

1 **Online monitoring of *N*-nitrosodimethylamine for the removal assurance of**
2 **1,4-dioxane and other trace organic compounds by reverse osmosis**

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19 **Abstract**

20 Public health protection and cost effectiveness of potable reuse can be improved by providing
21 reliable water quality assurance for removal of trace organic compounds (TOrcs) by reverse
22 osmosis (RO) membrane. This study evaluated the effectiveness of online monitoring of *N*-
23 nitrosodimethylamine (NDMA) removal by RO system to ensure the removal of low
24 molecular weight TOrcs. Among TOrcs, the main focus was placed on 1,4-dioxane due to
25 the limited information for RO. Laboratory-scale experiments showed that the rejection of
26 1,4-dioxane by two commercial RO membranes — ESPA2 and HYDRA (98 and 99%,
27 respectively) — was higher than that of NDMA (57 and 81%, respectively). Pilot-scale
28 experiments using a treated wastewater identified a strong linear correlation between 1,4-
29 dioxane and NDMA rejection over a range of feed temperature. Pilot-scale results also
30 demonstrated the applicability of NDMA a conservative performance indicator for 46 other
31 TOrcs at two different RO feed temperatures. These results suggest that online monitoring of
32 NDMA in RO feed and permeate can allow for ensuring the removal of larger TOrcs, which
33 could provide additional protection of public health in potable reuse.

34 **Keywords:** *N*-nitrosodimethylamine; 1,4-dioxane; trace organic compounds; potable reuse;
35 reverse osmosis.

36 1 Introduction

37 In response to frequent and severe drought, the use of advanced treatment processes to
38 reclaim wastewater for augmenting drinking water supply, also known as potable reuse, has
39 been increasingly adopted in many countries and regions of world.¹ High quality reclaimed
40 water is typically produced through conventional wastewater treatment followed by several
41 layers of advanced treatment processes including microfiltration/ultrafiltration (UF), reverse
42 osmosis (RO), and advanced oxidation process (AOP).² Among these advanced treatment
43 processes, RO is a critical physical barrier to remove trace organic compounds (TOrcs) such
44 as disinfection by-products, endocrine disrupting compounds, and pharmaceuticals and
45 personal care products that are ubiquitous in reclaimed wastewater.³⁻⁷ Thus, monitoring the
46 integrity of the RO process is essential during potable water reuse operation. In particular,
47 much of the recent attention has been given towards two specific TOrcs namely *N*-
48 nitrosodimethylamine (NDMA) and 1,4-dioxane.⁸⁻¹¹ The former is a disinfection by-product
49 occurring ubiquitously in reclaimed wastewater,^{9, 12} while the latter is a common industrial
50 solvent often accidentally released into the sewer and the environment.¹³ Both NDMA and
51 1,4-dioxane are probable carcinogens and thus are regulated in potable water reuse
52 applications. The occurrences of NDMA in RO permeate intended for potable water reuse
53 have occasionally been reported^{14, 15} at above the NDMA notification levels (10 ng/L) by the
54 authority in California, USA.¹⁶

55 Most advanced water treatment plants for potable reuse applications are equipped with AOP-
56 based post treatment to ensure adequate removal of NDMA and 1,4-dioxane in addition to
57 disinfection requirements. Photolysis by UV irradiation is sufficient for the decomposition of
58 NDMA,¹⁷ while reactive free radicals (e.g. HO[•] and Cl[•]) generated by AOP are necessary to
59 oxidize 1,4-dioxane. As a result, 1,4-dioxane removal has been to benchmark AOP
60 performance as an indicator for the removal of other TOrcs in California, USA. For potable

61 reuse application, AOP is required to achieve a minimum 0.5-log (69%) removal of 1,4-
62 dioxane by California Office of Administrative Law.¹⁸ Since 1,4-dioxane is an industrial
63 solvent, its occurrence in wastewater is site specific and is often associated with accidental
64 release in the wastewater catchment. 1,4-dioxane concentration as high as 100 µg/L has been
65 reported in treated wastewater while a lower concentration has been reported in the RO
66 feed.^{19,20} Thus, it is very difficult to directly validate the rejection of 1,4-dioxane by RO in a
67 full scale plant due to its intermittent occurrence of 1,4-dioxane in wastewater. For example,
68 Orange County Water District (CA, US)²¹ has reported that weekly sampling programs
69 identified 1,4-dioxane at an yearly average of 2.2 µg/L in the secondary effluent (i.e. inflow
70 of water recycling plant) but at below reportable detection limit (1 µg/L) in RO permeate.
71 Any surrogate performance indicator to reliably provide any credibility for 1,4-dioxane
72 removal by RO can enhance the safety of recycled water.

