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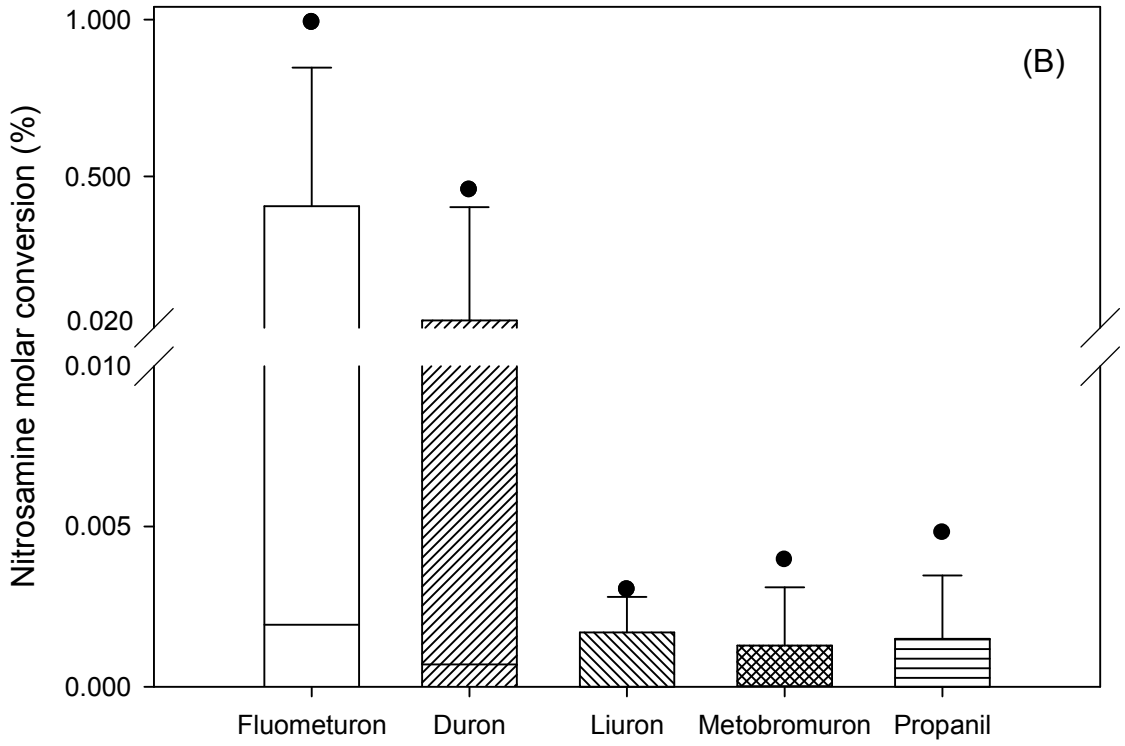

The true adverse environmental impacts of these phenylurea herbicides are important to emphasize given their high loadings as non-point source pollutants and typical environmental scenarios (e.g., a neutral pH or the co-occurrence of inorganic nitrogen) likely resulting in more efficient nitrosamine formation.

Environmental Impact Statement

Nitrosamines are disinfection byproducts of concern. This study investigates the formation of nitrosamines during chlor(am)ination of phenylurea herbicides, with the effects of disinfection approaches, additional inorganic nitrogen, and reaction pH being studied. Applying the results observed, the phenylurea herbicide concentrations ranging from several to tens μg/L will yield a N-nitrosodimethylamine (NDMA) concentration in drinking water above 0.7 ng/L, which is the level for a theoretical 10^{-6} lifetime cancer risk (assuming that molar conversion ratios of NDMA from phenylurea herbicides are between 0.01% to 0.2%). The formation of other nitrosamine (e.g., Ni-nitrosopyrrolidine) and their own toxicities will decrease the substituted phenylurea herbicide concentrations needed to cause a significant risk to downstream water users.

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ARTICLE

Effect of molecular characteristics on formation of nitrosamines during chlor(am)ination of phenylurea herbicides

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The objective of this study was to investigate the formation of different nitrosamines during chlorination or chloramination (chlor(am)ination) of five phenylurea herbicides (fluometuron, diuron, liuron, metobromuron, and propanil), with the effects of disinfection approaches, additional inorganic nitrogen, and reaction pH being studied. By analyzing six nitrosamines, N-nitrosodimethylamine (NDMA) and N-nitrosopyrrolidine (NPYR) formation was observed. The dimethylamine functional group was the key to determine whether a phenylurea herbicde is an important nitrosamine precursor, as the NDMA conversion ratios were much higher. Chlorination with ammonium or dichloramination enhanced the NDMA formation. The NPYR formation from the herbicides that did not form NDMA was detected and more vigorous during dichloramination or in the presence of either ammonium or nitrite. The NPYR formation was possibly relevant to the aniline molecular fragment from phenylurea herbicides. Both NDMA and NPYR formation were higher at pH 8. Overall, the maximum nitrosamine conversions decreased in the order: fluometuron>diuron>propanil>metobromuron>liuron (up to 0.99%, 0.46%, 0.005%, 0.004%, and 0.003% molar conversion rates, respectively) during chlorination or chloramination and dichloramine>free chlorine>monochloramine (up to 0.99%, 0.41%, and 0.005% molar conversion rates, respectively) for given herbicide, chlorine, and nitrogen doses. Applying the results of this study, the phenylurea herbicide concentrations ranging from several to tens μg/L will yield a NDMA concentration in drinking water above the level for a theoretical 10^{-6} lifetime cancer risk. The NPYR formation will increase the risks of these phenylurea herbicide concentrations to downstream water users. The true adverse environmental impacts of these phenylurea herbicides are important to emphasize given their high loadings as non-point source pollutants and typical environmental scenarios (e.g., a neutral pH or the co-occurrence of inorganic nitrogen) likely resulting in more efficient nitrosamine formation.

