1   **Online monitoring of *N*-nitrosodimethylamine rejection as a performance**

2   **indicator of trace organic chemical removal by reverse osmosis**

3   Revised manuscript submitted to

4   **Chemosphere**

5   February 2018

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16   **ABSTRACT**

17   The security of recycled water quality in potable reuse can be enhanced by improving the

18   credibility of reverse osmosis (RO) treatment for the removal of trace organic chemicals

19   (TOrCs). This study evaluated the potential of online monitoring of *N*-nitrosodimethlyamine

20   (NDMA) before and after RO treatment as a surrogate indicator for TOrC removal by RO.

21   This pilot-scale study monitored NDMA concentrations in RO feedwater (ultrafiltration-

22   treated wastewater) and RO permeate every 22 min using novel online NDMA analyzers—

23   high-performance liquid chromatography followed by photochemical reaction and

24   chemiluminescence detection. NDMA rejection by RO varied considerably in response to

25   changes in operating conditions (permeate flux and feedwater temperature). A high linear

26   correlation between NDMA rejection and the rejection of six other TOrCs was observed. The

27   linear correlation was also identified for an RO membrane damaged with chlorine. The

28   correlation between another potential surrogate indicator (conductivity rejection) and TOrC

29   rejection was relatively low. NDMA, which is the smallest compound among regulated

30   TOrCs, revealed rejections lower than the other TOrCs, indicating that NDMA rejection can

31   be a conservative surrogate indicator capable of predicting changes in TOrC removal.

32   **Keywords:** *N*-nitrosodimethylamine; *N*-nitrosamines; potable reuse; reverse osmosis;

33   surrogate indicator

1   INTRODUCTION

Potable water reuse (PR) has been increasingly important in many parts of the world as an attractive strategy to augment drinking water supplies. PR is typically performed by replenishing the drinking water sources (e.g. dams and aquifers) with recycled water that exceeds drinking water standards. This approach is referred as indirect PR. Direct PR, which transfers recycled water directly to a drinking water treatment plant, is also being considered as a feasible option, but it requires more stringent monitoring of water quality (Leverenz et al., 2011; Arnold et al., 2012; CSWRCB, 2016). In particular, pathogens and trace organic chemicals (TOrCs) (e.g. pharmaceuticals, personal care products, steroid hormones, pesticides, and disinfection by-products) that are ubiquitously present in wastewater are of great importance due to their adverse consequences for human health.

In typical PR, the removal of TOrCs below their regulated limits is achieved through an advanced water treatment process typically comprised of reverse osmosis (RO) treatment and an advanced oxidation process (AOP) such as ultraviolent (UV) irradiation with hydrogen peroxide (H_2O_2) (Poussade et al., 2009; Drewes and Khan, 2011). Although RO treatment can sufficiently remove most TOrCs, some low molecular weight TOrCs such as N-nitrosodimethlyamine (NDMA, disinfection by-product) (USEPA, 1993) are not well rejected. Since there is no tool or technology capable of ensuring membrane integrity for the removal of TOrCs by RO, most of recent PR schemes in the USA and Australia essentially rely on AOP-based post treatment for their removal. In contrast to RO, treatment performance of AOP for TOrC removal can be ensured through the online monitoring of UV power input, UV transmittance, and H_2O_2 dose (Plumlee et al., 2008). This indicates that only a single reliable barrier for TOrC removal is in place in PR.

57   A provision for the credible removal of TOrC by RO treatment can enhance the security of

58   recycled water quality. The analysis of TOrCs requires laboratory testing with labor intensive

59   pretreatment such as solid or liquid phase extraction and sophisticated analytical instrument

60   (e.g. gas chromatography and mass spectrometry) (Munch and Bassett, 2004). More

61   importantly, their occurrence could be site specific and they could often be detected at very

62   low concentrations in RO feed. In contrast, NDMA is commonly identified at concentrations

63   higher than 10–30 ng/L in RO feed due to its ubiquitous presence in raw wastewater (Fujioka

64   et al., 2012a). NDMA is also formed through the chloramination process intended for

65   mitigation of RO biofouling, increasing NDMA concentration prior to any RO process

66   (Krauss et al., 2009; Farré et al., 2011; Shah and Mitch, 2012; Krasner et al., 2013). Thus,

67   NDMA removal by RO could potentially be used as a surrogate indicator for TOrC removal.

68   A recent work by the authors (Fujioka et al., 2017) demonstrated the ability of online

69   monitoring of NDMA in RO permeate using a newly developed NDMA analyzer—high-

70   performance liquid chromatography followed by photochemical reaction and

71   chemiluminescence detection (HPLC-PR-CL). Monitoring NDMA concentrations in RO

72   permeate online allows for improved early warning of NDMA spikes, which could exceed

73   regulatory limits (e.g. 10 ng/L California regulatory notification level) in the final product

74   water (CDPH, 2015). In addition, the adaptation of this technique to both RO feedwater and

75   RO permeate can provide an online rejection data, which can be utilized as a surrogate

76   indicator for TOrC removal.

77   The primary objective of this study was to examine the applicability of online-monitored

78   NDMA rejection as a surrogate indicator of TOrC removal by RO treatment at the pilot scale.

79   Correlation of rejection between NDMA and representative TOrCs was evaluated through

80   monitoring NDMA concentrations every 22 min before and after RO treatment using

81   untreated and chlorine-treated RO membrane elements.

