



Research Paper

N-Nitrosamines and their precursors in wastewater effluents from selected industries in Spain

Maria José Farré^{a,b,*}, Sara Insa^{a,b}, Wolfgang Gernjak^{a,c}, Lluís Corominas^{a,b}, Mira Čelić^{a,b}, Vicenç Acuña^{a,b}

^a Catalan Institute for Water Research (ICRA), Carrer Emili Grahit 101, 17003 Girona, Spain

^b University of Girona, Plaça de Sant Domènec 3, 17004 Girona, Spain

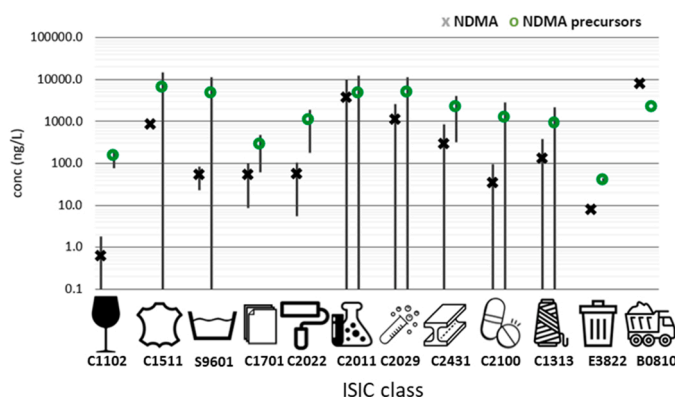
^c Catalan Institution for Research and Advanced Studies (ICREA), Passeig Lluís Companys 23, 08010 Barcelona, Spain



HIGHLIGHTS

- Industrial effluents are important sources of nitrosamines and their precursors.
- The highest N-nitrosodimethylamine conc. occurred in effluents of chemical industries.
- The highest N-nitrosodiethylamine conc. was found in an effluent of stone quarrying.
- Textile washing and dry cleaning is an important source of nitrosamine precursors.

GRAPHICAL ABSTRACT



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ABSTRACT

N-nitrosamines (NAs), and N-nitrosodimethylamine (NDMA) in particular, are hazardous disinfection byproducts (DBPs) relevant when wastewater impacts drinking water sources and, in water reuse practices. Our study investigates the concentrations of NDMA and five additional NAs and their precursors in industrial wastewater effluents. Aiming to identify potential differences between industrial typologies, wastewaters from 38 industries belonging to 11 types of the UN International Standard Industrial Classification of All Economic Activities system (ISIC) were analysed. Results show that the presence of most NAs and their precursors cannot be linked to a specific industry type as these were in general very different within the classes. Nevertheless, N-nitrosomethylethylamine (NMEA) and N-nitrosopiperidine (NPIP) as well as precursors for N-nitrosodiethylamine (NDEA), NPIP and N-nitrosodibutylamine (NDBA) could be rank with different concentrations between ISIC classes (p -value < 0.05). Specific industrial wastewater with notable high concentrations of NAs and their precursors were identified too. The effluents with the highest concentration of NDMA belong to the ISIC C2011 class (Manufacture of basic chemical), while the effluents with the highest concentration of NDMA precursors were from the ISIC C1511 class (Tanning and dressing of leather; dressing and dyeing of fur). Other relevant NAs

* Corresponding author at: Catalan Institute for Water Research (ICRA), Carrer Emili Grahit 101, 17003 Girona, Spain.

E-mail address: mjfarre@icra.cat (M.J. Farré).

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found were NDEA in ISIC class B0810 (Quarrying of stone, sand, and clay) and ISIC class C2029 (Manufacture of other chemical products).

1. Introduction

Unplanned indirect (*de facto*) wastewater potable reuse occurs when wastewater is discharged into surface waters upstream of drinking water treatment plant intake [1]. Wastewater is a source of a new pool of disinfection by-products (DBPs) precursors that are different from those related to natural organic matter, therefore, evaluating the formation of DBPs in potable reuse is crucial [2]. In particular, precursors of *N*-nitrosamines (NAs) are relevant in potable reuse scenarios. Among NAs, *N*-nitrosodimethylamine (NDMA) is the most studied one, as its formation is related to disinfection of wastewater with chloramines (or chlorine in the presence of ammonia) and ozone, which is a common disinfectant employed in water reuse [3]. NDMA is a hazardous compound whose guideline value is in the nanogram per liter range (ng/L), in contrast to the majority of regulated DBPs such as trihalomethanes (THMs) or haloacetic acids (HAAs), which are regulated in the range of micrograms per liter ($\mu\text{g/L}$). NDMA is included in the Contaminant Candidate List 4 of the USEPA [4,5]. California's Department of Public Health has established a 10 ng/L [6] notification level for NDMA in drinking water, while the California's Office of Environmental Health Hazard Assessment has defined 3 ng/L as a public health goal [7]. Massachusetts has a guideline value of 10 ng/L [8], Health Canada [9] has set a national guideline value, whereas the Ontario Ministry of the Environment [10] has a maximum allowable concentration for NDMA of 9 ng/L in drinking water. The World Health Organization guideline was established at 100 ng/L for NDMA in drinking water [11], which was adopted as a target value by Japan and Australia. *N*-nitrosodiethylamine (NDEA) is another relevant nitrosamine regulated for example in Australia's recycled water at 10 ng/L [12].