Introduction

Although carbonaceous disinfection byproducts (DBPs) like trihalomethanes and haloacetic acids have been regulated (e.g., the Stage 2 Disinfectants and Disinfection Rules developed by the U.S. Environmental Protection Agency (USEPA)) and substantially investigated since their discoveries in 70s, there has been a recent focus on the occurrence of nitrogenous DBPs including halonitriles, haloamides, haloacetamides, cyanogen halides, and halonitromethanes in drinking water treatment plants (DWTPs).[1-3] These compounds are known to be more genotoxic, cytotoxic, or carcinogenic than carbonaceous DBPs.[3] Of these emerging hazards, N-nitrosodimethylamine (NDMA) that belongs to the family of nitrosamines has caused regulatory attention since its discovery in a drinking water well in northern California in 1998.[4] It has been frequently detected in drinking water and recycled wastewater worldwide[2, 5] and is far more toxic than regulated DBPs.[4] For example, the concentration of NDMA in drinking water for a theoretical 10^{-6} lifetime cancer risk level is 0.7 ng/L, several orders of magnitude lower than that of dichlorobromomethane having the highest risk amongst the regulated trihalomethanes (THMs).[4, 6]

Considering their adverse health effects from trace levels, it is important to investigate potential precursors of these nitrosamines in the environment and associated formation mechanisms in DWTPs. Nitrosamines, mainly NDMA, are known to be formed through several pathways with the formation associated with chloramination likely to be more important. The reactions between chloramines and appropriate precursors such as natural organic matter (NOM)[7] or dimethylamine (DMA)[8, 9], a widely-tested NDMA precursor, have been substantially studied but limitedly model NDMA formation over a wide range of environmental conditions. Another pathway involves breakpoint chlorination or increase of chlorine dose to minimize free ammonia residual under the nitrification scenario.[10, 11] NDMA formation is enhanced at a specific free chlorine to ammonia molar ratio (e.g., near 1.7:1) when free chlorine is not detected during breakpoint chlorination. Nitrosation by reacting free chlorine with nitrite (NO_2^-)-containing water also results in NDMA formation.[8, 12] With a lower NDMA yield, this formation pathway is associated

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with production of a nitrosating agent (dinitrogen tetroxide) and is expected to occur in the cases such as NO_2^--polluted water treated by free chlorine. Nitrosamine formation during ozonation is another pathway of concern.[13, 14] The yields are contingent on the precursors considered, as high yields (e.g., >50%) have been observed for selected compounds such as N, N-dimethylsulfamide, a fungicide's decomposition product found in groundwater and surface water[15], and others with dimethylhydrazine-like functional groups.[16]

Researches have investigated a number of compounds for their potentials to form nitrosamines, mostly NDMA. A subset of dissolved organic nitrogen constituents present in water impacted by wastewater effluents is prone to NDMA formation.[2, 3, 17] These constituents include compounds with secondary, tertiary, or even quaternary amines[3, 18], such as ranitidine (e.g., >90% yield), a pharmaceutical used to inhibit stomach acid production[19, 20], and diuron, a herbicide widely used for pre- and post-emergent control of broad leaf and grassy weeds.[21, 22] Quaternary amine-based polymers and resins used for coagulation and anion exchange for drinking water and wastewater treatment such as poly(epichlorohydrin dimethylamine)-based polymers represent other groups of precursors with significant formation potentials.[13, 23]

Phenylurea herbicides are widely used and the family contains a number of substituted compounds[22], which also have the potentials to be present in water and pose adverse health risks to downstream users.[4] For example, fluometuron was detected in more than 40% of the lake water samples with a mean concentration above 0.5 μg/L in a study in the U.S.[24] Diuron has been detected in many environments including lakes[24], aquifers[25], stormwater[26], agricultural drainages[27], or seawater and sediments.[28] The concentrations of diuron in wastewater or groundwater impacted by municipal wastewater treatment effluents fell within the range of μg/L[29], while the concentrations up to the level of mg/L have been reported for propanil, another commonly-used phenylurea herbicide.[30] Ammonium (NH_4^+), NO_2^-, and nitrate (NO_3^-) from both natural and anthropogenic sources are common nitrogen forms in water. They represent the major nitrogen inputs for different drinking water sources (e.g., NH_4^+ and NO_3^- in surface water and groundwater, respectively) and may change the disinfection process employed.[12, 31] For example, monochloramine (NH_2Cl) and dichloramine ($NHCl_2$) coexist and are two products from the reactions between chlorine and ammonia, as the dominant species is determined by the reaction pH.[9] The objective of this study was to investigate possible formation of multiple nitrosamines during chlorination or chloramination (chlor(am)ination) of selected phenylurea herbicides (shown in Fig. 1). Fluometuron and diuron both contain a DMA functional group, while metobromuron and liuron have one methoxy-methyl-amine functional group. Diuron, propanil, and liuron have the similar ring structures. The effect of molecular characteristic was studied by analyzing nitrosamine formation from different phenylurea herbicides, with the influences of disinfection approaches, additional inorganic nitrogen, and reaction pH being also investigated.

