Image caption: Water holding pools at a drinking water plant. Photo from iStock.

Nitroxyl – The Missing Link in NDMA Formation in Chloramine Systems

Huong T. Pham[1] and Julian Fairey[2]*

[1]Graduate Student, Department of Civil Engineering, University of Arkansas, Fayetteville, Arkansas 72701; [2]Associate Professor, Department of Civil Engineering, University of Arkansas, Fayetteville, Arkansas 72701
*Corresponding author, julianf@uark.edu

Abstract: The NDMA formation pathway in chloraminated drinking water remains unresolved. The goal for this project was to investigate the role of nitroxyl and peroxynitrite, both hypothesized chloramine decay intermediates and RNS, in the NDMA formation pathway in drinking water systems. Profiles of dichloramine decomposition, nitrous oxide formation, and dissolved oxygen consumption indicated the formation of nitroxyl and peroxynitrite, both RNS, from dichloramine hydrolysis. Experiments with of uric acid, a peroxynitrite scavenger, implicated peroxynitrite as a central node in the N-nitrosodimethylamine (NDMA) formation pathway. Revised unified chloramine kinetic model with nitroxyl as the heretofore unidentified intermediate (*I*) of dichloramine hydrolysis accurately simulated kinetic profiles of dichloramine, monochloramine, dissolved oxygen, and NDMA between pH 7 and 10, the pH range of interest in chloramine systems. The State of Arkansas has twelve public water systems using chloramines, serving a total approximately 100,000 people. These facilities are located throughout the state and have limited resources to dedicate to NDMA control strategies. An accurate understanding of the NDMA formation pathway during chloramination would facilitate development of strategies to curb NDMA formation and promote monochloramine stability. The main findings of the project were published in the journal *Environmental Science & Technology* (Pham, Wahman, & Fairey, 2021).

Key Points:

- Dichloramine, nitrous oxide, and dissolved oxygen profiles indicated the formation of nitroxyl and peroxynitrite, both reactive nitrogen species (RNS), from dichloramine decomposition.

- Experiments with uric acid, a peroxynitrite scavenger, implicated peroxynitrite as a central node in the N-nitrosodimethylamine (NDMA) formation pathway.

- Revised unified chloramine kinetic model with nitroxyl as the heretofore unidentified intermediate (*I*) of dichloramine hydrolysis accurately simulated kinetic profiles of dichloramine, monochloramine, dissolved oxygen, and NDMA between pH 7 and 10, the pH range of interest in chloramine systems.

Introduction

The USEPA Technical Fact Sheet for *N*-nitrosodimethylamine (NDMA) issued in November 2017 states that NDMA is a priority pollutant, classified as a B2 probable human carcinogen, and is a significant concern as a drinking water contaminant. Although industrial production of NDMA no longer occurs in the United States, NDMA still forms as an unintended by product of drinking water disinfection.

NDMA forms through various reaction pathways, and yields are largely dependent on the type of disinfectant with chloramines > ozone = chlorine dioxide > free chlorine (Pham, Wahman, Zhang, & Fairey, 2019). In Northwest Arkansas, the Carroll Boone Water District uses chloramines, which provides drinking water to approximately 13,000 customers in Harrison, Green Forest, Berryville and Eureka Springs. There are twelve public water systems in Arkansas that use chloramines, including Magnolia, Texarkana, and Waldron. Many rural water systems use chloramines to help meet the Stage 2 Disinfectants/Disinfection Byproduct rule and hence may experience elevated levels of NDMA. An accurate understanding of the NDMA formation pathway may lead to strategies to minimize its formation in chloramine systems.

The goal of this project was *to investigate the role of nitroxyl and peroxynitrite, both hypothesized chloramine decay intermediates, in the formation of NDMA in drinking water systems*. The widely accepted reaction mechanism for NDMA formation involves a nucleophilic substitution between dichloramine and unprotonated amine-based precursors to form an unsymmetrical dimethylhydrazine (UDMH), which then reacts with dissolved oxygen to form NDMA (Schreiber & Mitch, 2006). However, this latter reaction is spin-forbidden, meaning is likely kinetically unfavorable and therefore is unlikely to occur rapidly. This runs counter to our preliminary data which show rapid formation of NDMA at pH 10. This could have important implications for NDMA control strategies and other nitrogen-containing disinfection byproducts. A recent study also showed that nitrification in storage facilities and distribution systems can lead to elevated NDMA levels (Zeng & Mitch, 2016) but the underlying reaction mechanism was not determined. In this research, an NDMA formation pathway was investigated that involved RNS generated from the decomposition of dichloramine.