73 In addition to the rejection of 1,4-dioxane, a reliable surrogate performance indicator to
74 monitor the rejection of TOrCs by RO can also improve treatment efficiency and reliability.
75 In the context of membrane integrity monitoring, a surrogate indicator is required to satisfy
76 three criteria for practical implementation. These criteria include: (a) ubiquitous occurrence
77 in the source water (i.e. RO feed), (b) online monitoring capability and (c) similar behaviour
78 with the target or can provide a conservative estimate. To date, surrogate performance
79 indicators such as conductivity or total organic carbon (TOC) rejection have been commonly
80 used for the integrity monitoring of RO for pathogen reduction. Nevertheless, no surrogate
81 indicators have been fully established to ensure of TOrC removal by RO.²²

82 The authors²³ have recently developed a very fast, sensitive, and reliable analytical technique
83 for quantifying NDMA concentration in reclaimed water online. NDMA analysis is based on
84 high-performance liquid chromatography followed by photochemical reaction and

85 chemiluminescence detection.²⁴ This technique is highly sensitive and can quantify NDMA in
86 RO feed water and permeate at 3 ng/L and below 1 ng/L, respectively. By contrast,
87 conventional techniques for NDMA analysis are not capable of online monitoring due mainly
88 to the requirement of pre-concentration steps including liquid or solid phase extraction.
89 NDMA, the smallest among TOrCs regulated in potable reuse, is ubiquitous in secondary
90 treated effluent and is formed as a by-product of chloramination.²⁵⁻²⁷ A recent study by the
91 authors²⁸ has also demonstrated that NDMA can be used as potential surrogate for monitoring
92 the rejection of six TOrCs by RO. NDMA has the potential of being a surrogate performance
93 indicator for 1,4-dioxane because of their similarity in chemical properties (e.g. molecular
94 weight, hydrophobicity, and uncharged species). Further studies are also needed to
95 demonstrate that NDMA rejection is actually lower than the rejection of many other TOrCs,
96 because there could be several hundreds of chemicals listed in potable reuse guidelines (e.g.
97 387 compounds in Queensland, Australia).²⁹

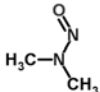
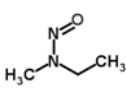



98 The objective of this study was to evaluate the potential of online monitoring of NDMA in
99 RO feed and permeate to ensure the removal of many TOrCs, which is highly relevant to
100 potable reuse. Due to the limited knowledge on 1,4-dioxane rejection by RO, 1,4-dioxane
101 was first tested at the laboratory scale to clarify the efficacy of monitoring NDMA rejection
102 as a surrogate indicator. In addition, the correlation between the rejection of NDMA and 1,4-
103 dioxane was evaluated using online NDMA monitors at the pilot scale. Further pilot-scale
104 experiments using other 46 TOrCs were conducted to clarify (a) whether NDMA has the
105 lowest rejection by RO and (b) which TOrC needs more attention for its rejection during
106 monitoring of NDMA.

107 2 Methods

108 2.1 Chemicals

109 Certified analytical grade solutions of *N*-nitrosamines – NDMA, *N*-nitrosomethylethylamine
110 (NMEA), *N*-nitrosopyrrolidine (NPYR), and *N*-nitrosomorpholine (NMOR) – were
111 purchased from Ultra Scientific (Kingstown, RI, USA). These solutions were used to prepare
112 working stock solution containing *N*-nitrosamines in pure methanol at 1 µg/mL of each
113 compound. Analytical grade 1,4-dioxane was purchased from Wako Pure Chemical
114 Industries (Osaka, Japan). A working stock solution containing 1000 µg/mL 1,4-dioxane was
115 also prepared in pure methanol. Physicochemical properties of four *N*-nitrosamines and 1,4-
116 dioxane are displayed in **Table 1**.

117 **Table 1:** Physicochemical characteristics of the selected *N*-nitrosamines and 1,4-dioxane.

Name	NDMA	NMEA	NPYR	NMOR	1,4-dioxane
Structure					
Molecular formula	C ₂ H ₆ N ₂ O	C ₃ H ₈ N ₂ O	C ₄ H ₈ N ₂ O	C ₄ H ₈ N ₂ O ₂	C ₄ H ₈ O ₂
Molecular weight [Da]	74.1	88.1	100.1	116.1	88.1
pKa ^{1,2}	3.5	3.4	3.3	3.1	Not ionized
Log <i>D</i> at pH8 ¹	0.04	0.40	0.44	-0.18	-0.09

118 ¹ Chemicalize (<https://chemicalize.com>)

119 ² Strongest base pKa between 0 and 14.

120 In addition, 46 TOrCs frequently detected in municipal wastewater were also investigated
121 (**Table S1**). A stock solution was prepared from analytical grade chemicals to contain 100
122 µg/mL of each of these compounds in pure methanol. In this study, TOrCs are categorised as
123 neutral (≤50% ionised) or charged (≥50% ionised) compounds at pH 6.5 which is the feed
124 solution pH in this study (**Table S1**). These charged TOrCs can be further classified as
125 positively or negatively charged or zwitterions. Neutral TOrCs can also be further classified

126 as hydrophilic ($\log D < 2$) or hydrophobic ($\log D \geq 2$) according to their Log D value at pH
127 6.5 ($\log D$ is the logarithm base 10 of the apparent water-octanol distribution coefficients at a
128 specific pH).^{30, 31}

129 A secondary effluent was further treated by ultrafiltration (UF) and used for all laboratory
130 and pilot scale RO experiments in this study. This UF-treated secondary effluent had a pH of
131 6.6 ± 0.1 .

132 **2.2 Laboratory-scale RO system and experiments**

133 Two commercial thin-film composite polyamide RO membranes – namely ESPA2 and
134 Hydrapro[®]501 – were provided by Hydranautics (Oceanside, CA, USA). The ESPA2 is a low
135 pressure membrane for water reuse applications. The HYDRAPRO[®]501 (HYDRA) is designed
136 for industrial applications where the feed stream can be at a high temperature (condensate
137 water) or contain proteins (e.g. for protein recovery), surfactants (e.g. laundry wastewater
138 recycling), and even aggressive chemicals (e.g. chemical recovery).