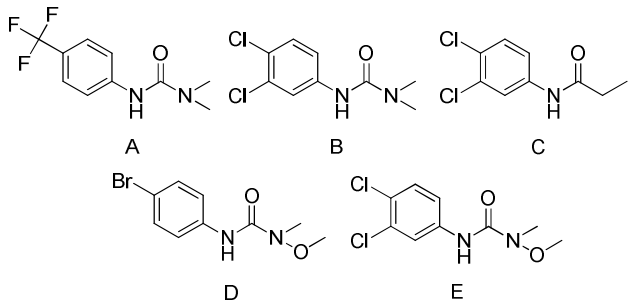

Figure 1. Five phenylurea herbicides of interest in this study (A: fluometuron, B: diuron, C: propanil, D: metobromuron E: liuron)

Materials and methods

Reagents

Phenylurea herbicide (Sigma-Aldrich, USA) and nitrosamine standards (Chem Service, USA) were used in the experiments without further purification. Deuterated NDMA (NDMA-d_6) and NDPA (NDPA-d_{14}) (Chem Service, USA) were added prior to extraction and instrumental analysis as the surrogate and internal standard to correct the recovery efficiencies, respectively. Ammonium chloride, sodium nitrite, and potassium nitrate (Fisher Scientific, USA) were used as the initial inorganic nitrogen in the experiments. Sodium hypochlorite (NaOCl, 4~6% purified grade) and ascorbic acid (Fisher Scientific, USA) were used to chlorinate water and to quench chlorination due to the presence of chlorine residual, respectively. Extraction cartridges consisting of 6-mL poly propylene tubes packed with 1.8 to 2.2 g of coconut charcoal (Sigma-Aldrich, USA) recommended in the USEPA Method 521 were used to extract nitrosamines from aqueous solutions.[32] All other reagents were obtained from Fisher Scientific in the U.S.

Chloramine preparation

As the chlorine to nitrogen molar ratio is below 1.5:1, NH_2Cl to $NHCl_2$ coexist without the presence of free chlorine. NH_2Cl solution was freshly prepared prior to experiments by slowly adding sodium hypochlorite to rapidly-stirred ammonium chlorine solution. The chlorine to nitrogen molar ratio was controlled at 1:1.2 to limit local excess of hypochlorite causing breakpoint chlorination. The pH was maintained at 8.5 to minimize the transformation of NH_2Cl to $NHCl_2$.[33] $NHCl_2$ solution was prepared by reducing the pH of NH_2Cl solution to below pH 3.7 and aging for at least 1 hour. Concentrations of all chlorine and chloramine solutions were standardized by using the colorimetric methods (Move 100 Colorimeter, Merck, USA).

Nitrosamine formation assays

Batch experiments were conducted to assess nitrosamine formation at room temperature in 2 L sealed amber jars under dark condition to avoid photolysis of nitrosamines. Herbicide

solutions were prepared by fully dissolving pre-determined amounts of herbicides in deionized water and selected reagents were added to simulate chlorination or chloramination. Solutions were buffered with sodium acetate (pH 3), sodium phosphate (pH 8), and carbonate (pH 10), as the pH was adjusted as needed using sodium hydroxide or sulfuric acid (0.2 N). Nitrosamine formation during chlorination or chloramination of phenylurea herbicides was studied by varying the herbicide added, disinfection approach, contact time, initial nitrogen source, and reaction pH. All experiments were at least duplicated to consider the reproducibility of results.

Nitrosamine analyses

Accurate and precise methods to analyse the nitrosamines in multiple water matrices have been reported[34, 35]. In this study, nitrosamine concentrations produced in chlorination or chloramination experiments were determined by the isotope dilution method, after extraction using a 12-port Visiprep Solid Phase Extraction (SPE) Vacuum Manifold (Supelco, Bellefonte, USA). The 6-ml glass SPE cartridges, packed with 2 g of coconut charcoal, were pre-cleaned with hexane followed by dichloromethane and pre-conditioned by passing methanol and deionized water. Prior to extraction, water samples were buffered to pH 8.2 by adding $NaHCO_3$ and NDMA-d_6 was spiked as a surrogate. After introducing samples to the SPE cartridges by vacuum, 15 ml of dichloromethane was used to elute nitrosamines adsorbed onto the bed and concentrated to 0.5 mL by nitrogen blow down. NDPA-d_{14} was added prior to the instrumental analysis as the internal standard. Six nitrosamines including NDMA, N-nitrosomethylethylamine (NMEA), N-nitrosodiethylamine (NDEA), N-nitrosodipropylamine (NDPA), N-nitrosodibutylamine (NDBA), and N-nitrosopyrrolidine (NPYR) were analyzed in this study. While the NDMA and NPYR concentrations were quantified using a gas chromatography coupled with mass spectrometry (GC/MS), other nitrosamines in dichloromethane were transferred into methanol by solvent exchange and analyzed by an ultra-high pressure liquid chromatography coupled with triple quadruple mass spectrometry (UPLC/MS-MS).

The GC (QP5050A, Shimadzu, Japan) was equipped with a 30 m x 0.25 mm I.D. DB-624 capillary column with 1.4 μm film thickness (Agilent, U.S.). Two μL of sample were injected in splitless mode. The column temperature was programmed as follows: initial oven temperature of 35 °C ramped at 10 °C/min to 120 °C, then 30 °C/min to 220 °C, and held 2 min. The MS was performed in electron ionization mode and the ion source temperature was 230°C. The target ions were 74 and 80 m/z for NDMA and NDMA-d_6, respectively. The other nitrosamine concentrations were analyzed by using an UPLC (Agilent 1290) coupled with electrospray positive ionization (ESI)-MS/MS (Agilent 6430) in multiple reaction mode (MRM). The chromatographic separation was performed using a Synergi Fusion-RP 80A C18 column (20 mm x 4.6 mm I.D., 4 mm particle size). Mobile phase A and B were 10 mM ammonium formate and methanol, respectively. The flow rate of the mobile phase was 0.4 mL/min, and the injection volume was 10 μL. Data acquisition was performed in the positive ion mode with a source temperature at 350°C. The minimum detection limits (MDLs) of nitrosamines in this study were determined by following the USEPA's Method Detection Limit procedure (40 CFR 136, Appendix B). The MDLs of NDMA and NDEA were 3 and 7 ng/L, respectively, while the MDLs for other nitrosamines were about 10 ng/L.