While NDMA precursors in domestic wastewater have been relatively well studied [3,13–15], much less is known on the concentrations of NAs and their precursors in industrial effluents, especially other than NDMA. In fact, Mitch and co-authors [16] reviewed the presence of NDMA and its precursors in drinking water and listed effluents from some industries such as production of pharmaceuticals, pesticides, rubber, and printed circuit boards as pollution source. Beyond that, NA contamination from industrial effluents has been historically associated with leather tanning, metal casting, metalworking using cutting fluids, electronic industry, and food processing [17–19]. Deeb and co-authors [20] identified dithiocarbamates from the metal plating industry and fumigants containing dimethyldithiocarbamates applied to sewer trunklines in residential or industrial areas to control tree root growth as the main precursors of NDMA. Furthermore, Chuang and co-authors [21] followed up on this finding and compared the concentrations of NDMA precursors in different effluents. They found out that domestic/commercial sewage and discharges from metal finishing and electronics-related facilities accounted for ~25% of the median NDMA concentration measured in primary effluent, even though the metal finishing/electronics facilities accounted for only 0.25% of the sewage flow. In addition, specific NDMA precursors from industrial effluents were identified by two major studies. The first study performed in the Yodo River basin in Japan demonstrated that a discharge from a photographic paper manufacturer employing 1,1,5,5-tetramethylcarbohydrazide, a chemical used to prevent photographic paper degradation, served as the predominant source of ozone-reactive NDMA precursors [22]. In another study, certain compounds added to plastics to prevent yellowing resulting from degradation in sunlight, acted as ozone-reactive NDMA precursors at this treatment plant [23]. In Southeast China, Chen et al. [24] investigated the compositions of NAs in eleven different wastewaters in the Pearl River Delta. High concentrations of NDMA (up to 4000 ng/L) were found in the wastewaters

mostly coming from the textile printing and dyeing, and the electroplating industries. Qiu and co-authors [25] recently investigated the concentrations of NAs and their precursors in urban water systems in China. Within this work they also investigated specific industrial effluents. They found high concentration of NDMA in textile printing and dyeing wastewater (772 ng/L) followed by electroplating wastewater (517 ng/L), chemical industry wastewater (209 ng/L), livestock breeding wastewater (177 ng/L), domestic wastewater treatment plants effluent (138 ng/L), mechanical industry wastewater (78 ng/L) and fishery wastewater (25 ng/L). Additionally, the highest concentrations of NDMA precursors also found in textile printing and dyeing wastewater (2184 ng/L), domestic wastewater treatment plant effluent (621 ng/L), mechanical industry wastewater (547 ng/L), chemical industry wastewater (385 ng/L), fishery wastewater (288 ng/L), electroplating wastewater (256 ng/L) and livestock breeding wastewater (103 ng/L). They also identified NDEA and their precursors in electroplating wastewater and textile printing and dyeing wastewater.

Recently, the presence of NDMA and its precursors in an indirect potable reuse pilot in the Llobregat river (main source of drinking water for Barcelona and metropolitan area) were investigated by our group [26]. In the mentioned study, river samples before discharge from tertiary treated wastewater were also collected and analyzed. Although the presence of NDMA was negligible in the river, the concentrations of NDMA precursors ranged between 90 and 270 ng/L assuming that their presence was related to the previous discharge of wastewater into the river (*de facto* reuse). To better understand the contribution of industrial effluents to the concentrations of NA precursors in the Llobregat river we monitored 38 industrial effluents corresponding to the 11 most polluting industrial types in Catalonia, according with the annual loads of hazardous priority pollutants discharged to the river networks. The UN International Standard Industrial Classification of All Economic Activities (ISIC) was used as classification system. The main purpose of ISIC is to provide a set of activity categories that can be utilized for the collection and reporting of statistics according to such activities.

Characterizing the concentrations of the NAs and their precursors in effluents from different types of industrial discharges is an important step toward source control efforts. To this end, the present study allowed the identification of industrial wastewater discharges with a very high concentrations of NA precursors that need to be considered when faced with a planned or unplanned application of potable water reuse, specifically in the studied region.

2. Material and methods

2.1. Study design

Water samples were collected as grab samples in selected industrial facilities from Catalunya, Spain during October 2021. Since the sampling of these industrial facilities was conducted under non-disclosure agreements, the locations and names have been anonymized. In total, 38 different industrial wastewater effluents were collected during daylight hours, accounting for 3–5 samples of each of the 11 ISIC classes. To select the ISIC classes to be considered, we ranked them according to the discharged loads of priority hazardous compounds as well as Biological Oxygen Demand (BOD). Specifically, we estimated the annual load by each ISIC class by summing the individual loads of all industrial facilities of each ISIC class, those estimated from their wastewater flow and the reported concentrations for BOD and priority hazardous substances. More information on water composition is found in [Table S11 of the supporting information](#) and more information on the selection criteria can be found elsewhere [27]. Further, the analytical results were

statistically analyzed to identify general patterns (differences between ISIC classes) and to indicate industries that produce high concentrations of NA and NA precursors.

Table 1 shows the number of samples collected in industries belonging to different ISIC classes. This assignment is built on a production-oriented or supply-based conceptual framework that groups producing units into detailed industries based on similarities in the economic activity, considering the inputs, the process and technology of production, the characteristics of the outputs and the use to which outputs are applied. Because of these principles of classification, it is commonly assumed that the composition of the generated wastewater would be similar within each ISIC class, and thus reporting on industrial wastewater flows commonly uses this classification.

2.2. Sample collection

Water samples were collected as grab samples at the effluents of the 38 selected industrial facilities during October 2021. 3 L of each sample were collected for the analysis of NAs, their precursors, and other basic parameters such as pH, conductivity, biological oxygen demand (BOD), chemical oxygen demand (COD), dissolved organic carbon (DOC), total nitrogen (TN), and ionic content (see Supporting Information (SI) Table S11). Samples for the formation potential test to quantify NA precursor and other parameters were processed immediately, while samples for NAs concentrations were frozen at -20°C until laboratory processing.