139 The rejection of four *N*-nitrosamines and 1,4-dioxane by RO was evaluated using a
140 laboratory-scale RO system (**Fig. S1**). The RO system was operated by recirculating the
141 feedwater and permeate at a permeate flux of 20 L/m²h, 40 mL/min cross-flow rate, and
142 20 °C feedwater temperature. The concentration of NDMA and 1,4-dioxane in the RO
143 feedwater were 500 ng/L and 500 µg/L, respectively. Prior to feed and permeate sample
144 collection (in amber vials) for TOrC analysis, the system was stabilised for at least 1 h.
145 Sample volumes for *N*-nitrosamines and 1,4-dioxane were 1.5 and 100 mL, respectively.

146 **2.3 Pilot-scale system and experiments**

147 Pilot validation was performed using an RO system equipped with one 4-in. spiral-wound
148 ESPA2 element (Hydranautics, Oceanside, CA, USA) (**Fig. S2**). This element contained 7.43

149 m² of membrane. The RO system was operated at a constant permeate flux of 20 L/m²h and
150 system recovery of 20%.

151 Two separate pilot-scale experiments were conducted. The first experiment was conducted
152 using a UF-treated wastewater containing NDMA and 1,4-dioxane for 7.5 h. It has been
153 established that the rejection of hydrophilic and neutral chemicals such as *N*-nitrosamines
154 reach a steady state condition within 1 h;³² thus, the impact of the short experimental period
155 on their rejection is negligible. Because the UF-treated wastewater contained negligible
156 concentrations of NDMA (3.2 ng/L) and 1,4-dioxane (<2 µg/L), their stock solutions were
157 added into the RO feed. From 0 to 2 h, the concentration of NDMA and 1,4-dioxane in the
158 RO feedwater was incrementally increased from zero to about 150 ng/L and 100 µg/L,
159 respectively. The feedwater temperature was adjusted between 15 and 33 °C. RO feedwater
160 and RO permeate were continuously fed to two separate online NDMA analysers. The second
161 experiment was performed using a UF-treated wastewater containing 46 TOxCs. The system
162 was operated over 46 h prior to the sample collection to ensure that their adsorption had
163 reached the steady state condition, and thus, minimise the effect of adsorption of hydrophobic
164 TOxCs to RO membrane on their rejection. TOxCs were introduced to the feedwater to obtain
165 45 µ/L of each compound. The feedwater temperature was adjusted at 20 °C. RO feed and
166 permeate samples were collected in 500 mL glass bottles for the analysis of TOxCs.

167 **2.4 Analytical techniques**

168 The *N*-nitrosamine concentration was determined by HPLC-PR-CL.³³ Sample volumes into
169 the HPLC-PR-CL were 20 µL for UF-treated wastewater (i.e. RO feedwater) and 200 µL for
170 RO permeate. For samples collected during laboratory-scale experiments, an auto-sampler
171 was used for the *N*-nitrosamine analysis. The method detection limits (MDLs) of NDMA,
172 NMEA, NPYR and NMOR for a 200 µL injection volume were 0.3, 0.7, 1.4 and 0.8 ng/L,

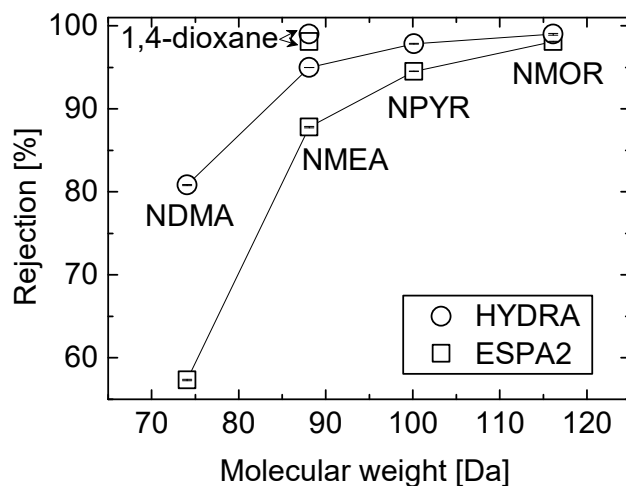
173 respectively. The MDLs of NDMA, NMEA, NPYR and NMOR for a 20 μ L injection volume
174 were 2.7, 6.3, 7.7 and 11.8 ng/L, respectively. For pilot-scale experiments, two online NDMA
175 monitoring systems were configured with two HPLC-PR-CL instruments, each of which was
176 equipped with a six-port valve (**Fig. S3**).²⁸ Concentrations of 1,4-dioxane were determined by
177 headspace (HS) solid-phase micro-extraction followed by gas chromatography (GC) and
178 mass spectrometry (MS) using an Agilent G1888/6890/5973 HS-GC-MS with a VF-624 ms
179 column (Agilent Technologies, Palo Alto, CA, USA). 1,4-Dioxane-d8 was used as the
180 surrogate standard. The detection limits of 1,4-dioxane was 2 μ g/L. Concentrations of TORCs
181 were determined using a method previously reported in literature.³⁴ This method involves
182 solid phase extraction followed by analytical quantification using an ultra-performance liquid
183 chromatography equipped with atmospheric pressure ionization and tandem mass
184 spectrometer.