2   MATERIALS AND METHODS

2.1 Chemicals

84   All chemicals used in this study **(Table 1)** were of analytical grade. Four *N*-nitrosamines—

85   NDMA, *N*-nitrosomethyethylamine (NMEA), *N*-nitrosopyrrolidine (NPYR), *N*-

86   nitrosomorpholine (NMOR)—were purchased from Ultra Scientific (Kingstown, RI, USA).

87   A stock solution of *N*-nitrosamines was prepared at 1 mg/L in pure methanol. The other

88   chemicals selected as TOrCs were purchased from Wako Pure Chemical Industries (Osaka,

89   Japan). A stock solution with a concentration of 1 mg/L of each chemical was prepared in

90   pure methanol. TOrCs were categorized as neutral (ionised by ≤50%) and charged (ionised

91   by >50%) **(Table S1)**. All chemicals used here can be classified as hydrophilic TOrCs (Log*D*

92   = <2.0) (Bellona et al., 2004; Van der Bruggen et al., 2006) except for carbamazepine; thus,

93   the impact of adsorption on the rejection of most of the TOrCs was expected to be negligible.

94   Ultrafiltration (UF)-treated wastewater was obtained by filtering an activated sludge effluent

95   from a municipal treatment plant in Japan. Total organic carbon (TOC), electrical

96   conductivity, and pH of the UF-treated wastewater were 6.5 mg/L, 895 µS/cm, and 7.0,

97   respectively.

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Table 1 – Properties of the selected TOrCs.

Name (charge)	Abbreviation	Formula	Molecular weight (Da)	LogD at pH 7
Uncharged at pH 7				
N-nitrosodimethlyamine	NDMA	$C_2H_6N_2O$	74.1	0.04
N-nitrosomethyethylamine	NMEA	$C_3H_8N_2O$	88.1	0.40
N-nitrosopyrrolidine	NPYR	$C_4H_8N_2O$	100.1	0.44
N-nitrosomorpholine	NMOR	$C_4H_8N_2O_2$	116.1	-0.18
Acetaminophen	ACE	$C_8H_9NO_2$	151.2	0.91
Caffeine	CAF	$C_8H_{10}N_4O_2$	194.2	-0.55
Carbamazepine	CAR	$C_{15}H_{12}N_2O$	236.3	2.77
Charged at pH 7				
Naproxen (-)	NAP	$C_{14}H_{14}O_3$	230.3	0.25
Sulfamethoxazole (-)	SUL	$C_{14}H_{18}N_4O_3$	253.3	0.15
Atenolol (+)	ATE	$C_{14}H_{22}N_2O_3$	266.3	-2.14
Trimethoprim (+)	TRI	$C_{14}H_{18}N_4O_3$	290.3	0.92
Diclofenac (-)	DIC	$C_{14}H_{11}Cl_2NO_2$	296.2	1.34

2.2 Pilot-plant validation test protocol

The validation test was performed using a pilot-scale cross-flow RO treatment system **(Fig. S2)**. The pilot system held a 4-in. spiral wound ESPA2 RO membrane element with a 7.43 m^2 effective membrane area (Hydranautics, Oceanside, CA, USA). RO treatment was performed using untreated or chlorine (Cl_2)-treated ESPA2 RO membrane element. The Cl_2-treated ESPA2 RO membrane was prepared by feeding the element a 20 mg/L NaOCl solution at a recovery of 25% and feedwater temperature of 15–20 °C for 28 days. RO treatment was conducted after spiking *N*-nitrosamines and TOrCs in the UF-treated wastewater at 150–550 ng/L and 45 µg/L for each chemical, respectively. Rejection of NMEA, NPYR, and NMOR by RO membranes is typically higher than NDMA due to their larger size in molecular dimension; thus, the three *N*-nitrosamines were dosed at high target concentrations (550 and 200 ng/L for the untreated and Cl_2-treated RO membranes, respectively) to identify a measurable concentration in the RO permeate. Unless otherwise stated, the RO system was operated under standard conditions (permeate flux = 20 L/m^2h, feed solution temperature = 15 °C and system recovery = 15%) for 21 h. *N*-nitrosamine concentrations in RO feedwater and permeate were monitored by drawing samples from the pilot system into the online

116   NDMA analyzers. The analysis of the TOrCs was conducted by collecting 250 mL grab

117   samples from the RO feedwater and 500 mL from the RO permeate.

2.3   Analytical techniques

119   Concentrations of *N*-nitrosamines in RO feedwater and permeate were determined by high-

120   performance liquid chromatography-photochemical reaction-chemiluminescence (HPLC-PR-

121   CL) analyzers (Fujioka et al., 2016; Kodamatani et al., 2016) equipped with a six-port valve

122   **(Fig. S3)** (Fujioka et al., 2017). Sample volumes of 20 μL (RO feedwater) and 200 μL (RO

123   permeate) were injected into the HPLC-PR-CL every 22 min. Conductivity and temperature

124   of RO feedwater and permeate were also monitored using conductivity meters (Orion Star™

125   A325, Thermo Fisher Scientific, MA, USA). Concentrations of TOrCs in RO feedwater and

126   permeate were determined using an ultra-performance liquid chromatography (UPLC)

127   equipped with an atmospheric pressure ionization (API) tandem mass spectrometer. The

128   analytical system comprised of ACQUNITY UPLC system and Quattro micro API mass

129   spectrometer (Waters, MA, USA) (Narumiya et al., 2013).