Formation kinetic

The reaction kinetic of a phenylurea herbicide to produce nitrosamines was investigated by employing fluometuron at a high concentration during monochloramination at pH 8±0.2. The concentration of fluometuron was 9 μM (~2 mg/L) and was higher than the concentration representative of water treatment operations to account for its anticipated low yields of nitrosamines. Although chlorine is more popular for disinfection in DWTPs, it has been investigated in our previous study[36] and NH_2Cl is present due to reactions between chlorine and nitrogen-containing compounds such as NH_4^+ in the water from natural and anthropogenic sources or those intentionally added for chloramination. NH_2Cl was added in the experiments at a concentration of 0.05 mM (3.6 mg/L), which was in excess compared to the concentration of herbicide and equal to those of hypochlorous acid or NH_2Cl used in the following experiments for later comparison. NDMA formation was measured for contact times up to 168 hours to allow complete reaction.

To investigate the reaction kinetics, two different models, the 1st-order and sigmoid functions, were used. The 1st-order function was used in the form of[37]:

$$Y = Y_{Max} \times (1 - \exp(-k_1 t))$$

where Y is the nitrosamine molar conversion at a given reaction time; Y_{Max} is the maximum molar conversion; k_1 is the pseudo 1st-order rate coefficient; and t is the reaction time. In this case, it was assumed that the model was a pseudo 1st-order model (d[C]/dt = -k [disinfectant] [precursor], where k [disinfectant] is a constant when the concentration of the disinfectant remains stable throughout the reaction). Another model, the sigmoid function, has been known to accurately model the formation of NDMA from pharmaceutical precursors and was employed in the form of:[38]

$$Y = \frac{Y_{Max}}{1 + \exp(k_2(Lag - t))}$$

where k_2 is the pseudo 1st-order rate coefficient of the sigmoid function model; Lag is the time required to achieve 50% of the maximum molar conversion.

Results and discussion

NDMA formation from fluometuron

The potentials of a phenylurea herbicide to produce nitrosamines was firstly investigated by employing fluometuron (9 μM) during monochloramination at pH 8±0.2

for contact times up to 168 hours, as shown in Fig. 2. Fluometuron was firstly tested as the base-case precursor, while the other four herbicides were used in the subsequent experiments to investigate the effects of different molecular characteristics of precursor compounds. While the other nitrosamines were not detected, the NDMA concentration increased rapidly at the beginning of reaction and continuously increased in 168 hours. The molar conversion was approximately 0.05%, which is relatively lower than the numbers reported for certain pharmaceuticals and personal care products (PPCPs) and close to those of other herbicides (Table 1).[38, 39] The NDMA concentration variation over time also suggested a rapid reaction between fluometuron and NH_2Cl in a short period of time (e.g., in 8 hours in Fig. 2). After 8 hours, the NDMA concentration continuously increased until 168 hours. Although the contact time needed to reach the maximum yield of NDMA formation was long (e.g., more than 7 days and longer than many precursors in Table 1), the continuous reactions of fluometuron or other phenylurea herbicides potentially remaining after treatment with chlorine residual in distribution systems are an important issue to consider, particularly as these herbicides are difficult to remove by conventional water treatment technologies.[21, 36]

Table 1. Maximum NDMA yields during monochloramination of herbicides (except that trifluralin forms NDPA) and pharmaceuticals and personal care products (PPCPs) in different studies

Precursor		NH_2Cl (mM)	pH	Time (hr)	Molar yield (%)
Herbicide	Isoproturon[1]	2.5	8.5	120	0.34 (0.2)
	Trifluralin[1,2]	2.5	8.5	120	0.18 (0.1)
	Diuron[1]	4.0	8.5	120	0.15 (0.1)
PPCP	Ranitidine[3]	0.6	7	8	82.7 (2.4)
	Ranitidine[1]	4.0	8.5	24	40.22 (1.43)
	Minocycline[1]	2.5	8.5	120	8.21 (0.72)
	Chlorophenamine[3]	0.6	7	24-48	1.8 (0.1)
	Doxepin[1]	2.5	8.5	120	2.32 (0.01)
	Doxylamine[3]	0.6	7	96	3.8 (0.1)
	Amitriptyline[1]	2.5	8.5	120	1.15 (0.04)
	Mifepristone[1]	2.5	8.5	120	0.39 (0.02)

1. Source from (Le Roux et al. 2011) [39]
2. Trifluralin forms NDPA during monochloramination[39].
3. Source from (Shen and Andrews 2011)[38]
4. Numbers in the bracket represent the standard deviation on 3 replicates.

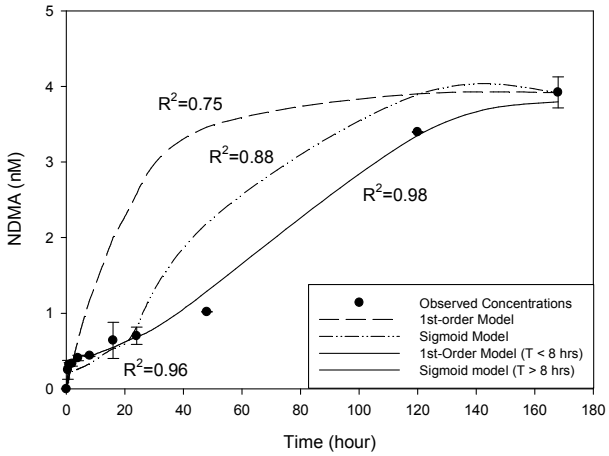

Figure 2. Observed and simulated kinetics of NDMA formation from fluometuron upon monochloramine disinfection (Error bars represent the 95% confidence level). The initial concentrations of fluometuron and NH_2Cl were 9 μM and 0.1 mM, respectively. The pH was at pH 8±0.2.