185 **3 Results and discussion**

186 ***3.1 Role of molecular size for the rejection of N-nitrosamines and 1,4-*** 187 ***dioxane***

188 The four *N*-nitrosamines investigated here and 1,4-dioxane are neutral and hydrophilic. Thus,
189 their rejection was governed mostly by size interaction.³⁰ As expected, the rejection of these
190 neutral and hydrophilic *N*-nitrosamines by both ESPA2 and HYDRA RO membranes
191 increased with increasing molecular weight. It is noteworthy that 1,4-dioxane rejection (i.e.
192 >98%) was markedly higher than that of NDMA (**Fig. 1a**). Indeed, 1,4-dioxane rejection by
193 the HYDRA and ESPA2 RO membranes (98 and 99%, respectively) was higher than NMEA
194 rejection (which is also better rejected by RO than NDMA) (**Fig. 1a**) despite their identical
195 molecular weight (88.1 Da) (**Table 1**). Our results are consistent with a previous study by

196 Schoonenberg Kegel et al.³⁵ who also reported higher rejection of 1,4-dioxane (96%) than
197 that of NDMA (74%) by an RO membrane.



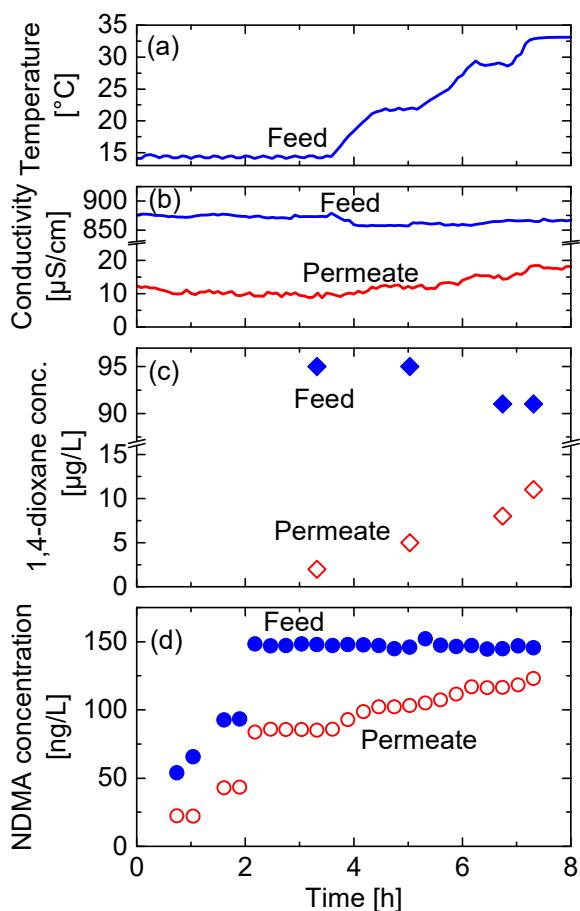
198
199 **Fig. 1** – Rejection of 1,4-dioxane and four *N*-nitrosamines by RO membranes as a function of
200 their molecular weight at the laboratory scale (permeate flux = 20 L/m²h, feed temperature =
201 20.0 ± 0.1 °C). Values reported here are the average and ranges of duplicate analytical results.

202 **3.2 Online monitoring of NDMA for 1,4-dioxane removal**

203 The potential of online monitoring of NDMA as a surrogate indicator for 1,4-dioxane
204 rejection by RO was evaluated at the pilot scale by identifying the correlation between their
205 rejection at various feedwater temperatures. Permeate flux, system recovery, and feed flow
206 rate (indicating the cross flow velocity in the feed channel) were constant at 20 L/m²h, 20%
207 and 12.5 L/min, respectively. In response to the changes in feedwater temperature between 15
208 to 33 °C, transmembrane pressure across the RO element decreased from 0.45 to 0.26 MPa.
209 Accordingly, in the RO permeate, conductivity increased from 10 to 18 μS/cm, NDMA
210 concentration increased from 85 to 123 ng/L, and 1,4-dioxane concentration increased from 2
211 to 11 μg/L (**Fig. 2**). The increase in solute concentration in RO permeate is very likely due to
212 the increased permeation of these chemicals. NDMA and 1,4-dioxane are both very
213 hydrophilic. Thus, their adsorption onto the membrane surface and consequently desorption

214 from the membrane surface are not expected. In fact, NDMA concentration in the RO feed
215 was constant throughout all experiments. The increase in solute permeation due to increasing
216 temperature led to a decrease in the rejection of conductivity, NDMA and 1,4-dioxane from
217 98.8% to 97.9%, from 43% to 16% and from 98% to 88%, respectively.

218 It is important to note that NDMA rejection by ESPA2 membrane at the pilot scale (29%)
219 was far lower than that at the laboratory scale (57%) despite their similar operating
220 conditions: same permeate flux (20 L/m²h) and similar temperature 20–22 °C. Indeed, this is
221 usually observed when the RO process is up-scaled.³⁶ In the spiral wound module, NDMA
222 concentration in the feed increases toward the end of the module, subsequently causing an
223 increase in solute concentration in RO permeate. In addition, hydrodynamic distribution in a
224 spiral wound module is not uniform and the flux also decreases toward the end of the module.
225 This non-uniform hydraulic distribution can also increase solute transport to RO permeate
226 stream, resulting in a reduction in overall solute rejection.