The research hypothesis was that nitroxyl (HNO/NO⁻) was the key intermediate in NDMA formation, shown in Figure 1. Nitroxyl is known to react with dissolved oxygen to form peroxynitrite (Smulik et al., 2014), which is a known nitrosating agent, followed by the reaction with dimethylamine (DMA) to form NDMA.

Nitroxyl may form through at least four pathways, which are (1) abiotic pathway from the breakdown of dichloramine ($NHCl_2$), (2) biotic pathway in which monochloramine (NH_2Cl) reacts with hydroxylamine generated by nitrifying bacteria, (3) abiotic pathway through the reaction of hydroxide ion with monochloramine to form hydroxylamine, which then reacts with NH_2Cl and (4) free chlorine reaction with hydroxylamine generated through nitrification. In this project report, Pathway #1 was investigated.

Methods

Batch kinetic experiments were conducted using DMA, a model NDMA precursor, and dichloramine at pH 7, 8, 9, 10. All NDMA formation kinetic experiments were performed headspace free in 25 mL amber glass vials sealed with PTFE-lined screw top lids. DMA solutions were diluted with Milli-Q water to 25 µM DMA in a volumetric flask and adjusted with 40 mM buffer to the desired pH, along with peroxynitrite scavenger (uric acid) in certain experiments. Buffers used were bicarbonate for pH 10, borate for pH 9, and phosphate for pH 8 and 7. Monochloramine
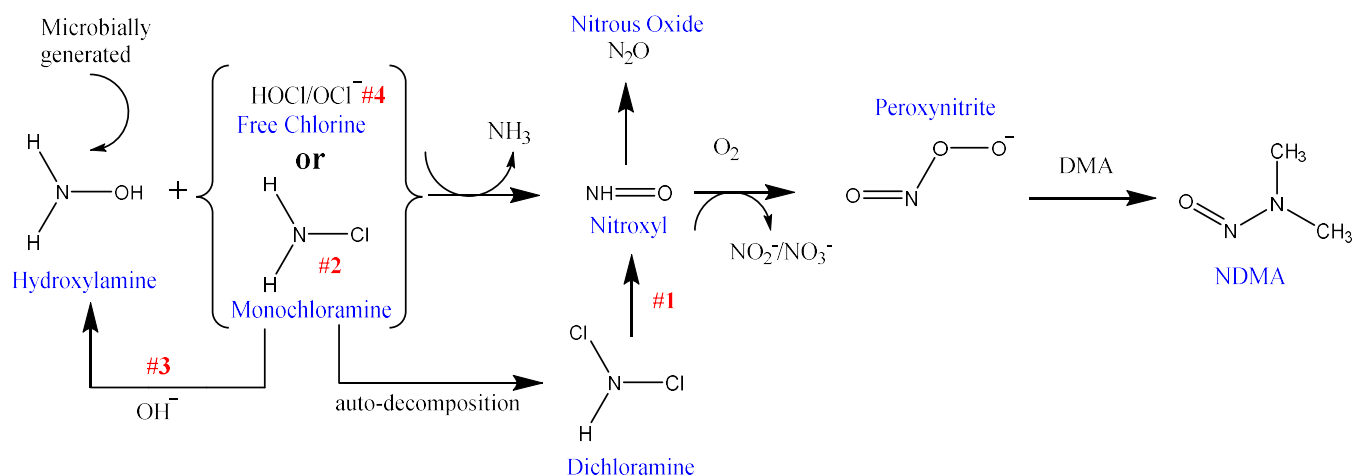

Figure 1: Proposed NDMA formation pathways (#1, #2, #3 and #4) with nitroxyl as the intermediate.

solutions at 2 mM were freshly prepared before each experiment following the procedure developed by Do, Chimka, and Fairey (2015) then adjusted to pH 3.7 with 2 N sulfuric acid and aged for 1 hour to make dichloramine. The pH of the dichloramine was not adjusted before mixing with DMA stock solution due to its fast decomposition at these conditions. Precisely 5 mL of the dichloramine solution was added to 10 mL of 25 µM DMA at the same pH and 5 mL of the corresponding buffer at 200 mM. Nitrous oxide (N_2O) and dissolved oxygen (DO) microelectrodes (Unisense) were used to quantify concentrations of these species kinetically.