2.3. Chemicals and reagents

EPA 521 Nitrosamine Mix containing: *N*-nitrosodimethylamine (NDMA, CAS 62–75–9), *N*-nitrosomethylethylamine (NMEA, CAS 10595–95–6), *N*-nitrosodiethylamine (NDEA, CAS 55–18–5), *N*-nitrosopyrrolidine (NPYR, CAS 930–55–2), *N*-nitrosodipropylamine (NDPA, CAS 621–64–7), *N*-nitrosopiperidine (NPIP, CAS 100–75–4), and *N*-nitrosodibutylamine (NDBA, CAS 924–16–3), each at 2000 $\mu\text{g}/\text{mL}$ in dichloromethane, was obtained from Supelco (Merck, Darmstadt, Germany). Isotopically labeled compound, used as internal standard (IS) was NDMA- d_6 (Cambridge Isotope Laboratories, Inc, Tewksbury, MA), NDEA- d_{10} (Cambridge Isotope Laboratories, Inc, Tewksbury, MA) and NDPA- d_{14} (*N*-nitrosodipropylamine, Restek, Bellefonte, PA). The NDMA formation potential test was performed by using NH_4Cl (>99.5%, Merck, Darmstadt, Germany), NaOH (ACS, ISO, Scharlau, Barcelona, Spain), and NaClO (reagent grade, available chlorine $\geq 4\%$, Merck, Darmstadt, Germany). For the same test Na_2SO_3 (>98%, Merck, Darmstadt, Germany) was used to quench residual disinfectant. pH buffer solutions were prepared with KH_2PO_4 (>99%, Merck, Darmstadt,

Germany) and Na_2HPO_4 (>99%, Merck, Darmstadt, Germany). Commercial DPD test kits (LCK310, Hach Lange, Loveland, CO) were used for the analysis of free and total chlorine using a Hach DR2800 spectrophotometer. Ultrapure water and methanol (Optima® LC/MS grade) were purchased from Fisher Chemical (Madrid, Spain). Formic acid 98–100% (ACS / Reag. Ph Eur grade) was acquired from Merck (Darmstadt, Germany). Sulfuric acid 95–97% (Reag. Ph Eur grade) was obtained from Scharlau (Barcelona, Spain). Nitrogen (99.995% purity) for extract drying was purchased from Linde Gas España. Glass fiber filters (GF/F, 0.7 μm) were obtained from Whatman-Merck Darmstadt, Germany). Activated charcoal cartridges (6 mL, 2 g) used for NDMA extraction were purchased from Resteck (Bellefonte, PA).

2.4. NDMA formation potential and chemical analysis

NA precursors were quantified by means of NDMA formation potential (FP) tests followed the protocol published by Mitch et al [28]. In summary, 10 mM buffered filtered samples were disinfected with a monochloramine concentration of 140 mg/L and kept in the dark and at ambient conditions ($T = 21 \pm 1^{\circ}\text{C}$) for seven days in an amber glass reactor. After this contact time chloramines were quenched with 2.5 g/L of sodium sulfite prior to NDMA extraction for the analysis by gas chromatography/tandem mass spectrometry (GC-MS/MS). The method used for NDMA extraction was based on EPA Method 521 [29]. The solid phase extracted (SPE) samples were injected in a TSQ™ 9000 triple quadrupole GC-MS/MS system from Thermo Scientific using advanced electron ionization (AEI) to investigate the presence of NAs in the industrial effluent samples but also after the formation potential tests. A volume of 1 μL of the nitrosamine mixture extract was injected in splitless for 1 min. The injector temperature was set at 240°C . The GC separation of extracted components was carried out on a Thermo Scientific TraceGOLD TG-1701MS (30 m \times 0.25 mm (id) \times 0.5 μm) with the following GC temperature program: initial temperature of 35°C held for 1 min, increased at a rate of $25^{\circ}\text{C}/\text{min}$ to 130°C , followed by increase at a rate of $20^{\circ}\text{C}/\text{min}$ to 250°C , then held for 2 min (total run 12.8 min). The GC was interfaced with the TSQ™ 9000 instrument via a transfer line heated at 290°C . The source temperature was set at 280°C . MS analyses were performed using electron ionization (EI) at 70 eV in timed-SRM mode [30]. Each sample was analyzed in duplicates. The limit of quantification (LOQ) for NDMA and all additional NAs was 0.5 ng/L, except for NDEA, whose limit was 1.9 ng/L. Recovery of NDMA and NDEA was assessed and corrected by spiking known concentrations of NDMA- d_6 and NDEA- d_6 to each sample (25 ng/L). The performance of the method for the remaining NAs was assessed by evaluating the compound recoveries determined from three separate extractions of a water sample, fortified with a mix of 50 ng/L of each analyzed nitrosamine. The results showed that the average recovery values ranged between 80.7% and 111.1%. Additionally, NDPA- d_{14} was used as IS for injection error correction. Further details of the method can be found elsewhere [31]. Data were acquired using timed-SRM and final data processing was done using Trace Finder 4.1 software (Thermo Fisher Scientific Inc., Waltham, U.S.).

For sample characterization different parameters were measured using the following equipment: pH with a pH meter GLP21 + (Crison, Düsseldorf, Germany), conductivity with a conductivity meter GLP31 + (Crison, Düsseldorf, Germany), BOD with pressure sensor Oxitop control OC 100 (WTW, Weilheim, Germany), and COD was measured with an automatic titrator 814 USB sample processor (Metrohm, Herisau, Switzerland). Bromide, nitrate, nitrite, phosphate, and ammonium and other ions were analyzed by ionic chromatography, on a Dionex ICS-5000 ion chromatography system (Dionex, Sunny Vale, U.S). Total dissolved organic carbon was analyzed by following catalytic oxidation, on a TOC-V CSH (230 V) analyzer (Shimadzu, Tokyo, Japan), which includes the TNM-1 modules for the total nitrogen determinations.

Table 1
ISIC classes and number of samples.