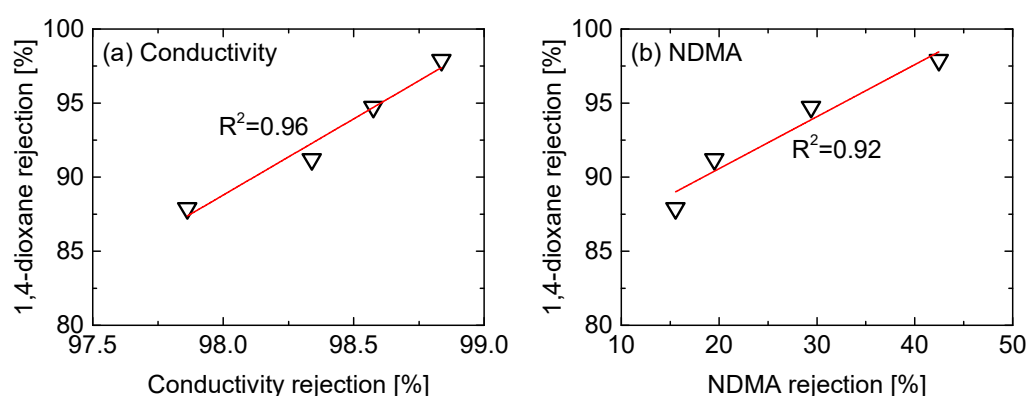


227

228 **Fig. 2** – The effects of changes in (a) feed temperature on (b) conductivity, (c) 1,4-dioxane
 229 and (d) NDMA concentrations during the system operation using the UF-treated wastewater
 230 by ESPA2 RO membrane at the pilot scale (permeate flux = 20 L/m²h).

231 Data from **Fig. 2** were also used to evaluate the correlation between the rejections of 1,4-
 232 dioxane and NDMA as well as conductivity as potential surrogate indicators. Pilot-scale data
 233 show a strong correlation ($R^2 = 0.96$) between conductivity and 1,4-dioxane rejection (**Fig.**
 234 **3a**). Nevertheless, conductivity rejection varied only slightly by 0.9% (i.e. from 97.9 to
 235 98.8%), which was much narrower than 1,4-dioxane rejection by 10% (i.e. from 88 to 98%).
 236 A high correlation ($R^2 = 0.92$) was also obtained between NDMA rejection and 1,4-dioxane
 237 rejection (**Fig. 3b**). The variation in NDMA rejection was over a broad range (16–43%) when
 238 1,4-dioxane rejection varied from 88% to 98%. Results in **Fig. 3** suggest that, compared to
 239 conductivity, NDMA is a more sensitive surrogate indicator, one that can adequately indicate
 240 changes in separation performance due to variation in operating conditions. By contrast,

241 conductivity rejection is not significantly affected by operating conditions. The successful
242 pilot-scale demonstration confirms potential for using online monitoring of NDMA rejection
243 to continuously ensure 1,4-dioxane rejection by RO for potable water reuse. However, further
244 validations focusing on the effect of membrane variety (e.g. high rejection RO membranes)
245 and long-term changes (e.g. membrane fouling, chemical cleaning and membrane aging) are
246 still necessary prior to the implementation in the full scale.



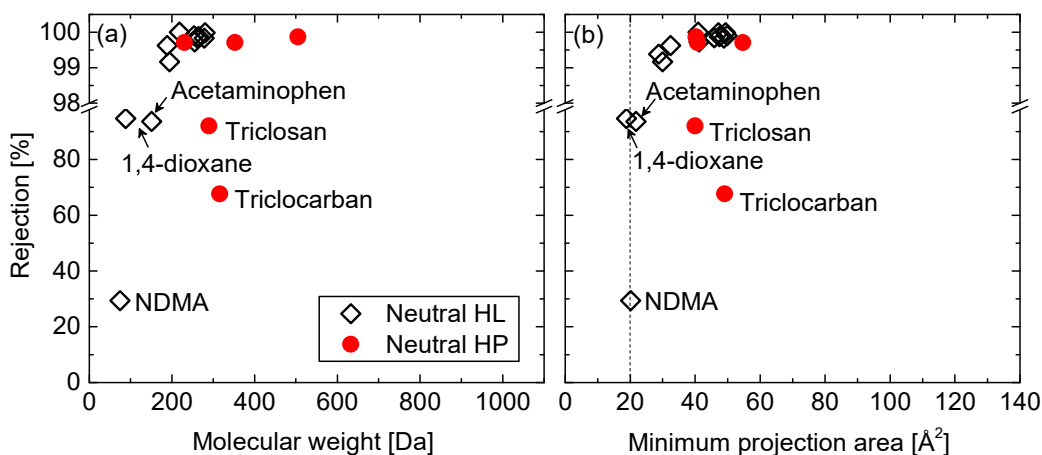
247
248 **Fig. 3** – Correlation between 1,4-dioxane rejection and (a) conductivity rejection and (b)
249 NDMA rejection by ESPA2 RO membrane at pilot-scale operation.