3   RESULTS AND DISCUSSION

3.1   Online analysis of N-nitrosamines

132   Monitoring *N*-nitrosamine concentrations in RO feedwater and RO permeate were performed

133   using two online HPLC-PR-CL analyzers during RO treatment of a UF-treated wastewater.

134   The concentration of *N*-nitrosamines in the RO feedwater showed a gradual decrease possibly

135   due to their sorption to the components of the pilot-scale RO system (e.g. a reservoir, pipes

136   and RO membrane) **(Fig. 1 and Fig. S4)**. During the first 12–13 h filtration under a permeate

137   flux of 20 L/m^{2}h and feed temperature of 20°C, NDMA concentrations in RO permeate

138   remained almost constnat **(Fig. 1a,b)**. A stepwise decrease in permeate flux (20, 10 and 5

139   L/m²h) at 13–16 h caused a substantial increase in conductivity and *N*-nitrosamine

140   concentration in the RO permeate **(Fig. 1 and Fig. S4)**. In response to the increased RO

141   feedwater temperature, the NDMA concentration in the permeate also increased, from 99 to

142   151 ng/L and from 88 to 145 ng/L for untreated and Cl$_2$-treated ESPA2 RO membranes,

143   respectively. At 16 h, the permeate flux was reestablished at 20 L/m²h and thereafter RO

144   feedwater temperature was increased from 20 to 27 °C. The increase in RO feedwater

145   temperature caused an increase in permeate conductivity and *N*-nitrosamine. The NDMA

146   concentration in RO permeate increased from 94 to 132 ng/L and 95 to 135 ng/L for

147   untreated and Cl$_2$-treated RO membranes, respectively. The operating conditions used in this

148   study led to a wide range of solute permeation with respect to *N*-nitrosamines and

149   conductivity, which allowed for a systematic examination of the correlation between a

150   potential surrogate parameter (i.e. conductivity or NDMA rejections) and TOrC rejection in

151   the following tests. It should be noted that this study used very high NDMA concentrations

152   (160–190 ng/L) in RO feedwaters. NDMA in RO feedwater is typically identified below 20–

153   30 ng/L; therefore the high NDMA concentration used here is a limitation of this study when

154   applying the findings to on-site use.

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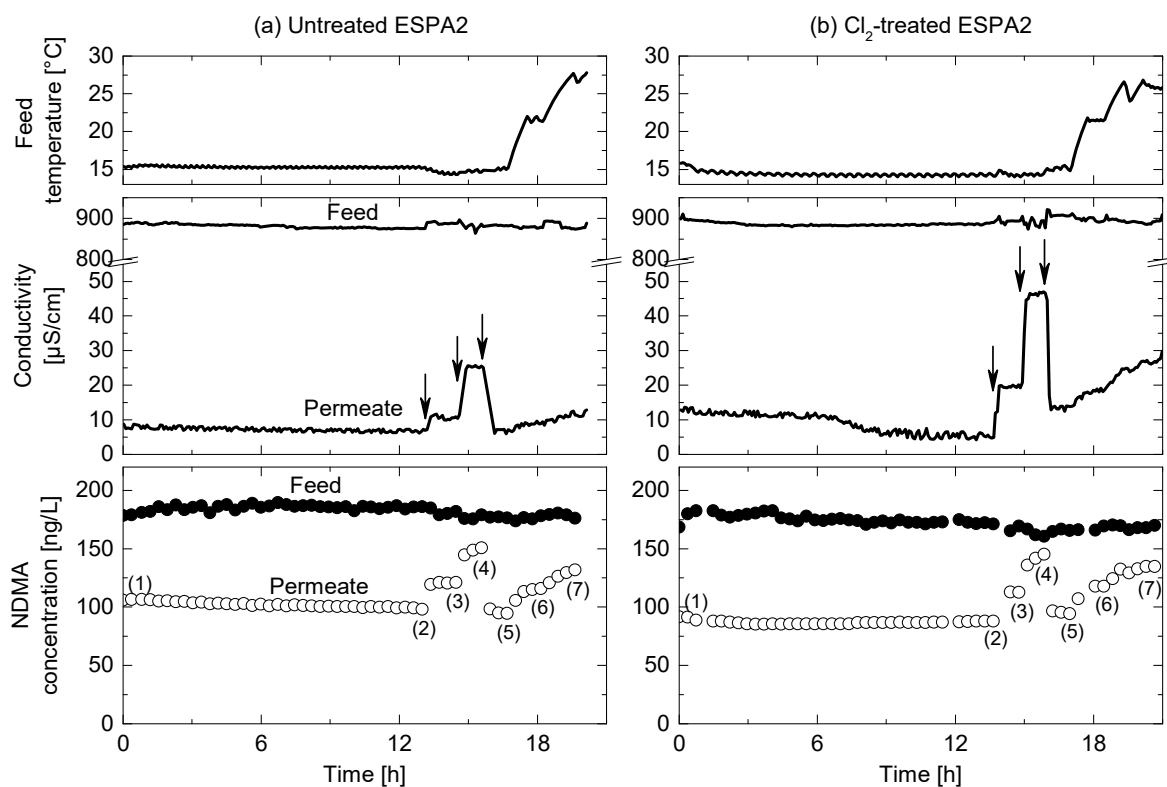
Fig. 1 – Online analysis of feed temperature, conductivity and NDMA concentration during RO treatment of a UF-treated wastewater using (a) untreated and (b) Cl$_2$-treated ESPA2 RO membranes. Numbers in bracket indicate grab sampling event number. Arrows indicate the time when permeate flux was changed. Permeate flux was 20 L/m^{2}h except for 13–16 h (5 or 10 L/m^{2}h).