ISIC class description	ISIC class	Number of samples
Quarrying of stone, sand, and clay	B0810	1
Manufacture of wines	C1102	4
Finishing of textiles	C1313	4
Tanning and dressing of leather; dressing and dyeing of fur	C1511	2
Manufacture of pulp, paper and paperboard	C1701	5
Manufacture of basic chemicals	C2011	3
Manufacture of paints, varnishes and similar coatings, printing ink and mastics	C2022	3
Manufacture of other chemical products n.e.c.	C2029	2
Manufacture of pharmaceuticals, medicinal chemical and botanical products	C2100	4
Casting of iron and steel	C2431	4
Treatment and disposal of hazardous waste	E3822	2
Washing and (dry-) cleaning of textile and fur products	S9601	4

2.5. Statistical evaluation

We performed a series of analysis to identify which compounds were more spread among ISIC classes and which were unique to one or few classes. First, we assessed the homoscedasticity using Levene's test and normality using the Shapiro-Wilk test. The homoscedasticity and normality tests were done using the 'homoscedasticity' and 'normality' functions from the 'pingouin' library of Python (version 3.10.0). Because of the high number of cases in which homoscedasticity and normality were violated, we selected nonparametric (or distribution-free) inferential statistical methods. Specifically, we used the Kruskal-Wallis test by ranks for each compound to assess the differences between the ISIC classes, followed by a posteriori Dunn's test with two stage false discovery rate correction of the p-values for assessing differences between specific sample pairs. An additional advantage of using these nonparametric tests is that these allow comparing samples of different sizes, which is our case. The Kruskal-Wallis analyses were done using the 'Kruskal' package, from the 'stats' section of the 'scipy' library of Python, whereas the Dunn's test was done using the 'posthoc_dunn' package, from the 'scikit_posthocs' library of Python (version 3.10.0). Only categories with 3 or more samples could be included in this statistical analysis.

3. Results

3.1. Overview of N-nitrosamines and their precursors in industrial effluents

Fig. 1 shows the average NDMA concentration (ng/L) per ISIC class of the selected industries, whereas the concentrations of other NAs are displayed in Table 2. The number of industrial effluents used to calculate the average values is given in Table 1. Likewise, Fig. 2 shows the average concentrations of NDMA precursors, while the concentrations of other NA precursors is detailed in Table 2. NA precursor concentrations were obtained by subtracting the concentrations of NAs found in the effluent from the NAs measured after formation potential tests. Individual data for Figs. 1 and 2 is presented in Table S12. Finally, the entire data set showing the individual concentrations of NAs and their precursors and relative standard deviation for each sample is summarized in Table S13.

NDMA was the NA measured at the highest concentration in all industries with a maximum concentration measured around 11 µg/L.

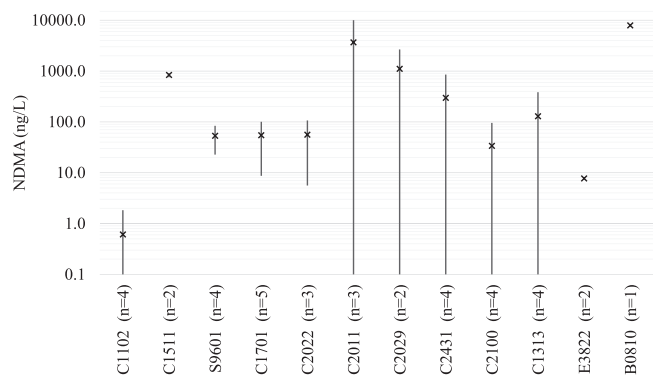


Fig. 1. Average concentration of NDMA per industry class (x) and range (line). Manufacture of wines (C1102), Tanning and dressing of leather; dressing and dyeing of fur (C1511), Washing and (dry-) cleaning of textile and fur products (S9601), Manufacture of pulp, paper and paperboard (C1701), Manufacture of paints, varnishes and similar coatings, printing ink and mastic (C2022), Manufacture of basic chemicals (C2011), Manufacture of other chemical products n.e.c. (C2029), Casting of iron and steel (C2431), Manufacture of pharmaceuticals, medicinal chemical and botanical products (C2100), Finishing of textiles (C1313), Treatment and disposal of hazardous waste (E3822), Quarrying of stone, sand, and clay (B0810).

Likewise, maximum concentrations of NDMA precursors were around 14 µg/L. Both values were substantially higher than previous values reported by Qiu and co-authors [25] when investigating the industrial discharge concentrations of NAs and their precursors in a Chinese river catchment. When evaluating the entire data set, 23% occurrence corresponds to NDMA and 72% to NDMA precursors (see Fig. S11). Hence, industries already discharge appreciable amounts of NDMA and not just NDMA precursors, confirming what has been published in literature before [17-19]. NDMA accounts for 91% of the total NA concentration, while 96% of the precursors were also from NDMA (see Fig. S12). Concentration as function of percentile when rating all the industries by NDMA concentration, showed that NDEA is the most important NA after NDMA, and NPYR precursors are the most abundant after NDMA precursors (Fig. 3). Fig. 3 shows for example that 6.6% of the industrial effluents contained all the analyzed NAs and 9.3% all the NA precursors. Focusing only on the individual samples, Fig. 3a shows that 75% of all samples contained NDMA and this was the only NA present in 35% of the total analyzed samples. NMEA was the NA less frequently detected as was only measured in 6.5% of all samples, closely followed by NPYR that was detected in 9.2% of the total. Considering NA precursors, 100% of the samples contained those related to NDMA formation (Fig. 3b), while precursors of NMEA were only measured at 9.2% of the samples, confirming this NAs as the less relevant in the selected industries considered for this study.

3.2. N-nitrosamines and their precursors per ISIC class

As shown in Fig. 1, the highest concentration of NDMA (11 ± 0.6 µg/L) was found in an effluent of ISIC class C2011 corresponding to the manufacture of basic chemicals. Similar concentrations (13.6 ± 0.3 µg/L) of NDMA precursors (i.e., NDMA FP - NDMAo), was found in that same industry (Fig. 2), highlighting this category as the one with higher NA pollution potential among the selected ISIC classes. However, within the same category, the other two industries had negligible concentrations of NDMA and their precursors were below 70 ng/L (M_0157 and M_0178 industries, see Table SI 3). The industrial effluent with the highest concentrations of NDMA and NDMA precursors also contained 62 ± 1.2 ng/L of NDEA and 34 ± 0.5 ng/L of NDEA precursors (NDEA FP - NDEAo), the latter also found at 31 ± 0.7 ng/L in another industry of the same ISIC category. Concentrations of 2.3 ± 0.1 ng/L for NPYR and 18.1 ± 1 ng/L for NPYR precursors were found in the same industry type (Table 2). Recently, Acuña et al [27] published the concentrations of priority and preferent pollutants in the effluent obtained from the industry within the same ISIC class (C2011). Up to 46.2 µg/L of chloroform was found in the same sample. However, no conclusions were reached from the analysis of correlations with other pollutants, which emphasizes the uniqueness of NA contamination that must be investigated independently.

