk	*Accipiter gentilis*
Northern Harrier	*Circus cyaneus*
Northern Pintail	*Anas acuta*
Northern Saw-Whet Owl	*Aegolius acadicus*
Northern Shoveller	*Anas clypeata*
Northern Shrike	*Lanius excubitor*
Northwestern Crow	*Corvus caurinus*
Oriole	*Icterus spp.*
Pacific Loon	*Gavia pacifica*
Pelagic Cormorant	*Phalacrocorax pelagicus*
Peregrine Falcon	*Falco peregrinus*
Pied-billed Grebe	*Podilymbus podiceps*
Pileated Woodpecker	*Dryocopus pileatus*
Red-breasted Merganser	*Mergus serrator*
Red-Necked Grebe	*Podiceps grisegena*
Red-tailed Hawk	*Buteo jamaicensis*
Red-throated Loon	*Gavia stellata*
Ring-billed gull	*Larus delawarensis*
Ring-necked Duck	*Aythya collaris*
Ring-necked Pheasant	*Phasianus colchicus*
Rough-legged Hawk	*Buteo lagopus*
Ruddy Duck	*Oxyura jamaicensis*
Sandhill Crane	*Grus canadensis*
Sharp-shinned Hawk	*Accipiter striatus*
Short-eared Owl	*Asio flammeus*
Short-billed Dowitcher	*Limnodromus griseus*
Snow Goose	*Chen caerulescens*
Sooty Shearwater	*Ardenna grisea*
Sora	*Porzana carolina*
Spotted Sandpiper	*Actitis macularia*
Thayer Gull	*Larus thayeri*
Tree Swallow	*Tachycineta bicolor*
Trumpeter Swan	*Cygnus buccinator*
Violet green swallow	*Tachycineta thalassina*
Western Grebe	*Aechmophorus occidentalis*
Western Meadowlark	*Sturnella neglecta*
Western sandpiper	*Calidris mauri*
Whimbrel	*Numenius phaeopus*
Wilson's Snipe	*Gallinago delicata*

Table S. 6. List of species at risk based on the Species At Risk Act and Committee on the Status of Endangered Wildlife in Canada that can be potentially found in Alaksen National Wildlife Area. Adapted from ECCC 2021, Alaksen National Wildlife Area: Management Plan.

Status	Species	Status
Endangered	Little brown myotis, *Myotis lucifugus*	SARA: 1-Endangered (2014) COSEWIC: Endangered (2013) BC list: Yellow Provincial Rank: S4 (2015)
Endangered	Painted turtle: Pacific Coast population *Chrysemys picta*	SARA: 1-Endangered (2007) COSEWIC: Threatened (2016) BC list: Red Provincial Rank: S1S2 (2018)
Endangered	Brassy minnow *Hybognathus hankinsoni*	SARA: No Schedule COSEWIC: Not Listed BC list: No Status Provincial Rank: S4(2011)
Threatened	Barn owl *Tyto alba*	SARA: 1-Threatened (2018) COSEWIC: Threatened (2010) BC list: Red Provincial Rank: S2 (2015)
Threatened	Barn swallow, *Hirundo rustica*	SARA: 1- Threatened (2017) COSEWIC: Threatened (2011) BC list: Blue Provincial Rank: S3S4B (2015)
Threatened	Northern goshawk, laingi subspecies *Accipiter gentilis laingi*	SARA: 1-Threatened (2013) COSEWIC: Threatened (2013) BC list: Red Provincial Rank: S2 (2010)
Threatened	Northern saw-whet owl *Aegolius acadicus*	SARA: 1-Threatened (2007) COSEWIC: Threatened (2017) BC list: Yellow Provincial Rank: S5B, S5N (2009)
Special concern	Black swift, *Cypseloides niger*	SARA: No schedule, no status COSEWIC: Endangered (2015) BC list: Blue Provincial Rank: S2S3B (2015)
Special concern	Great blue heron, fannini subspecies	SARA: 1-Special Concern (2010) COSEWIC: Special Concern (2008) BC list: Blue Provincial Rank: S2S3B, S4N (2018)
Special concern	Peregrine falcon, anatum/tundrius subspecies *Falco peregrinus anatum*	SARA: 1-Special Concern (2012) COSEWIC: Not at Risk (2017) BC list: Red Provincial Rank: S2 (2011)
Special concern	Peregrine falcon, pealei subspecies *Falco peregrinus pealei*	SARA: 1-Special Concern (2003) COSEWIC: Special Concern (2017) BC list: List Provincial Rank: S3 (2010)
Special concern	Horned grebe *Podiceps auritus*	SARA: 1-Special Concern (2017) COSEWIC: Special Concern (2009) BC list: Yellow Provincial Rank: S4B, SNRN(2015)
Special concern	Short-eared owl *Asio flammeus*	SARA: 1-Special Concern (2012) COSEWIC: Special Concern (2008) BC list: Blue Provincial Rank: S3B, S2N (2015)
Special concern	Barrow's goldeneye *Bucephala islandica*	SARA: 1-Special Concern (2003) COSEWIC: Special Concern (2011)

Special concern	Western grebe *Aechmophorus occidentalis*	BC list: Yellow Provincial Rank: S4S5(2015) SARA: 1-Special Concern (2017) COSEWIC: Special Concern (2014) BC list: Red Provincial Rank: S1B, S2N (2015)

Table S. 7. Aquatic toxicity reference values (TRV) for pharmaceuticals and personal care products detected in abiotic media of the Alaksen National Wildlife Area.