250 **3.3 Online monitoring of NDMA for other 46 TOrcs**

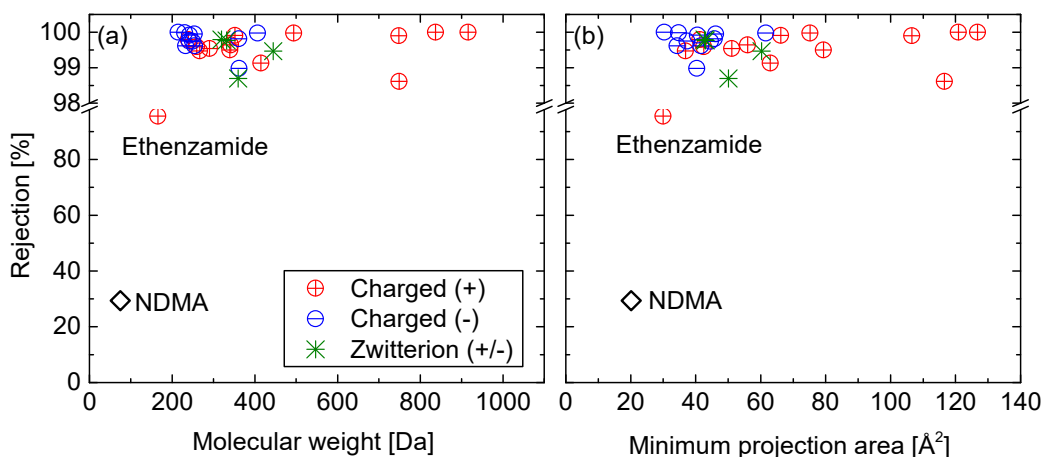
251 In addition to other *N*-nitrosamines and 1,4-dioxane, the potential use of online monitoring of
252 NDMA as a surrogate indicator for TOrcs was evaluated by comparing the rejection of
253 NDMA and that of 46 TOrcs at pilot-scale operation (**Fig. S4**). Similar to the results reported
254 in **Fig. 2**, the rejection of neutral TOrcs at 20 °C increased with increasing molecular weight
255 (**Fig. 4a**), indicating that their rejection was mainly governed by a size exclusion mechanism.
256 A similar trend in TOrc rejection was observed at an elevated feed temperature of 30 °C (**Fig.**
257 **S5**). A plot of the “minimum projection area”, which is the area of the compound projected
258 with the minimum plane of its circular disk (**Fig. S6**), revealed a better correlation in
259 rejection for hydrophilic TOrcs (**Fig. 4b**). It is clear that a minimum projection area of

260 approximately 20 \AA^2 is the critical boundary for determining the permeation of TOrCs
261 through the ESPA2 RO membrane.

262 Among all TOrCs investigated here, NDMA had the lowest rejection by RO; thus, NDMA is
263 a conservative surrogate indicator. All neutral TOrCs were rejected at greater than 98% with
264 only a few exceptions. These exceptions included one small hydrophilic TOrC
265 (acetaminophen, 94%) and two hydrophobic TOrCs (triclosan, 92%; and triclocarban, 68%).
266 Acetaminophen was the smallest pharmaceutical selected in the study; thus, it is reasonable to
267 attribute the low rejection to a molecular size interaction. The low rejection of triclosan and
268 triclocarban could be due to their adsorption to the polymeric RO membrane surface.
269 Triclosan and triclocarban are relatively large in molecular size (MW = 290 and 316 Da,
270 respectively) but are also very hydrophobic (Log D = 4.93 and 4.95, respectively) compared
271 to all other TOrCs selected here. Hydrophobic interaction between these compounds and the
272 membrane polymeric matrix can lower their rejection.^{37, 38} Due to adsorption, these chemicals
273 can accumulate at the membrane surface, and subsequently result in more diffusion through
274 the membrane active skin layer. The low rejection of hydrophobic TrOCs has been reported
275 with polyamide RO membranes.³⁹⁻⁴² Thus, it is important to include these two TOrCs when
276 validating a surrogate indicator for TOrC rejection. More importantly, because the rejection
277 of triclocarban is the lowest amongst all TOrCs investigated here (although it is still higher
278 than the rejection of NDMA), online monitoring of NDMA can play an important role to
279 ensure its removal by RO when triclocarban concentrations in RO feed exceed its regulated
280 limit.



281
 282 **Fig. 4** – Rejection of NDMA, 1,4-dioxane and 17 neutral TOxCs by ESPA2 RO membrane as
 283 a function of their (a) molecular weight and (b) minimum projection area at the pilot scale
 284 treatment of UF-treated wastewater (permeate flux = 20 L/m²h, feed temperature = 20–22 °C).
 285 It has been well demonstrated in the literature that the rejection of ionised compounds by RO
 286 membranes are typically much higher than neutral compounds.^{30, 43} As expected, the rejection
 287 of most of the charged TOxCs by the ESPA2 RO membrane was high (>98 and >97%) at 20
 288 and 30°C, respectively (**Fig. 5** and **Fig. S7**). Nevertheless, the rejection of one positively
 289 charged compound (ethenzamide, 96% at 20 °C) appeared to be lower than the other charged
 290 TOxCs presumably due to its small size (MW = 165 Da and minimum projection area = 30 Å)
 291 and positive charge. In fact, the rejection of positively charged TOxCs was generally lower
 292 than that of negatively charged TOxCs. Despite of the low rejection of some TOxCs, the low
 293 rejection can generally be explained by mechanisms related to size, charge or hydrophobic
 294 interactions. More importantly, the results here confirmed that NDMA is a conservative
 295 surrogate indicator for monitoring the rejection of all TOxCs selected in this study.