The second highest concentration of NDMA (7.9 ± 0.4 µg/L) was found in a quarrying of stone, sand, and clay industry effluent (ISIC B0810). The same sample also contained 1.4 ± 0.1 µg/L of NDEA, 18.2 ± 0.1 ng/L of NPIP, 5.3 ± 0.2 ng/L of NDBA and 6.1 ± 0.2 ng/L of NMEA. Regarding the measured NA precursors, the effluent contained 2.2 ± 0.1 µg/L of NDMA precursors. Formation potential tests also reveal a concentration of 167.3 ± 0.3 ng/L of NMEA precursors, 65 ± 3 ng/L of NPYR precursors, and 60 ± 2 ng/L of each NPIP and NDBA precursors as well. Interestingly, despite the high concentration of NDEA found, no additional NDEA precursors were quantified after the formation potential test, which means that on this occasion, all NDEA found was already present in the industry effluent. Large amounts of waste, fuel and oil may be the reason for this pollution, as NDEA is commonly used as gasoline and lubricant additive [32].

Concentration of 2.2 ± 0.1 µg/L of NDMA were found in one manufacture of other chemical products industry (ISIC class C2029), while the other industry in this same category only contained 5.6 ± 0.9 ng/L of NDMA. The effluent with the highest concentration in this

Table 2

Concentration of N-nitrosamines other than NDMA and their precursors (ng/L) in ISIC groups. The standard deviation is shown in parentheses. Manufacture of wines (C1102), Tanning and dressing of leather; dressing and dyeing of fur (C1511), Washing and (dry-) cleaning of textile and fur products (S9601), Manufacture of pulp, paper and paperboard (C1701), Manufacture of paints, varnishes and similar coatings, printing ink and mastics (C2022), Manufacture of basic chemicals(C2011), Manufacture of other chemical products n.e.c. (C2029), Casting of iron and steel (C2431), Manufacture of pharmaceuticals, medicinal chemical and botanical products (C2100), Finishing of textiles (C1313), Treatment and disposal of hazardous waste (E3822), Quarrying of stone, sand, and clay (B0810).

ISIC class	NMEA _o	NDEA _o	NPYR _o	NPIP _o	NDBA _o	NMEAFP-NDEA _o	NDEAFP-NDEA _o	NPYRFP-NPYR _o	NPIPFP-NPIP _o	NDBA-NDBA _o
C1102	<LOD	<LOD	<LOD	0.9	4.6	<LOD	7.2	28.6 (17.0)	4.9	<LOD
C1511	<LOD	<LOD	42.9	6.1	<LOD	<LOD	<LOD	44.4 (13.5)	4.9	3.0
S9601	<LOD	24.1(28.6)	<LOD	7.1 (6.8)	6.8 (6.3)	<LOD	28.8 (13.6)	115.9 (78.6)	10.6 (7.0)	6.7 (3.5)
C1701	<LOD	14.8(11.4)	<LOD	<LOD	1.0	<LOD	7.4 (84.6)	24.0 (22.3)	5.4	2.6
C2022	<LOD	13.6	2.8	<LOD	<LOD	<LOD	23.9	45.1 (50.8)	9.9 (5.0)	8.0
C2011	<LOD	61.6	2.3	<LOD	<LOD	<LOD	32.1 (2.3)	23.6 (7.7)	8.2	<LOD
C2029	<LOD	732.1	<LOD	<LOD	<LOD	<LOD	230.2	33.8	<LOD	21.1
C2431	5.2(0.7)	<LOD	29.0	6.2 (3.6)	<LOD	110.1 (129.4)	15.2 (11.8)	146.4 (102.2)	42.4 (39.6)	<LOD
C2100	<LOD	22.4	<LOD	<LOD	28.3	22.3	118.6 (148)	18.4 (11.1)	8.9	<LOD
C1313	<LOD	19.8 (28.1)	<LOD	<LOD	<LOD	<LOD	114.4 (149)	29.8 (32.2)	<LOD	<LOD
E3822	<LOD	10.1	<LOD	<LOD	3.5	<LOD	<LOD	5.1	<LOD	2.5
B0810	6.0	1368.3	<LOD	18.2	5.3	167.3	<LOD	65.0	59.8	59.7

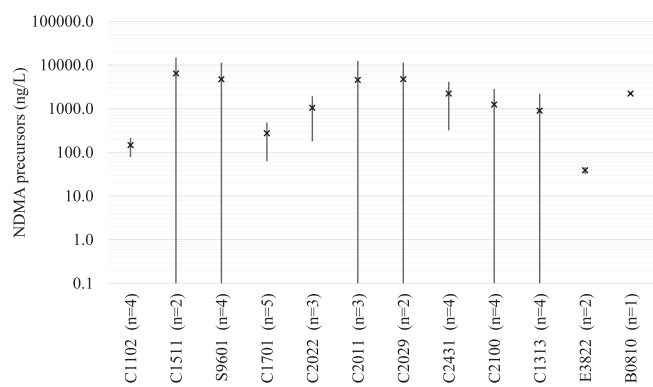


Fig. 2. Average NDMA precursor concentration per industry class (x) and range (line). Manufacture of wines(C1102), Tanning and dressing of leather; dressing and dyeing of fur (C1511), Washing and (dry-) cleaning of textile and fur products (S9601), Manufacture of pulp, paper and paperboard (C1701), Manufacture of paints, varnishes and similar coatings, printing ink and mastics (C2022), Manufacture of basic chemicals(C2011), Manufacture of other chemical products n.e.c. (C2029), Casting of iron and steel (C2431), Manufacture of pharmaceuticals, medicinal chemical and botanical products (C2100), Finishing of textiles (C1313), Treatment and disposal of hazardous waste (E3822), Quarrying of stone, sand, and clay (B0810).