3.2   Rejection of NDMA and other TOrCs

The rejection of TOrCs by the untreated RO membrane increased with increasing molecular weight **(Fig. 2)**. In particular, *N*-nitrosamines showed a considerable increase in rejection according to increase in molecular weight, which was in line with previous laboratory-scale studies (Fujioka et al., 2012b; Fujioka et al., 2013). In addition to *N*-nitrosamines, acetaminophen, another low molecular weight TOrC, showed a relatively low rejection of 97.1%. The rejection of the other high molecular weight TOrCs were typically very high (>99.7%) throughout the tests **(Tables S5 and S6)**. The results suggest that monitoring RO membrane integrity for TOrC removal is important for low molecular weight compounds. It

170　has been well demonstrated in the literature that the rejection of ionised chemicals is much

171　greater than that of non-ionised chemicals similar in molecular size (Bellona et al., 2004;

172　Verliefde et al., 2008). However, the impact of the electrostatic interactions was not

173　identified in this study. In addition to *N*-nitrosamines, two small and uncharged TOrCs (i.e.

174　acetaminophen and caffeine) and one positively charged TOrC (atenolol) were selected for

175　further evaluation.
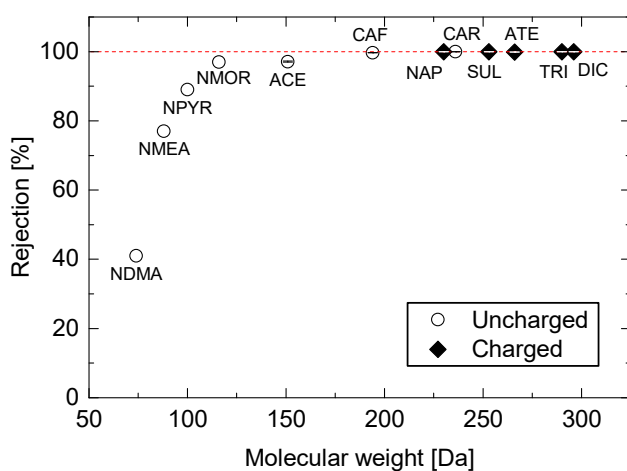
176

177　**Fig. 2** – Rejection of TOrCs by untreated ESPA2 RO membrane as a function of their

178　molecular weight. The data was obtained from the analytical results of the sampling event (1)

179　in **Fig. 1**. Values reported for TOrCs excluding *N*-nitrosamines are the average and ranges of

180　triplicate samples.

181　*3.3 Surrogate indicator*

182　Conductivity rejection by the untreated RO membrane generally correlated well with TOrC

183　rejection. For example, R-squared values for the rejection of NDMA, NMEA and

184　acetaminophen were 0.81, 0.80 and 0.85, respectively **(Fig. 3a)**. Likewise, R-squared values

185　for the rejection of NPYR, NMOR, caffeine and atenolol showed a high correlation in the

186　range of 0.80–0.98. The correlation was also observed for the Cl$_2$-treated ESPA2 RO

187　membrane (R^2 = 0.79–0.93) with the exception of atenolol (R^2 = -0.18) **(Fig. 3b)**.

188　Nevertheless, the feasibility of using conductivity rejection as a surrogate indicator of TOrC

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189 rejection still remains questionable. For example, the majority of conductivity measurements

190 obtained in this study lie in a very narrow range of 98.7–99.3% and 96.9–99.5% for the

191 untreated and Cl_2-treated RO membranes, respectively. In the region of high conductivity

192 rejection (98.5–99.5%) by the Cl_2-treated RO membrane, *N*-nitrosamine rejection did not

193 correspond with changes in conductivity rejection. Moreover, conductivity rejection appeared

194 to be sensitive to changes in permeate flux, so that a low permeate flux of 5 L/m^{2}h resulted in

195 a conductivity rejection distinctly lower than the others (97% and 95% for untreated and Cl_2-