Chemical	Species	Biota	Endpoint	Duration	TRV (µg/L)	Reference
Erythromycin	*Synechococcus leopoldensis*	Cyanobacteria	NOEC - Growth	6 d	2	Ando et al., 2007
	Anabaena cylindrica	Cyanobacteria	NOEC - Growth	6 d	3.1	Ando et al., 2007
	Microcystis wesenbergii	Cyanobacteria	NOEC - Growth	6 d	4.7	Ando et al., 2007
	Pseudokirchneriella subcapitata	Green algae	NOEC - Growth	72 h	10.3	Eguchi et al., 2004
	Chlorella vulgaris	Green algae	NOEC - Growth	72 h	12.5	Eguchi et al., 2004
	Lemna minor	Aquatic plant	NOEC - Growth	7 d	10	Pomati et al., 2004
	Daphnia magna	Crustacean	NOEC - Reproduction	21 d	248	Meinertz et al., 2010
	Oryzias latipes	Fish	NOEC - Growth	40 d	100000	Ji et al., 2012
DEET	*Pseudokirchneriella subcapitata*	Green algae	NOEC - Growth	96 h	521	Harada et al., 2008
	Chlorella protothecoides	Green algae	EC50 -Growth	24 h	388000	Costanzo et al., 2007
	Daphnia magna	Crustacean	LOEC Growth	21 d	7500	Minderhout et al., 2008
	Chironomus riparius	Crustacean	NOEC Growth	10 d	8800	Campos et al., 2016
	Macrobrachium nipponense	Crustacean	LC10	28 d	2730	Gao et al., 2020
	Rhodeus sinensis Gunther	Fish	LC10	28 d	8680	Gao et al., 2020
Metformin	*Pimephales promelas*	Fish	NOEC – NR	32 d	780	Moermond et al., 2016
Ibuprofen	Gammarus pulex	Invertebrate	LOEC – Behaviour	2 h	0.01	De Lange et al., 2006
Naproxen	Selanastrum capricornutum	Green algae	IC25 – Growth	72 h	32	Brun et al., 2006
Tylosin	*Lemna minor*	Aquatic plant	NOEC – Growth	7 d	100	Brain et al., 2004
Moxifloxacin	*Microcystis aeruginosa*	Green algae	LOEC – Growth	96 h	5	Wan et al., 2021
Sulfamethoxazole	*Caenorhabditis elegans*	Invertebrate	EC10 – Growth	96 h	0.0157	Yu et al., 2011
Cloxacillin	-	Fish	NOEC – NR	Chronic	3040	ECOSAR 2.2
Thiabendazole	NR	Fish	NOEC – NR	21 d	12	US EPA 1992
Caffeine	*Rana pipiens*	Amphibian	NOEC – Growth	28 d	0.6	Fraker et al., 2004
Cocaine	*Anguilla anguilla*	Fish	LOEC – Histology	50 d	0.02	Capaldo et al., 2019
Benzoylecgonine	*Dreissena polymorpha*	Invertebrate	LOEC – Oxidative stress	11 d	0.5	Parolini et al., 2013
Amphetamine	-	Fish	NOEC – NR	Chronic	348	ECOSAR 2.2
Cotinine	*Lemna minor*	Aquatic plant	NOEC – Growth/reproduction	7 d	1000	Brain et al., 2004
Citalopram	Poecilia wingei	Fish	NOEC – Behaviour	21 d	0.2	Olsén et al., 2014
Venlafaxine	*Oncorhynchus mykiss*	Fish	NOEC – Glucose reduction	3 h	2.774	Ings et al., 2012
Atenolol	*Pimephales promelas*	Fish	NOEC – Growth	32 d	3200	Winter et al., 2008
Metoprolol	*Oncorhynchus mykiss*	Fish	LOEC – Histology	28 d	1	Triebskorn et al., 2007
Carbamazepine	-	EQG	-	-	10	CCME 2018
Theophylline	*Danio rerio*	Fish	EC10 - Development	48 h	90983	Pruvot et al., 2012

NR – Not reported
NOEC – No observed effect concentration
LOEC – Lowest observed effect concentration