category corresponded to a treatment and management of industrial waste, as well as in the recovery of solvents and water treatment industry. The concentration of NDMA precursors in this industry was $9.5 \pm 0.4 \mu\text{g/L}$. NDEA concentration in this sample was $732.1 \pm 3.6 \text{ ng/L}$ and the concentration of NDEA precursors was $230.2 \pm 2.3 \text{ ng/L}$. Finally, $21.1 \pm 0.4 \text{ ng/L}$ of NDBA precursors were also measured in this effluent.

A concentration of NDMA of up to $1.1 \pm 0.1 \mu\text{g/L}$ was found in an industry corresponding to the casting of iron and steel (ISIC class C2431), where four different industries were investigated. For the other 3, the maximum concentration of NDMA measured was $30.5 \pm 1.4 \text{ ng/L}$. Low concentrations of NMEA ($5.7 \pm 0.3 \text{ ng/L}$), NPIP ($5.8 \pm 0.5 \text{ ng/L}$), and $29.0 \pm 1.6 \text{ ng/L}$ of NPYR were also found in the industry within the same ISIC class. Regarding precursors, $2200 \text{ ng/L} \pm 2000 \text{ ng/L}$, 110.1 ± 129.4 , $15.2 \pm 11.8 \text{ ng/L}$, 146.4 ± 102.2 , and 42.4 ± 39.6 for NDME, NMEA, NDEA, NPYR and NPIP were measured, respectively where the error corresponds to the standard deviation (SD) within industries of the same category. Results showed that the composition in this category was more homogeneous. This observation was supported by data evaluation by principal component analysis (PCA) that showed that this group clustered, but mostly because they give a more varied profile of nitrosamines and not because of their abundance of NDMA (see Fig. S14).

Another industry with high concentrations of NDMA and NDMA precursors was the tanning and the dressing of leather and dressing and dyeing of fur (ISIC class C1511) with $836 \pm 81 \text{ ng/L}$, and $6.4 \pm 8.4 \mu\text{g/L}$ of NDMA and NDMA precursors, respectively, where the error

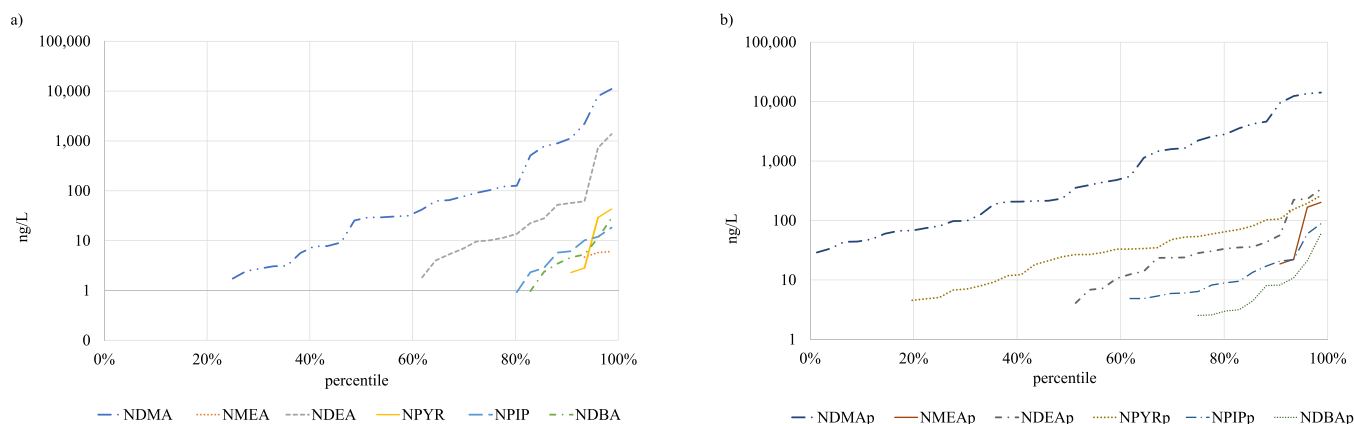


Fig. 3. Concentration as a function of the percentile of presence in an industrial sample for A) N-nitrosamines and B) N-nitrosamine precursors (p). NDMA= N-nitrosodimethylamine, NMEA= N-nitrosomethylethylamine, NDEA= N-nitrosodiethylamine, NPYR= N-nitrosopyridine, NPIP= N-Nitrosopiperidine, NDBA= N-nitrosodibutylamine.

corresponds to the SD within all the industries of the same category, showing that although the concentration of formed NDMA was relatively homogeneous, the concentrations of NDMA precursors varied considerably (i.e. maximum concentration $12.4 \pm 0.2 \mu\text{g/L}$ and minimum concentration $480 \pm 36 \text{ ng/L}$). In fact, one sample from the class ISIC C1511 was the industry with highest concentration of NDMA precursors among all measured samples (M_0172, Table S13). The leather industry has previously been reported to negatively impact environment due to the discharge of toxic chemicals [33]. NPYR ($42.9 \pm 4.1 \text{ ng/L}$) and NPIP ($6.1 \pm 0.5 \text{ ng/L}$) were also measured in industries from ISIC class C1511. Precursors of NPYR ($44.4 \pm 13.4 \text{ ng/L}$), PIP ($4.9 \pm 1.0 \text{ ng/L}$), and NDBA ($3.0 \pm 0.3 \text{ ng/L}$) were also measured in the same industry class.