196 treated RO membranes, respectively) despite a minor variation in TOrC rejection **(Fig. 3b)**.
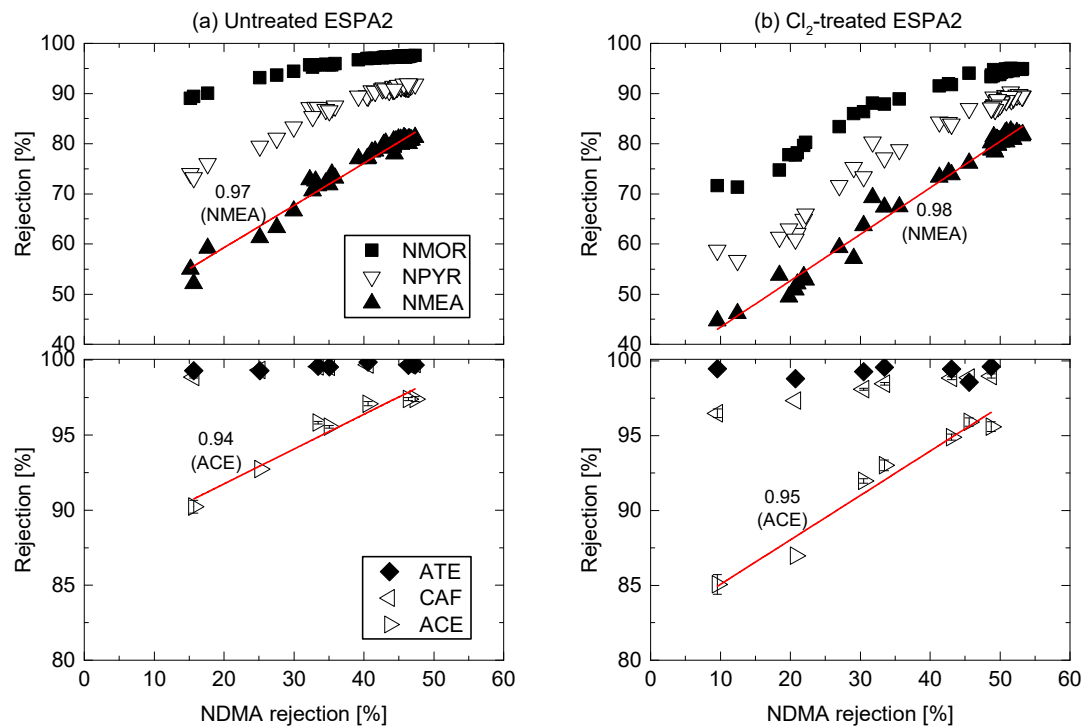
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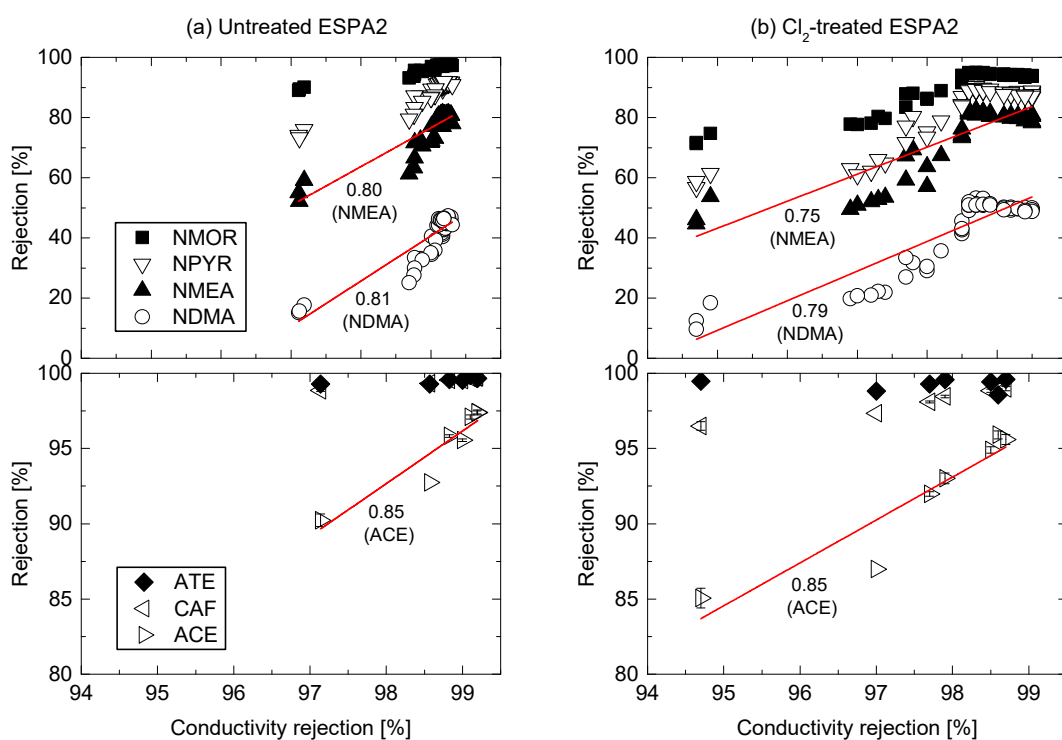
Fig. 3 – The rejection of TOrCs as a function of conductivity rejection using (a) untreated
199 and (b) Cl_2-treated ESPA2 RO membranes. R-squared values are only shown for NDMA,
200 NMEA and acetaminophen (ACE). Values reported for ATE, CAF and ACE are the average
201 and ranges of triplicate samples.

202 Compared with conductivity rejection, a higher linear correlation in rejection was obtained

203 between NDMA and TOrCs for the untreated RO membrane (e.g. R^2 = 0.97 and 0.95 for

204   NMEA and acetaminophen, respectively) **(Fig. 4a)**. A high correlation was also identified for

205   Cl_2-treated ESPA2 RO membrane **(Fig. 4b)**. Because this study used two separate RO

206   membrane elements (i.e. untreated and Cl_2-treated ESPA2 RO membranes), whether the

207   NDMA monitoring approach can be used to track the deterioration in TOrC rejection was not

208   fully demonstrated. To fully demonstrate the applicability of NDMA monitoring approach,

209   further evaluation may be necessary by tracking changes in TOrC rejection during

210   chlorination to the same RO membrane element.