The reaction kinetic of NDMA formation during chloramination of fluometuron was investigated. In Fig.2, the NDMA concentration variation over time was limitedly described by the widely-used pseudo 1st-order models[12, 36] (R^2=0.75). Using the sigmoid function, which has been found to accurately model the NDMA formation during monochloramination of different PPCPs[9], drew a better fit regression through the data (R^2=0.88). However, the best fit regression was observed when the 1st-order and sigmoid models were applied for the concentration variations within and after 8 hours (R^2=0.96 and 0.98), respectively. The analysis of variance (ANOVA) also showed that the NDMA formation was in better agreement with this approach (both $p<0.05$) compared to those of the1st-order or sigmoid function models ($p>0.05$). The estimated k_1 (before 8 hours) and k_2 constant values (after 8 hours) were 0.913/hour and 0.015/hour, respectively. This finding suggested that NDMA formation occurred rapidly when fluometuron reacted with NH_2Cl in a short contact time (the 1st-order function in 8 hours). The disproportionation products of fluometuron, such as those amine and aniline fragments[12, 21], maintained the reactions with NH_2Cl to form NDMA for longer contact times (the sigmoid function after 8 hours).

Effects of ammonium and chloramines

Fig. 3A exhibits the effects of adding NH_4^+ during chlorination or using chloramines on NDMA formation from fluometuron or other phenylurea herbicides. The influence of molecular characteristic was also studied by changing the substituted herbicides used in the experiments. In the results, NDMA formation was not observed during chlorination of fluometuron but found in the presence of NH_4^+ or during monochloramination or dichloramination. The maximum molar conversion ratio was about 0.99% during dichloramination of fluometuron. Given the same reagent

doses, NDMA formation increased in the order: NH_2Cl<chlorine plus NH_4^+<$NHCl_2$. Although studies have mentioned that $NHCl_2$ is a more potent NDMA-forming oxidant toward a list of precursors[12, 40], $NHCl_2$ can quickly transform to NH_2Cl that becomes the dominant species at neutral pH. The pH 8 in the experiments did not limit the NDMA formation during dichloramination, suggesting a fast reaction between fluometuron and $NHCl_2$ to form NDMA. NDMA formation during chlorination in the presence of NH_4^+ was higher than that during monochloramination. Separately adding chorine and NH_4^+ might result in formation of appreciable levels of $NHCl_2$ that enhanced the NDMA formation[33], whereas using preformed NH_2Cl minimized the presence of $NHCl_2$ in the experiments. The co-existence of phenylurea herbicides and NH_4^+, which are common in the waters impacted by agriculture or pastures, represents an issue of concern with respect to NDMA formation during chlorination of these waters. A similar NDMA formation trend was observed in the diuron experiments (r=0.997 by correlation analysis. r represents the linear correlation coefficient between the NDMA formation in fluometuron and diuron experiments). Both fluometuron and diuron contain DMA group, which appeared to be the key for NDMA formation from phenylurea herbicides.

NDMA formation was not observed in the experiments using liuron or metobromuron, attributed to the methoxy-methyl-amine group in the molecular structures of liuron or metobromuron that substitutes for the more efficient NDMA-forming DMA group in fluometuron. A similar finding was observed in the experiments using propanil with an ethyl group in the same location of the molecular structure (Figs. 1 and 3A), further suggesting the negative impact on NDMA formation by replacing the DMA group in a precursor's structure. It has been reported that the presence of bromide ion enhanced NDMA formation at pH 8 after 24 hours of reaction time, with a mechanism involving the formation of bromochloramine.[23, 41] Although bromine is contained in the molecular structure of metobromuron and its concentration in the experiments was sufficiently higher than those reported in the publications, its effect on NDMA formation was not observed due to the absence of bromine-containing intermediates with correct forms (e.g., bromochloramine) in the experiments.

While the other nitrosamines including NMEA, NDEA, NDPA, and NDBA were not detected, NPYR formation was observed in the liuron, metobromuron, and propanil experiments during chlorination in the presence of NH_4^+ or during dichloramination (Fig. 3B). The molar conversions of NPYR (<0.005%) were much lower than the molar conversions of NDMA in Fig. 3A or those listed in Table 1. Studies have reported that amine and aniline fragments are two main products from degradation of phenylurea herbicides by breaking the bonds between carbon and nitrogen near the carbonyl group.[12, 21] NPYR is known to be produced during disinfection of pyrrolidine (PYR).[42] However, these phenylurea herbicides do not contain a PYR group. A detailed literature review was conducted to investigate if it is possible to produce PYR through reactions of aniline or nitrobenzene, known products from degradation of fluometuron.[43, 44] Hussain et al. reported that the oxidative degradation of aniline in aqueous solution produces maleic acid and oxalic acid.[45] Maleic acid can be hydrogenated to form 1,4-butanediol [46], which can be further reacted with NH_4^+ to form PYR.[47] Although catalysts are required for hydrogenation to proceed and non-catalytic hydrogenation occurs at high temperatures, the NPYR yields observed here were very low and possibly still relevant to the proposed reaction mechanism. The low NPYR concentrations in these experiments also increased the difficulty and decreased the concern to investigate the NPYR formation pathway, as the NDMA was the more important product to address. Additional discussions are provided below given more results of other experiments using different herbicides as the precursors.