In the finishing of textiles category (ISIC class C1313), only one industry showed high concentration of NDMA ($512 \pm 14 \text{ ng/L}$) in its effluent, while the remaining 3 ones had negligible concentration of NDMA. However, the concentrations of NDMA precursors was high for the 4 industries investigated with an average value of $0.9 \pm 1.3 \mu\text{g/L}$, ranging from $207 \pm 5 \text{ ng/L}$ to $2.8 \pm 0.1 \mu\text{g/L}$. NDEA was the only NA relevant in this ISIC class with a maximum concentration measured of $52.2 \pm 0.8 \text{ ng/L}$. Cheng et al. [24] found mean NDMA concentrations of $4.3 \pm 0.09 \mu\text{g/L}$ in similar industries, which is in the same range with our findings. In the present study, the precursors of NDEA and NPYR were also measured, the former found at a higher concentration ($114.4 \pm 149 \text{ ng/L}$). Decolorization and disinfection with sodium hypochlorite could be the main reason for the formation of NDMA. This could be explained by the contact of chlorine as oxidants with NA precursors, which include naphthols, antiyellowing agents, azo dyes, and aromatic amines, among others. As it was mentioned before, Kosaka et al. [23] already has been identified antiyellow agents as potent NDMA precursors.

Concerning 5 effluents from pulp, paper, and paperboard industry manufacture (ISIC class C1701), contained an average of $54.5 \pm 45.8 \text{ ng/L}$ of NDMA and $274.3 \pm 212.1 \text{ ng/L}$ of NDMA precursors. The concentration of NDMA in this industry type was in the same range as it was reported by Chen et al. [24] (i.e., $97 \pm 4.8 \text{ ng/L}$) for the effluents coming from facility producing papers and printing materials [22]. NDEA was also measured in the present study at 3 industrial effluents of this category at an average value of $14.8 \pm 11.4 \text{ ng/L}$. NDEA and NPYR were also relevant industry effluents at concentrations of 7.4 ± 84.6 and $24.0 \pm 22.3 \text{ ng/L}$, respectively.

Washing and dry-cleaning of textile and fur products industry effluents (ISIC class S9601) contained low concentrations of NDMA ($53.1 \pm 30.4 \text{ ng/L}$) and other NAs, such as NDEA ($24.1 \pm 28.6 \text{ ng/L}$), NPIP ($7.1 \pm 6.8 \text{ ng/L}$), and NDBA ($6.8 \pm 6.3 \text{ ng/L}$), while the concentration of precursors was much higher. For instance, the concentrations of NDMA precursors was $4.7 \pm 6.6 \mu\text{g/L}$ with a maximum value of $14.2 \pm 0.3 \mu\text{g/L}$ in a specific laundry. The precursors of NPYR, NDEA, NPIP, and NDBA were 115.9 ± 78.6 , 28.8 ± 13.6 , 10.6 ± 7.0 , and 6.7 ± 3.5 , respectively in this ISIC class. These precursors were present in the 5 investigated industries of this category showing homogeneity in the presence of NA precursors in these effluents. In fact, Zeng and Mitch [15] previously identified laundry as a potential source of NDMA contamination. Moreover, PCA clustered this industry category as well (Fig. S14).

Manufacture of paints, varnishes and similar coatings, printing ink and mastics industries (ISIC class C2022) contained an average NDMA concentration of $56.0 \pm 50.5 \text{ ng/L}$, with a maximum value measured of $103.1 \pm 0.5 \text{ ng/L}$ in one specific industry. NDEA was found in one effluent of this category at $13.6 \pm 0.2 \text{ ng/L}$ as well as NPYR at $2.8 \pm 0.1 \text{ ng/L}$. The average concentration of NDMA precursors was $1.1 \pm 0.9 \mu\text{g/L}$, with a maximum concentration of $1.6 \pm 0.1 \mu\text{g/L}$. Precursors of NDEA, NPYR, NPIP, and NDBA were also found at lower concentrations (Table 2).

NDMA was only measured at a relevant concentration in an effluent of manufacture of pharmaceuticals, medicinal chemicals, and botanical

products industry (ISIC class C2100). This effluent contained $126.1 \pm 2.1 \text{ ng/L}$ of NDMA, $22.4 \pm 0.1 \text{ ng/L}$ of NDEA, and $28.3 \pm 0.5 \text{ ng/L}$ of NDBA. These were not found in any of the other industries of ISIC class C2100. Chen et al. [24], found NDMA in wastewaters from the pharmaceutical industry at a maximum concentration of $28 \pm 0.1 \text{ ng/L}$. Regarding precursors of NDMA, an average value of $1.2 \pm 1.6 \mu\text{g/L}$ was measured in the present study, which is not surprising as it is well known that precursors of NAs often occur in wastewaters during manufacturing of pharmaceuticals [34]. Precursors of other NAs such as NMEA ($22.3 \pm 0.3 \text{ ng/L}$), NDEA ($118.6 \pm 148 \text{ ng/L}$), NPYR ($18.4 \pm 11.1 \text{ ng/L}$) and NPIP ($8.9 \pm 0.4 \text{ ng/L}$) were also measured, where the error corresponds to the SD within this category.

Finally, the manufacture of wines (ISIC class C1102) did not contain NAs at relevant concentrations and the precursors were also low in average (NDMA precursor = $146.5 \pm 68.4 \text{ ng/L}$, NPYR precursors = $28.6 \pm 17.0 \text{ ng/L}$). NAs concentrations of treatment and disposal of hazardous waste (ISIC class E3822) did not contain NAs at relevant concentrations either and precursors were also low with a maximum concentration of $44 \pm 6 \text{ ng/L}$ for NDMA precursors in one specific industry of this type.