211   Chlorination to polyamide-based RO membranes typically lead to the deterioration in the

212   rejection of salts and TOrCs including NDMA (Kwon and Leckie, 2006; Simon et al., 2009;

213   Tin et al., 2017). In this study, the impact of chlorine treatment on TOrC rejection was more

214   apparent at higher feedwater temperature. At 27 °C, the rejection of NDMA and

215   acetaminophen by the untreated RO membranes (25% and 93%, respectively) was greater

216   than that by the Cl_2-treated RO membrane (21% and 87%, respectively), while at 15 °C the

217   difference in rejection between these two RO membranes was negligible **(Fig. 4)**. A similar

218   observation was identified for the other TOrCs.

219   The advantage of using NDMA rejection over conductivity rejection is the high sensitivity of

220   NDMA rejection in response to changes in membrane and system operating conditions.

221   NDMA is one of the smallest TOrCs that are regulated in PR. This indicates NDMA rejection

222   could be a conservative surrogate indicator for the rejection of most regulated TOrCs by RO.

223   Before full-scale implementation, further long-term investigation is necessary to evaluate the

224   influence of membrane fouling, chemical cleaning, and membrane aging on TOrC and

225   NDMA rejection.

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Fig. 4 – The rejection of TOrCs as a function of NDMA rejection using (a) untreated and (b) Cl2-treated ESPA2 RO membranes. R-squared values are only shown for NMEA and acetaminophen (ACE). Values reported for ATE, CAF, and ACE are the average and ranges of triplicate samples.

3.4 Conclusions

This pilot-scale study demonstrated online monitoring of NDMA concentrations in RO feedwater and RO permeate and identified a high linear correlation between NDMA rejection and the rejection of six other TOrCs by RO. The results suggest a potential for online monitoring of NDMA rejection as a conservative surrogate indicator of TOrC rejection by RO. Although the current integrity management strategy for RO membranes using conductivity (or TOC) has been successfully implemented in PR, online monitoring of NDMA is more relevant as a surrogate indicator of TOrC removal. However, it should be noted that the optimization of water recycling treatment processes and the minimization of NDMA formation during water recycling treatment can limit the use of NDMA as a surrogate indicator. In spite of this potential limitation in future potable reuse schemes, the suggested

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242 monitoring strategy using online NDMA analyzers could enable water utilities to ensure the

243 safety of recycled water quality with more stringent security management against trace

244 organic contaminants, which is crucial when shifting PR schemes from indirect PR to direct

245 PR.

4   ACKNOWLEDGEMENT

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Online monitoring of *N*-nitrosodimethylamine rejection as a performance indicator of trace organic chemical removal by reverse osmosis

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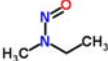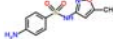[‡]*Research Center for Environmental Quality Management, Kyoto University, 1-2 Yumihama, Otsu, 520-0811, Japan*
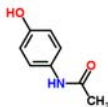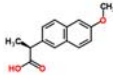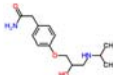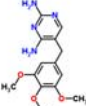
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Supplementary Material

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Table S1 – Properties of the selected TOrCs.

| Name	Structure*	pKa*	Charged species at pH 7*	California Code of Regulations **
NDMA		3.5	0	N/A
NMEA		3.4	0	N/A
NPYR		3.3	0	N/A
NMOR		3.3	0	N/A
Acetaminophen		9.46	0	(A) hydroxy Aromatic
Caffeine		-1.16	0	(D) deprotonated Amine
Carbamazepine		15.96	0	(C) nonaromatic C=C
Naproxen		4.19	100	(E) alkoxy polyaromatic
Sulfamethoxazole		1.97, 6.16	87	(B) amino/acylamino aromatic
Atenolol		9.68, 14.07	100	N/A
Trimethoprim		0.1, 7.16	59	(D) deprotonated amine
Diclofenac		4.00	100	N/A

* Chemicalize (https://chemicalize.com)