Following the desired reaction time (up to 4 hours unless stated otherwise), 20 mL aliquots were quenched of chloramines with 0.5 g dry quenching mix containing 1.8 g ascorbic acid, 1 g KH_2PO_4 and 39 g Na_2HPO_4 (12.5 mM ascorbic acid in solution). After quenching, 10 mL samples were immediately extracted with dichloromethane at a 10:1 water:dichloromethane volume ratio using a back-and-forth shaker table at high speed for 15 minutes. Following a 5-minute quiescent settling period, dichloromethane was extracted with a Pasteur pipette and stored for NDMA analysis.

Monochloramine was kinetically quantified using Hach Method 10171 and total chlorine was quantified by DPD Method 8167. The difference between the total chlorine and monochloramine was assumed to be dichloramine.

NDMA was identified and quantified using gas chromatography–mass spectrometry (GC-MS). Splitless injections of 5 µL were used with an injector temperature was 250 °C. The separation column used was a RESTEK 12497 FAME-WAX with a length of 30 m, inner diameter 0.25 mm, with a stationary phase film thickness of 0.25 µm. Helium carrier gas was used with constant flow rate at 1.0 mL/min. The oven program was 45 °C for 3 minutes followed by a ramp of 25 °C/min to 130 °C and then 12 °C/min to 230 °C hold for 1 minute. The full scan and selected ion monitoring (SIM) mode were simultaneously. Six-point NDMA standard curves (10 – 1000 µg-L^{-1}) were used to quantify the concentrations of the unknown samples ($R^2 > 0.999$). Blanks and check standards were run after at least every ten injections. Standard solutions are prepared following the same procedure as samples.

The data were used for model validation because the key reactants (dichloramine and dissolved oxygen), stable intermediates (nitrous oxide) and products (NDMA) were kinetically quantified. The model was composed of i) the unified model of chloramine chemistry developed by Jafvert and Valentine (1992) ii) the nitroxyl kinetic reactions measured by Lymar and Shafirovich (2007) iii) the decomposition of peroxynitrite developed by Kirsch, Korth, Wensing, Sustmann, and de Groot (2003), and iv) the hypothesized NDMA formation reactions stemming from peroxynitrite. The three underlying models - Jafvert and Valentine (1992), Lymar and Shafirovich (2007) and Kirsch et al. (2003) –

were previously validated. However, this work is the first to combine the unified model with the nitroxyl and peroxynitrite models and, as such, adjustments to the empirically derived RNS rate expressions were expected.

Results and Discussion

Figure 2 shows the impact of uric acid on NDMA formation at pH 7 – 10. A dose of uric acid at 200 µM and higher changed the dichloramine profiles and therefore, the upper limit was set at 160 µM. NDMA formation at pH 7, 8, and 9 had a dose-response relationship with uric acid. At pH 10, a decrease in NDMA formation was observed only after the uric acid concentration increase from 140 µM to 170 µM. The NDMA concentration decreased by about 50% with 120 µM uric acid at pH 9, 80% with 160 µM uric acid at pH 8, and 100% with 140 µM uric acid at pH 7.

Uric acid is a known scavenger for peroxynitrite and its decomposition products, such as $NO_2^\bullet$ and $CO_3^{\bullet-}$ radi-
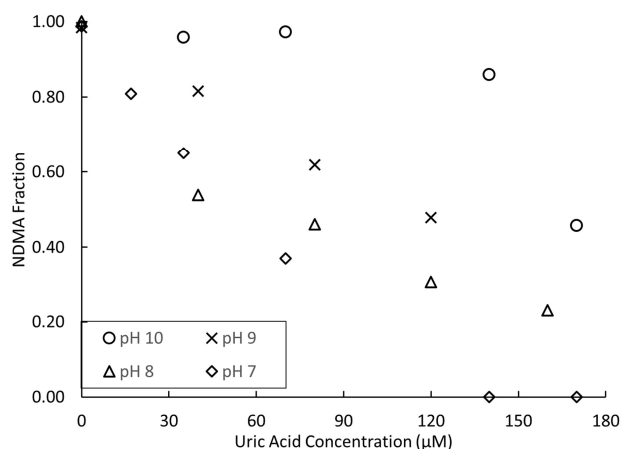