We statistically analyzed the industry classes with more than 3 samples assessing their differences between ISIC classes for each NA. To this aim, the Kruskal-Wallis test by ranks was performed followed by an a posteriori Dunn's test for assessing differences between specific sample pairs. The results of the Kruskal-Wallis tests by ranks are summarized in Table 3 and show that NMEA, NPIP, NDEAp, NPIPp, and NDBAp had p-values lower than 0.05, thus indicating statistically significant differences between the ISIC classes for these specific compounds. Results comparing NAs and NA precursors between pairs of ISIC class using the Dunn test (as p-value) are shown in Table S14. Regarding NAs, NMEA and NPIP were only present in C2431 (i.e., Casting of iron and steel) but always at low concentration (maximum $5.7 \pm 0.2 \text{ ng/L}$ and $10.1 \pm 0.1 \text{ ng/L}$, respectively). Precursors of NDEA, NPIP and NDBA were more spread between ISIC classes but the concentration ranges could statistically group them.

3.3. Implication for water industry

The discharge of NAs is a direct environmental hazard due to their toxic properties [35], hence the removal of these contaminants prior to discharge is crucial. In our study, ISIC class C2011 corresponding to the manufacture of basic chemicals and ISIC class B0810 quarrying of stone, sand and clay are the two classes where NDMA concentration has been measured at the highest concentration. ISIC class B0810 and ISIC class C2029 corresponding to the manufacture of other chemical products also contained relevant concentrations of NDEA which is even more toxic than NDMA. NDEA has the highest cancer potency, with only 0.2 ng/L in drinking water associated with a 10^{-6} lifetime excess cancer risk (compared to that of NDMA at 0.7 ng/L) [5]. With regard to

Table 3

Results of the different comparisons, using the Kruskal Wallis test by ranks (as H statistic and P-value) to identify NAs and NA precursors with different concentrations between ISIC classes.

	H statistic	p-value
NDMA	8.73	0.273
NMEA	13.95	0.052
NDEA	8.52	0.288
NPYR	6.82	0.448
NPIP	15.13	0.034
NDBA	6.47	0.486
NDMAp	5.74	0.570
NMEAp	10.59	0.157
NDEAp	15.61	0.029
NPYRp	8.68	0.276
NPIPp	15.04	0.035
NDBAp	21.96	0.003

previous assessments of the hazard, IARC [36], has classified NDMA and NDEA as group 2A carcinogens (probably carcinogenic to humans) and NMEA, NDPA, NPIP, and NPYR as group 2B carcinogens (possibly carcinogenic to humans).

This study demonstrates that industrial effluents can be an important source of NA precursors, other than NDMA, which has been the main class studied so far. Therefore, if an industry from the relevant ISIC category is involved in a reuse scenario with the specific conditions studied (i.e., chloramine or chlorine in the presence of ammonia), NAs other than NDMA can be formed and should be under control. The specific ISIC industries potentially related to high concentrations of NDMA and other NAs precursors in their effluents are S9601 washing and dry cleaning of textile and fur products, C2011 manufacture of basic chemicals, and C1511 tanning and dressing of leather, dressing, and dyeing of fur (NDMA up to 11 µg/L in C2011 and NDMA precursors above 12 µg/L in all three classes). As reported in the introduction, both NDMA and NDMA precursors were investigated in a similar recent study in China [25], that covered machinery, textile, chemical, metallurgy and electronics facilities as the pillar industries in the studied region. This study reported values as high as 772 ng/L for NDMA and 2184 ng/L for NDMA precursors in textile printing and dyeing wastewater, which is much lower than the values in the present study.

4. Conclusions

This study provides a general overview of the occurrence of NAs and their precursors in wastewater from selected industries. The concentrations of NAs and their precursors varied greatly among the types of industries investigated, but NMEA and NPIP as well as precursors for NDEA, NPIP and NDBA could be ranked with different concentrations between ISIC classes (p -value < 0.05). Also, NDMA was the nitrosamine most present in the effluents (91%). Similarly, NDMA precursors were also the most abundant (96%) among the investigated species.

The highest concentration of NDMA (11 ± 0.6 µg/L) was found in an effluent from an industry of ISIC class C2011 corresponding to the manufacture of basic chemicals followed by an industry from ISIC class B0810 quarrying of stone, sand and clay (7.9 ± 0.4 µg/L). Subsequently, NDEA was the most abundant NA measured with a concentration as high as 1.4 ± 0.1 µg/L in the effluent of an ISIC class B0810. An industry from ISIC class C2029 corresponding to the manufacture of other chemical products also contained 732.1 ± 3.6 ng/L of NDEA.

Remarkable high concentrations of NDMA precursors were measured in industrial effluents from ISIC classes S9601 washing and (dry) cleaning of textile and fur products (14.2 ± 0.3 µg/L), manufacture of basic chemicals C2011 (13.6 ± 0.3 µg/L) and tanning and dressing of leather; dressing and dyeing of fur C1511 (12.4 ± 0.2 µg/L). Nevertheless, only two industry types clustered in the principal component analysis (C2431, casting of iron and steel, and S9601, washing and dry-cleaning of textile and fur products) showing the great variability within industries. In the other extreme, manufacturing of wines (ISIC class C1102) and treatment and disposal of hazardous waste (ISIC class E3822) did not contain NAs at relevant concentrations and the precursors were also low.

Environmental implications

NAs, and NDMA in particular, are hazardous disinfection byproducts. Domestic wastewater discharges are considered the main sources of NDMA precursors to the aquatic environment. However, not much is known on the likely contribution of NA precursors by industrial effluents, especially for NAs other than NDMA. The results here presented suggest that industrial effluents could contribute to the presence of NAs and their precursors in rivers and estimating their formation is useful when planning reuse applications.

CRedit authorship contribution statement

Maria José Farré: Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Funding acquisition, Project administration, Visualization. **Sara Insa:** Investigation, Validation, Writing – review & editing. **Wolfgang Gernjak:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Funding acquisition, Visualization. **Lluís Corominas:** Conceptualization, Methodology, Writing – review & editing, Funding acquisition. **Mira Celić:** Investigation, Writing – review & editing. **Vicenç Acuña:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Funding acquisition, Project administration, Visualization.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Maria Jose Farre reports financial support was provided by Catalan Water Agency. Maria Jose Farre reports financial support was provided by Spanish Scientific Research Council.

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2023.131159.

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