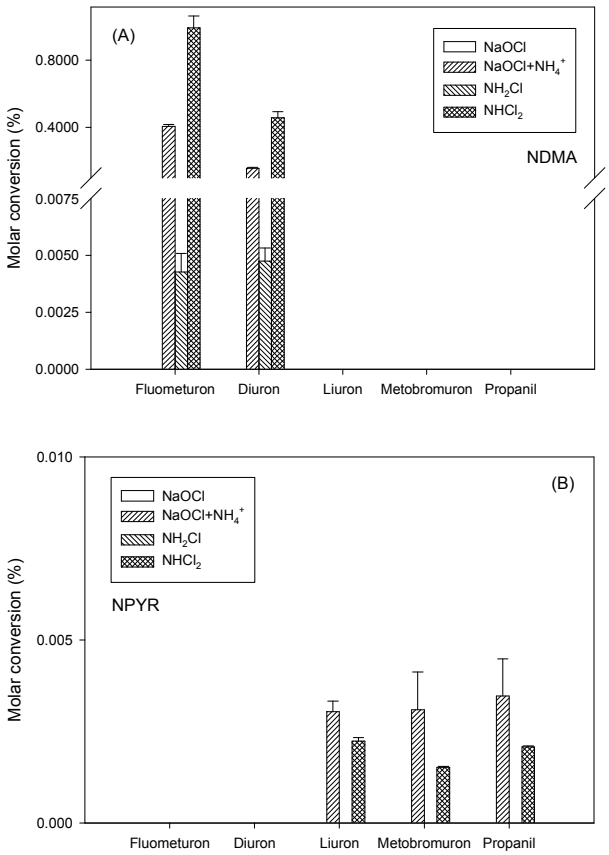

Figure 3. (A) NDMA and (B) NPYR molar conversions from different phenylurea herbicides under different disinfection scenarios at pH 8±0.2 for a contact time of 24 hours. The initial concentrations of herbicides, NH_4^+, and disinfectants were 9 μM, 0.12 mM, and 0.1 mM, respectively. The error bars depict one standard deviation. Blanks indicate that nitrosamine formation was non-detected.

Fig. 3B also shows the effect of adding NH_4^+ during chlorination or using chloramines on NPYR formation from phenylurea herbicides. It seemed that NH_4^+ or $NHCl_2$ represents important roles for NPYR formation, as the NPYR formation was relatively more vigorous in the presence of

NH_4^+ during chlorination ($p<0.05$). Because the experiments were conducted at pH 8, NH_4^+ might also be formed by disproportionation of $NHCl_2$. This result corresponded to the proposed mechanism above indicating that NH_4^+ is important for PYR formation and possibly becomes an effective nitrogen source for NPYR formation. Interestingly, the NPYR formation occurred in the experiments that did not form NDMA (the liuron metobromuron, and propanil experiments). The more efficient NDMA formation pathways somehow inhibited the reactions to form NPYR from these phenylurea herbicides.

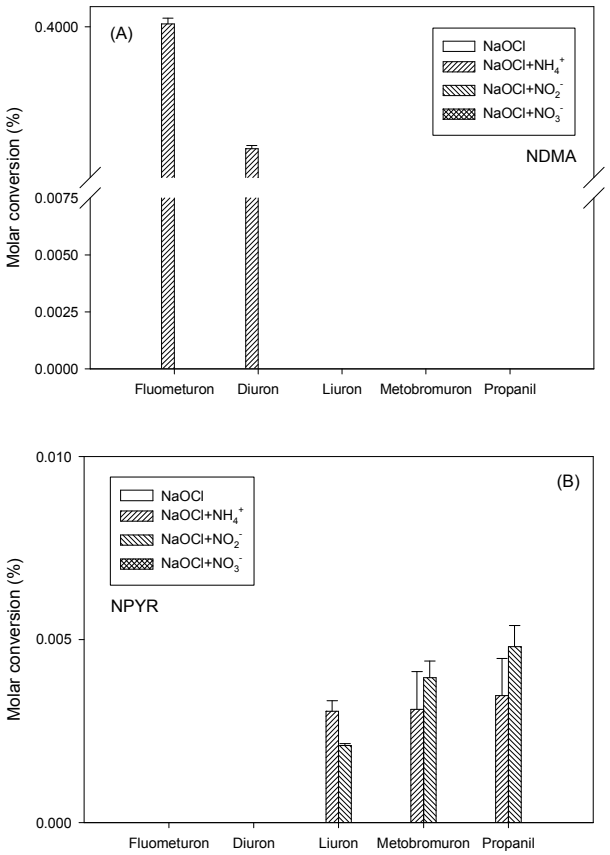

Figure 4. (A) NDMA and (B) NPYR molar conversions during chlorination of different phenylurea herbicides with/without the presence of additional nitrogen sources at pH 8±0.2 for a contact time of 24 hours. The initial concentrations of herbicides, nitrogen, and disinfectants were 9 μM, 0.12 mM, and 0.1 mM, respectively. The error bars depict one standard deviation. Blanks indicate that nitrosamine formation was non-detected.

Effect of additional nitrogen

Figs. 4A and 4B show the effects of different inorganic nitrogen species on NDMA and NPYR formation during free chlorination of phenylurea herbicides, respectively. In Fig. 4A, the NDMA formation was only observed during chlorination of fluometuron or diuron with NH_4^+ added. The NDMA concentration was not observed in the experiments using phenylurea herbicides without a DMA group or with addition of either NO_2^- or NO_3^-. The finding further demonstrated that the DMA group in the structure of phenylurea herbicides plays an important role (e.g., a possible nitrogen source) for NDMA formation. More importantly, the finding regarding the effects of adding NO_2^- or NO_3^- were similar to the results of preceding studies using DMA as the precursor. NDMA formation through the pathway that involved the reaction of NH_4^+ and production of unsymmetrical dimethyl hydrazine (UDMH)-containing intermediates was more potent than through another pathway driven by the presence of NO_2^- and free chlorine.[3, 48]

Similar to Fig. 3B, additional nitrogen sources (NH_4^+ and NO_2^-) in the experiments enhanced the NPYR formation from phenylurea herbicides (Fig. 4B), except in the NO_3^- experiments. The results were associated with the reactions of chloramination[40] or nitrosation[8], both of which are known to be important mechanisms for NDMA formation. It is worth noting that although diuron, liuron, and propanil have similar molecular characteristics (e.g., two chlorines) for their ring structures, the trends of NPYR formation were different in different herbicide experiments. Various molecular structures and compositions amongst these phenylurea herbicides such as different functional groups linked to the amine (e.g., between the cases of diuron and propanil) and ring structures (e.g., between the cases of fluometuron and diuron) may hinder the characterization of NPYR formation from these precursors. For example, Shen and Andrew investigated the NDMA formation during chloramination of eight pharmaceuticals, which all have one DMA group bound to an electron-rich moiety but different NDMA formation potentials.[49] It was found that certain pharmaceuticals (e.g. ranitidine) had higher NDMA formation potentials because their DMA groups are bound to a heterocyclic ring that is a strong electrophilic site due to the electron-donating effect of the oxygen heteroatom, whereas the NDMA formation potential of the other pharmaceuticals were lower due to additional elements present between their DMA groups and electron-donating groups weakening the electron donating effects (e.g., sumatriptan and diltiazem).[49] As more than one nitrosamine was formed, the effect of molecular structure on nitrosamine formation from phenylurea herbicides might become more complicated.