** California Office of Administrative Law (2015) California Code of Regulations, Title 22: Social Security, Division 4: Environmental Health, Chapter 3: Water Recycling Criteria.
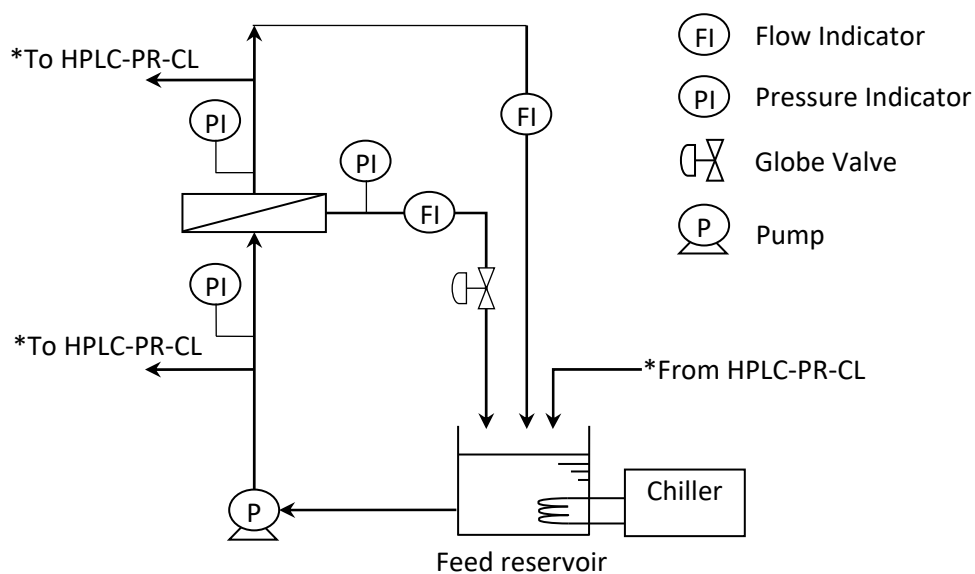
Fig. S2 – Schematic diagram of the pilot-scale RO treatment system. The system comprised of a 4-in. glass-fibre pressure vessel (ROPV, Nangang, China), 65-L stainless steel reservoir, a high-pressure pump (25NED15Z, Nikuni Co., Ltd., Kawasaki, Japan), digital flow meters (FDM, Keyence Co., Osaka, Japan), digital pressure indicators (GPM, Keyence Co., Osaka, Japan), a pressure gauge, stainless steel pipes in the feed stream and PVC pipes and PTFE tubing in the permeate stream). The membrane element was rinsed with pure water to eliminate residual preservatives on the RO element. Feed solution temperature was maintained in the reservoir using a titanium heat exchanging pipe connected to a chiller unit (CA-1116A, Tokyo Rikakikai Co. Ltd., Tokyo, Japan).
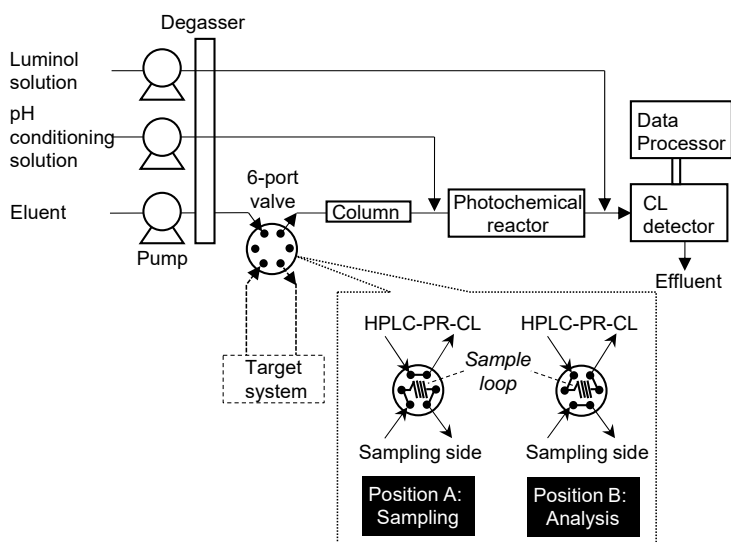
Fig. S3 – Schematic diagram of the online HPLC-PR-CL analyzer with a 6-port valve. The online HPLC-PR-CL monitor was assembled with commercially available components: DGU-20A$_3$ degasser (Shimadzu), six-port valve (HV-2080-01, JASCO, Tokyo, Japan), valve controller (Nichiri Mfg. Co. Ltd., Chiba, Japan), CTO-20AC column oven (40 °C), InertSustain C18-AQ column (5 μm, 4.6 mm i.d., 250 mm GLsciences, Tokyo, Japan), CL-2027 chemiluminescence detector (JASCO, Tokyo, Japan), and Chromato-PRO data processor (Runtime Instruments, Kanagawa, Japan). In addition, a low-pressure mercury lamp (15 W, CL-15, Panasonic, Tokyo, Japan) was used to construct the photochemical reactor. Eluent solution (10 mM phosphate buffer with 5% methanol) was fed to the instrument in isocratic mode at a flow rate of 1.5 mL/min. The method detection limits (MDLs) were determined based on the Method Detection Limit Procedure of the U.S. Environmental Protection Agency (40CFR 136, Appendix B, revision 1.11). The MDLs of NDMA, NMEA, NPYR and NMOR for a 200 μL injection volume were 0.3, 0.7, 1.4 and 0.8 ng/L, respectively. The MDLs of NDMA, NMEA, NPYR and NMOR for a 20 μL injection volume were 2.7, 6.3, 7.7 and 11.8 ng/L, respectively.
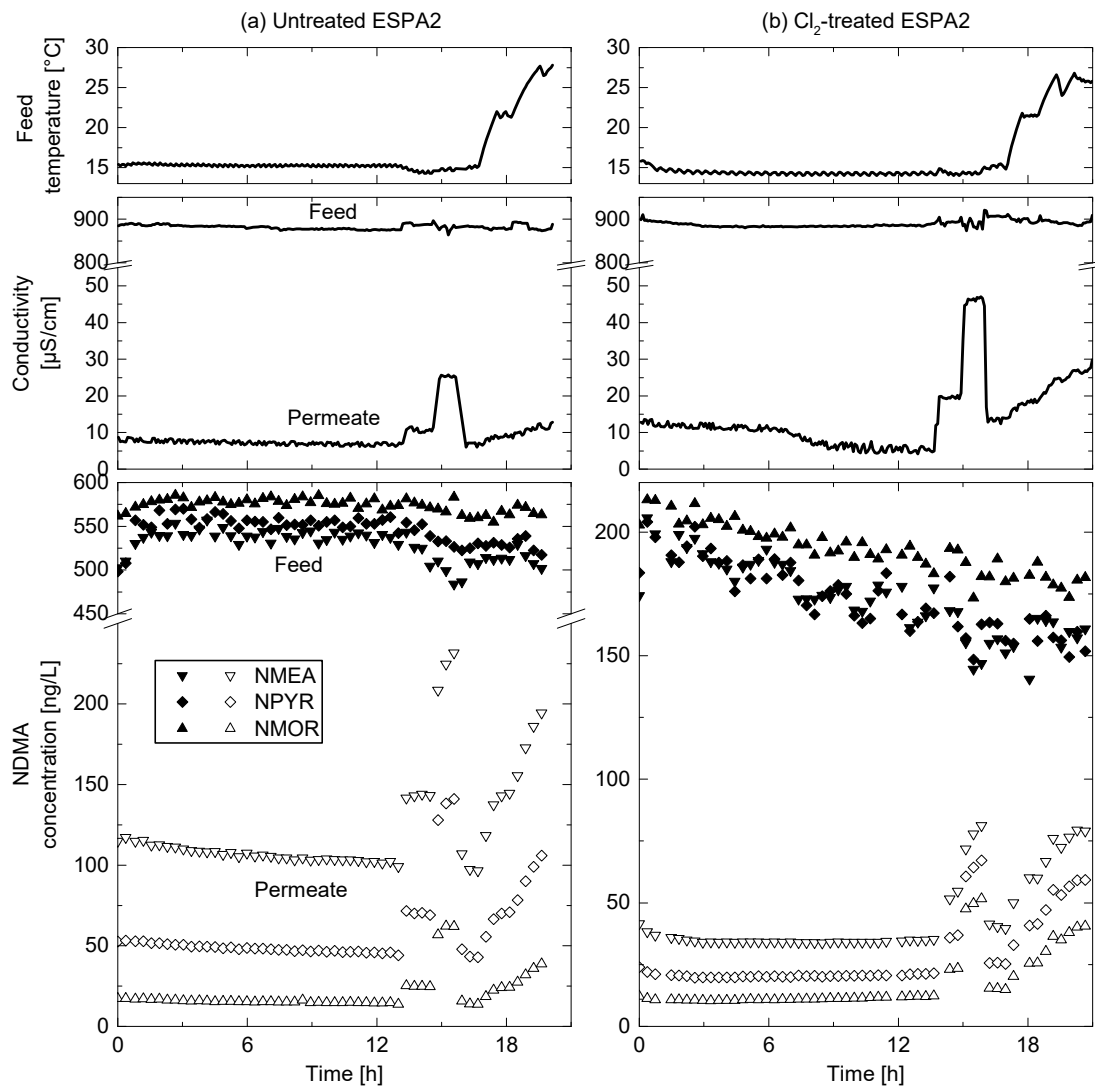
Fig. S4 – Online analysis of feed temperature, conductivity and concentrations of NMEA, NPYR and NMOR using (a) untreated and (b) chlorine-treated ESPA2 RO membranes.