Figure 2: NDMA formation at 4 hours versus uric acid does in waters amended with 10 µM DMA, ca. 800 µeq Cl_2/L $NHCl_2$ and 40 mM corresponding buffer at pH 7, 8, 9 and 10.

cals (Hooper et al., 2000; Hooper et al., 1998). While uric acid is non-selective and can also scavenge reactive oxygen species such as hydroxyl and superoxide radicals, Schreiber and Mitch (2006) ruled out the role of these species in the NDMA formation pathway by conducting scavenging experiments using tert-butanol and superoxide dismutase. Therefore, Figure 2 supported that (i) the majority of the NDMA formation occur through a peroxynitrite mediated pathway and (ii) peroxynitrite was associated with $NHCl_2$ decomposition.

Dichloramine hydrolysis was hypothesized to form nitroxyl, which can react with itself to form nitrous oxide (N_2O), a stable end-product. In a competing reaction, nitroxyl can also react with dissolved oxygen (DO) to form peroxynitrite. Therefore, detection of N_2O formation and DO consumption during dichloramine decomposition served as a nitroxyl formation marker. Figure 3 shows di-

chloramine, N_2O, NDMA, and DO kinetic profiles at pH 7 – 10. N_2O, NDMA and DO profiles track with $NHCl_2$ decomposition, indicating their linkage to $NHCl_2$ decomposition.

To assess the NDMA formation pathway through nitroxyl, a kinetic model, referred as UF+RNS model, was implemented in AQUASIM. The model was composed of the i) unified model of chloramine chemistry developed by Jafvert and Valentine (1992), ii) nitroxyl kinetic reactions in water measured by Lymar and Shafirovich (2007), iii) decomposition of peroxynitrite developed by Kirsch et al. (2003), and iv) NDMA formation through a direct

reaction between DMA and dichloramine developed by Schreiber and Mitch (2006) along with v) the hypothesized formation of NDMA through peroxynitrite.

Table 1 shows the revised rate constants along with the corresponding standard errors. The reactions that needed revisions were (1) the hydrolysis of dichloramine, proposed to form nitroxyl, (2) nitroxyl and dichloramine, and (3) the reaction between DMA and dichloramine. The rate constants for these reactions were empirical, formulated to match chloramine species and NDMA formation only. Therefore, they were considered for re-estimation in the current project. The revised UF+RNS captured the kinetic
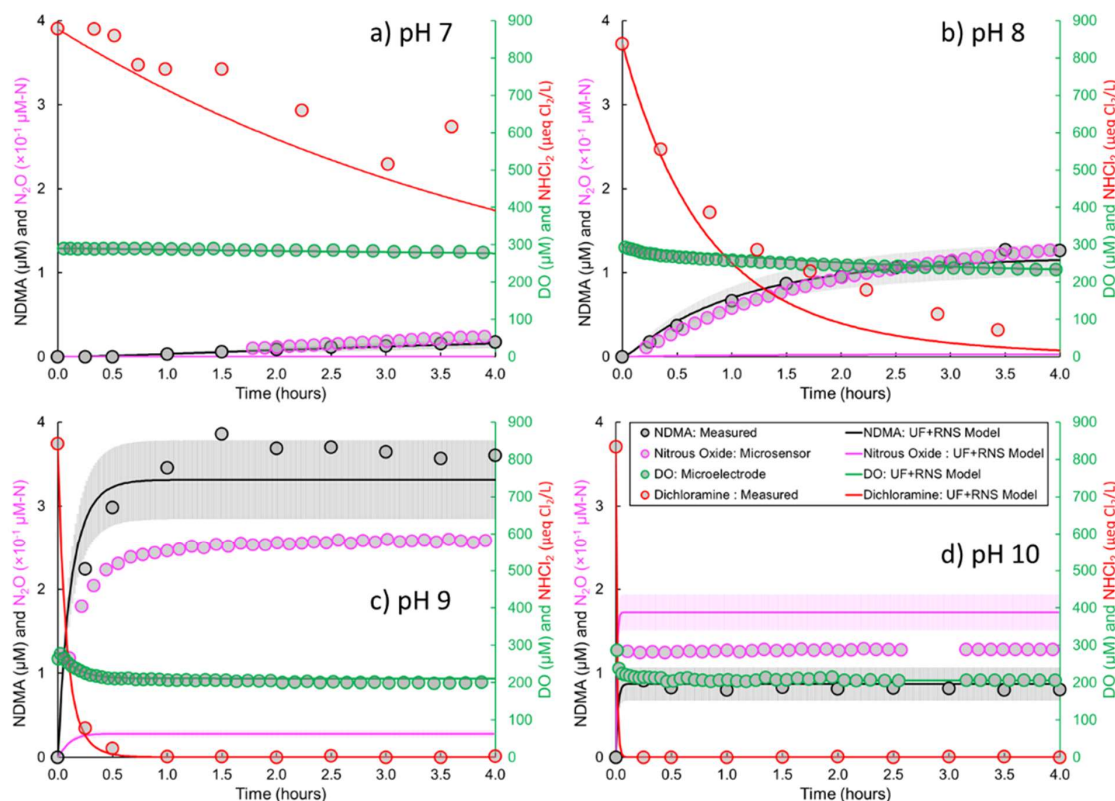