The pH effect

The influence of pH on NDMA and NPYR formation from phenylurea herbicides during dichloramination was studied (Figs. 5A and 5B). The pH 3 and 10 were chosen to understand the effects of acidic and basic conditions on nitrosamine formation from these herbicides. NDMA formation from fluometuron or diuron at different pH was studied, while liuron, metobromuron, and propanil were tested for NPYR formation in these experiments. The effect of molecular characteristic of a herbicide precursor is more important than that of pH on NDMA formation. NDMA formation during dichloramination was affected by pH with a maximum formation rate occurring at pH 8. The result was similar to the previous studies using DMA and wastewater effluent as the precursors, which indicated a maximum formation within a

neutral pH range.[48, 50] The pH dependence of NDMA formation appeared to be similar between the fluometuron and diuron experiments over the pH ranges (r=0.89). Besides the molecular features (e.g., whether containing a DMA group), water quality at neutral pH is of more concern in terms of NDMA formation from these phenylurea herbicides during chlorine disinfection. The NDMA yields were higher at pH 8 than at pH 3 possibly due to self-disproportionation of $NHCl_2$ at pH 8 producing higher NH_2Cl concentrations enhancing the NDMA formation. The pH 10 further caused chloramines to dissociate into ammonium and hypochlorite ions and reduced the NDMA yields. In Fig. 5B, the acidic or basic conditions did not help the NPYR formation from fluometuron or diuron. In the experiments using liuron or metobromuron as the precursor, the highest NPYR formation occurred at neutral pH 8, whereas the NPYR formation from propanil was not significantly different amongst the pH values tested.

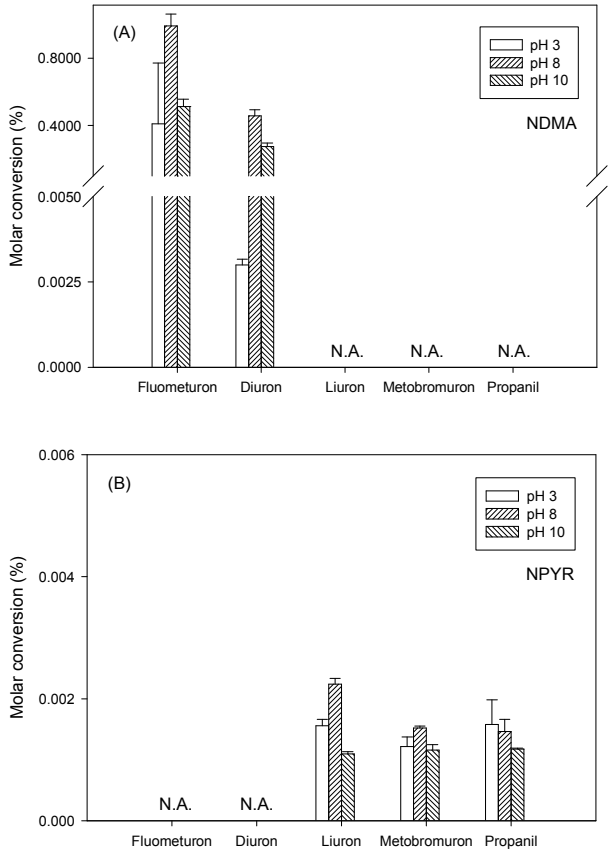

Figure 5. (A) NDMA and (B) NPYR molar conversions during dichloramination of phenylurea herbicides at pH 8±0.2 for a contact time of 24 hours. The initial concentrations of herbicides, ammonia, and disinfectants were 9 μM, 0.12 mM, and 0.1 mM, respectively. The error bars depict one standard deviation. N.A. (non-available) indicates that the experiments were not conducted.

Differences amongst disinfection approaches and phenylurea herbicides

Fig. 6 compares the nitrosamine formation potentials amongst different disinfection approaches (Fig. 6A) and nonpoint-source phenylurea herbicides (Fig. 6B), as two nitrosamines (NDMA and NPYR), five herbicides (fluometuron, diuron, liuron, metobromuron, and propanil), three disinfection approaches (chlorination, monochloramination, and dichloramination), three inorganic nitrogen species (NH_4^+, NO_2^-, and NO_3^-), and three pH (pH 3, 8, and 10) were considered. In Fig. 6A, the ranges of nitrosamine molar conversions increased in the order: NH_2Cl<free chlorine<$NHCl_2$ for given herbicide, chlorine, and nitrogen doses. The molar conversions of nitrosamines during dichloramination ranged from non-detected to 0.99%, whereas the results of free chlorination and monochloramination were lower than 0.41% and 0.005%, respectively. $NHCl_2$ is the disinfectant/oxidant that provides a more effective and efficient nitrogen source to produce nitrosamines from five phenylurea herbicides. Although chlorination is typically considered to reduce the NDMA formation as compared to monochloramination, our results suggested that with additional nitrogen sourced from inorganic nitrogen in water (e.g., NH_4^+) or precursor themselves, nitrosamine formation is still an issue of concern for chlorination.