Table S5 – Rejection of TOrCs by the untreated ESPA2 RO membrane. The average rejection was calculated from three RO feed and three RO permeate samples.

Sampling event #		1	2	3	4	5	6	7
Operating conditions	Flux (L/m^{2}h)	20	20	10	5	20	20	20
	Temperature (°C)	15	15	15	15	15	21	27
TOrCs	Acetaminophen	97.1	97.4	95.8	90.2	97.4	95.6	92.7
	Caffeine	99.7	99.7	99.6	98.9	99.7	99.5	99.3
	Carbamazepine	99.9	99.7	99.8	99.7	99.7	99.7	99.7
	Naproxen	99.94	99.96	99.94	99.87	99.97	99.96	99.92
	Sulfamethoxazole	99.98	99.94	99.95	99.84	99.93	99.92	99.96
	Atenolol	99.9	99.7	99.6	99.3	99.7	99.5	99.3
	Trimethoprim	99.99	99.6	99.6	99.4	99.5	99.5	99.5
	Diclofenac	99.9	99.8	99.6	99.5	99.8	99.8	99.9

Table S6 – Rejection of TOrCs by the Cl_2-treated ESPA2 RO membrane. The average rejection was calculated from three RO feed and three RO permeate samples.

Sampling event #		1	2	3	4	5	6	7
Operating conditions	Flux (L/m²h)	20	20	10	5	20	20	20
	Temperature (°C)	15	15	15	15	15	21	27
TOrCs	Acetaminophen	95.9	95.6	93.0	85.1	94.9	92.0	97.3
	Caffeine	98.9	99.0	98.5	96.5	98.8	98.1	97.3
	Carbamazepine	99.6	99.5	99.5	99.4	99.4	99.3	99.2
	Naproxen	99.8	99.8	99.8	99.6	99.8	99.8	99.8
	Sulfamethoxazole	99.9	99.9	99.9	99.7	99.9	99.9	99.9
	Atenolol	98.6	99.6	99.6	99.5	99.4	99.3	98.8
	Trimethoprim	99.6	99.2	99.3	99.0	99.2	99.0	99.2
	Diclofenac	99.9	99.8	99.9	99.8	99.8	99.8	99.9