Figure 3: NDMA (black, primary y-axis), Nitrous Oxide (N_2O, magenta, primary y-axis), DO (green, secondary y axis) and Dichloramine ($NHCl_2$, red, secondary y-axis) profiles in waters dosed with ca. 800 µeq Cl_2/L $NHCl_2$ and containing 10 µM DMA buffered at (a) pH 7, (b) pH 8, (c) pH 9 and (d) pH 10. Points are measured values, lines are UF+RNS model simulations, and shaded areas are simulations encompassing one standard error in the estimated parameters (see Table 1).

Table 1. Revised reactions and rate constants implemented in the UF+RNS model. Estimated rate constants provided with their standard error.

#	Reaction	Rate Constant (M^{-1} s^{-1}, unless state otherwise)	
		Published	This work
U7	$NHCl_2 + H_2O \xrightarrow{k_{u7}} HNO + 2H^+ + 2Cl^-$	110	186 ± 6
U8	$HNO + NHCl_2 \xrightarrow{k_{u8}} HOCl + products$	2.7×10^4	$(8.2 \pm 0.8) \times 10^4$
P5	$NHCl_2 + (CH_3)_2NH \xrightarrow{k_{P5}} (CH_3)_2NNHCl + H^+ + Cl^-$	52	28 ± 8
R7	$ONOOH + (CH_3)_2NH \xrightarrow{k_{r7}} (CH_3)_2NNO + products$	NA	$k_{r7}=k_{r7A} [\exp(-k_{r7B}/[H^+])]$ $k_{r7A} = (2.1 \pm 0.4) \times 10^7$ M^{-1} s^{-1} $k_{r7B} = (4.4 \pm 0.3) \times 10^{-10}$ M
R8	$ONOOH + (CH_3)_2NNHCl \xrightarrow{k_{r8}} (CH_3)_2NNO + products$	NA	$(1.3 \pm 0.8) \times 10^7$

profiles and yields of $NHCl_2$, DO, and NDMA at pH 7-10 (see Figure 3). Notably, at pH 9 and 10, the simulated DO and NDMA profiles matched the measured data in terms of kinetics and yields throughout the 4-hour time-course.

For additional discussion, please refer to Pham et al. (2021).

Conclusions

This project presented multiple lines of evidence to support that $NHCl_2$ hydrolysis resulted in HNO formation, heretofore referred as a unidentified reactive intermediate in the Jafvert and Valentine (1992) model. Once formed, nitroxyl reacted with dissolved oxygen to produce peroxynitrite, both RNS. Peroxynitrite and/or its decomposition products then reacted with unprotonated amine to form NDMA in the presence of DMA. Therefore, scavenging RNS such as nitroxyl and/or peroxynitrite may curb NDMA formation in chloramine systems.

Further research should consider additional nitroxyl formation pathways independent of $NHCl_2$ (Figure 1, pathway #3 and #4). The reaction of NH_2Cl with NH_2OH implicated nitroxyl and peroxynitrite formation (Wahman, Speitel, & Machavaram, 2014), providing a potential mechanism to evaluate and explanation of enhanced NDMA formation during nitrification episodes (Zeng & Mitch, 2016).

Acknowledgements

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