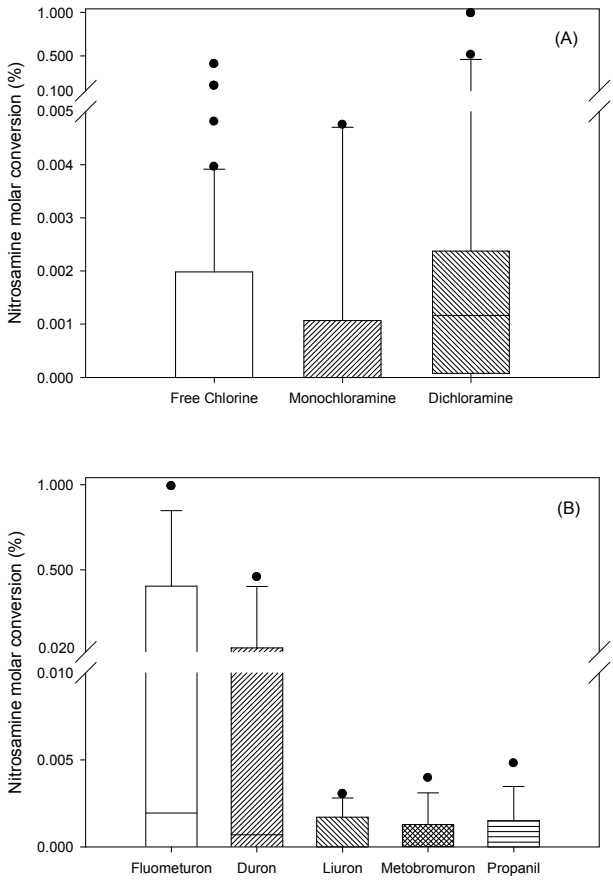

Figure 6. Nitrosamine molar conversions observed in all experiments using (A) different disinfectants (the free chlorine data includes those from the experiments with additional nitrogen sources) and (B) different phenylurea herbicides. The contact time

was 24 hours and three pH values were considered. The initial concentrations of herbicides and disinfectants were 9 μM and 0.1 mM, respectively. The line in the middle and at the bottom and top of the boxes represent the median, 25%, and 75% of the percentiles, respectively. The line below and above denotes 10% and 90% of the percentiles, while the dots represent the outliers.

In Fig. 6B, fluometuron and diuron that contain a DMA group in the chemical structures exhibited higher nitrosamine molar conversion ratios (up to nearly 0.99%), attributable to their more efficient NDMA formation. The NPYR formation from these two phenylurea herbicides was not detected. The NDMA conversion from liuron or metobromuron was inhibited because the original DMA group in the chemical structures of fluometuron or diuron became a methoxy-methyl-amine group in the structure of liuron or metobromuron or an ethyl group in propanil, significantly decreasing the overall nitrosamine conversion ratios.

Conclusions

Phenylurea herbicide-contaminated water such as those from agricultural activities are typically at neutral pH with the occurrence of inorganic nitrogen like NH_4^+ in surface water and NO_3^- in groundwater. Given the results of this study, these circumstances are likely to result in nitrosamine formation from phenylurea herbicides during oxidation or disinfection in water treatment processes. To take some drinking water treatment plants in southern Taiwan as examples, the source water qualities were regularly deteriorated by upstream activities such as the dam cleanup and agricultural and municipal discharges, resulting in the presence of low levels of organics or NH_4^+ (near or lower than 0.1 mg/L as N) in drinking water. The free chlorine residual in drinking water is regulated in Taiwan and maintained between 0.2 and 1.0 mg/L as Cl_2[51]. Applying the results observed in this study (assuming that chorine is present with NH_4^+ or as NH_2Cl with low levels of $NHCl_2$ by reactions between chlorine and NH_4^+ or organics), the phenylurea herbicide concentrations ranging from several to tens μg/L will yield a NDMA concentration in drinking water above 0.7 ng/L, which is the level for a theoretical 10^{-6} lifetime cancer risk (assuming that molar conversion ratios of NDMA from phenylurea herbicides are between 0.01% to 0.99%).

As mentioned in the introduction, the presences of these phenylurea herbicides within the ranges from μg/L to mg/L in different environments have been reported. Although it is important to take into account the possible removal of these herbicides by conventional or advanced water treatment technologies such as activated carbon or membrane filtration, the treatments are not definitely complete and many water treatment facilities do not have these advanced treatment technologies.[36] More importantly, the USEPA[6] and California Office of Environmental Health Hazard Assessment (OEHHA)[52] have 20 and 15 ng/L risk levels for NPYR in drinking water derived from 10^{-6} lifetime cancer risk levels. Also, in the Drinking Water Directive (98/83/EC) and the Groundwater Directive (2006/118/EC) by the European Union, the concentrations of single ad total pesticides in drinking water may not exceed 0.1 and 0.5 μg/L, respectively. The NPYR formation and their own toxicities will further decrease the phenylurea herbicide concentrations needed to cause a significant risk that were originally determined by only considering the formation of NDMA during post-chlorination.

Besides post disinfection, pre-oxidation commonly used to treat drinking water is another process of concern for nitrosamine formation. High concentrations of phenylurea herbicides in water can directly react to form nitrosamines during the process. Whether the pre-oxidation forms nitrosamines from these phenylurea herbicides or inhibits the formation of nitrosamines during post-disinfection is being investigated in our ongoing studies. While the nitrosamine formation potentials of these phenylurea herbicides may be less substantial than those from certain known precursors (e.g., PPCPs listed in Table 1), the true adverse impacts of these herbicides are potentially compensated by their high loadings as non-point source pollutants and typical environmental scenarios (e.g., a neutral pH or the occurrence of co-existing inorganic nitrogen) resulting in for more efficient nitrosamine formation.

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