296

297 **Fig. 5** – Rejection of NDMA and 29 charged TOxCs by ESPA2 RO membrane as a function
 298 of their (a) molecular weight and (b) minimum projection area at the pilot scale treatment of
 299 UF-treated wastewater (permeate flux = 20 L/m²h, feed temperature = 20–22 °C).

300 **3.4 Implication to full-scale operation**

301 NDMA meets all three key attributes for a good surrogate indicator for monitoring TOxC
 302 rejection by RO membranes. NDMA is ubiquitous in reclaimed water used as the feed
 303 solution to RO at well above the instrument detection limit (1–2 ng/L).^{14, 44} Recent analytical
 304 development has resulted in a reliable and affordable technique for online NDMA monitoring
 305 at concentrations relevant to their occurrence in reclaimed water. This can allow for
 306 monitoring NDMA online to continuously ensure the removal of 1,4-dioxane, *N*-nitrosamines,
 307 and other TOxCs by RO during potable water reuse. It is noted that the monitoring of the
 308 surrogate performance indicator is achievable only when the online instrument is installed in
 309 both RO feed and permeate streams. In other words, two online instruments are required. The
 310 online monitoring of NDMA in both RO feed and permeate could also provide significant
 311 benefits for detecting malfunctions of RO systems in terms of TOxC removal. However, this
 312 study used high NDMA concentrations (about 150 ng/L) in the RO feedwater. Because the
 313 online instrument is theoretically capable of analysing much lower concentrations (e.g. 2
 314 ng/L) in treated wastewater as demonstrated in a previous study using a bench-top

315 instrument,⁴⁵ further online validation tests using reclaimed wastewater (with NDMA
316 concentration in the typical range of 20–30 ng/L) at an advanced water treatment plant will
317 be the scope of our future study. Moreover, this study has demonstrated the rejection of only
318 51 TOrCs in total, which is far less than the number of compounds for potential regulation
319 (e.g. 387 compounds in Queensland, Australia).²⁹ Thus, further validation study with more
320 chemicals is needed to identify that NDMA rejection is the most conservative chemical
321 among regulated TOrCs.

322 **4 Conclusion**

323 Results from this study demonstrate the potential of using online monitoring of NDMA to
324 ensure the removal of other TOrCs including 1,4-dioxane by RO in potable reuse applications.
325 A strong correlation between NDMA and 1,4-dioxane rejections was validated. In addition,
326 NDMA rejection was lower than all TOrCs investigated in this study. In other words, a
327 conservative result can be expected for NDMA as a surrogate indicator. Using NDMA as a
328 surrogate indicator for monitoring the rejection of other TOrCs can allow water utilities to
329 provide a higher removal credit for difficult-to-analyse compounds such as 1,4-dioxane. This
330 study demonstrated that NDMA rejection by the HYDRA RO membrane at 81%, which
331 could also provide the minimum rejection credit of 81% for 1,4-dioxane. This result is
332 significant as the current removal credit by RO for 1,4-dioxane is zero since 1,4-dioxane does
333 not occur continuously in the RO feed and it cannot be artificially introduced to the feed for
334 validation.

335 **4 Conflicts of interest**

336 There are no conflicts to declare.

337 **5 Acknowledgements**

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Online monitoring of *N*-nitrosodimethylamine for the removal assurance of 1,4-dioxane and other trace organic compounds by reverse osmosis

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Supplementary Information

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Table S1 – Physicochemical characteristics of the selected TOrcs.

Compound	Structure	MW [Da]	Minimum projection area* [Å ²]	Log <i>D</i> at pH 6.5*	pK _a *	Ionisatio n at pH 6.5* [%]	Sup plier **
Neutral & hydrophilic							
<i>N</i> -nitrosodimethylamine	C ₂ H ₆ N ₂ O	74.08	20.10	0.04	3.52	0	US
1,4-dioxane	C ₄ H ₈ O ₂	88.10	18.80	-0.09	-	0	WA
<i>N</i> -nitrosomethylthylamine	C ₃ H ₈ N ₂ O	88.11	22.03	0.40	3.42	0	US
<i>N</i> -nitrosopyrrolidine	C ₄ H ₈ N ₂ O	100.12	25.04	0.44	3.30	0	US
<i>N</i> -nitrosomorpholine	C ₄ H ₈ N ₂ O ₂	116.12	26.92	-0.18	3.14	0	US
Acetaminophen	C ₈ H ₉ NO ₂	151.17	21.75	0.91	9.46	0	WA
Theophylline	C ₇ H ₈ N ₄ O ₂	180.17	28.75	-0.79	7.82, -0.78	5	WA
Antipyrine	C ₁₁ H ₁₂ N ₂ O	188.23	32.41	1.22	0.49	0	WA
Caffeine	C ₈ H ₁₀ N ₄ O ₂	194.19	30.01	-0.55	-1.16	0	WA
Primidone	C ₁₂ H ₁₄ N ₂ O ₂	218.26	40.90	1.12	11.5	0	WA
Sulfathiazole	C ₉ H ₉ N ₃ O ₂ S ₂	255.31	41.22	0.86	6.93, 2.04	27	WA
Cyclophosphamide	C ₇ H ₁₅ Cl ₂ N ₂ O ₂ P	261.08	45.84	0.10	13.43, 0.08	0	WA
Sulfamerazine	C ₁₁ H ₁₂ N ₄ O ₂ S	264.30	47.43	0.41	6.99, 2	24	WA
Sulfadimidine	C ₁₂ H ₁₄ N ₄ O ₂ S	278.33	48.80	0.54	6.99, 2	24	WA
Sulfamonomethoxine	C ₁₁ H ₁₂ N ₄ O ₃ S	280.30	47.18	0.66	7.15, 2.63	18	WA
Sulfadimethoxine	C ₁₂ H ₁₄ N ₄ O ₄ S	310.33	49.84	1.14	6.91, 1.95	28	WA
Thiamphenicol	C ₁₂ H ₁₅ Cl ₂ NO ₅ S	356.21	49.34	-0.22	8.75	1	WA
Neutral & hydrophobic							
Crotamiton	C ₁₃ H ₁₇ NO	203.29	40.23	3.09	-0.60	0	LKT
Isopropylantipyrine	C ₁₄ H ₁₈ N ₂ O	230.31	40.75	2.35	0.87	0	WA
Triclosan	C ₁₂ H ₇ Cl ₃ O ₂	289.54	40.00	4.95	7.68	6	WA
Triclocarban	C ₁₃ H ₉ Cl ₃ N ₂ O	315.58	49.11	4.93	11.42	0	SA
Griseofulvin	C ₁₇ H ₁₇ ClO ₆	352.77	54.74	2.17	-	0	MP
Positively charged							
Ethenzamide	C ₉ H ₁₁ NO ₂	165.19	29.99	1.53	6.2, 7.9	51	WA
Salbutamol	C ₁₃ H ₂₁ NO ₃	239.32	41.28	-2.01	9.4, 10.12	100	WA
Propranolol	C ₁₆ H ₂₁ NO ₂	259.35	42.47	-0.32	9.67, 14.09	100	WA
Atenolol	C ₁₄ H ₂₂ N ₂ O ₃	266.34	36.85	-2.48	9.68, 14.07	100	WA
Trimethoprim	C ₁₄ H ₁₈ N ₄ O ₃	290.32	51.14	0.60	7.16	82	WA
Disopyramide	C ₂₁ H ₂₉ N ₃ O	339.48	79.36	0.11	10.42	100	WA
Sulpiride	C ₁₅ H ₂₃ N ₃ O ₄ S	341.43	55.95	-1.55	8.39, 10.24	99	WA
Pirenzepine	C ₁₉ H ₂₁ N ₅ O ₂	351.41	66.19	0.19	7.2, 14.78	82	WA
Diltiazem	C ₂₂ H ₂₆ N ₂ O ₄ S	414.52	62.99	1.05	8.18, 12.86	98	WA
Tiamulin	C ₂₈ H ₄₇ NO ₄ S	493.75	75.23	1.61	9.51, 14.43	100	WA
Clarithromycin	C ₃₈ H ₆₉ NO ₁₃	747.97	106.52	1.36	8.38, 12.46	99	WA
Azithromycin	C ₃₈ H ₇₂ N ₂ O ₁₂	749.00	116.57	-2.89	9.57, 12.43	100	LKT
Roxithromycin	C ₄₁ H ₇₆ N ₂ O ₁₅	837.06	126.79	0.47	9.08, 12.45	100	WA
Tylosin	C ₄₆ H ₇₇ NO ₁₇	916.11	120.92	1.54	7.2, 12.45	83	WA
Negatively charged							
Clofibric acid	C ₁₀ H ₁₁ ClO ₃	214.65	30.34	-0.08	3.37	100	AA
Naproxen	C ₁₄ H ₁₄ O ₃	230.26	34.77	0.70	4.19	100	WA
Nalidixic acid	C ₁₂ H ₁₂ N ₂ O ₃	232.24	34.30	0.33	4.66, 5.77	84	WA
Mefenamic acid	C ₁₅ H ₁₅ NO ₂	241.29	37.30	2.83	3.89, -1.58	100	WA
Fenoprofen	C ₁₅ H ₁₄ O ₃	242.27	40.56	1.15	3.96	100	LKT
Sulfapyridine	C ₁₁ H ₁₁ N ₃ O ₂ S	249.29	44.58	0.64	6.24, 2.13	65	WA
Sulfamethoxazole	C ₁₀ H ₁₁ N ₃ O ₃ S	253.28	46.11	0.38	6.16, 1.97	69	WA
Ketoprofen	C ₁₆ H ₁₄ O ₃	254.29	41.68	1.05	3.88	100	WA
Levofloxacin	C ₁₈ H ₂₀ FN ₃ O ₄	361.37	45.74	0.27	5.29, 6.16	67	LKT
Bezafibrate	C ₁₉ H ₂₀ ClNO ₄	361.82	40.35	1.37	3.83, -0.84	100	LKT
Lincomycin	C ₁₈ H ₃₄ N ₂ O ₆ S	406.54	61.56	-1.80	7.97, 12.37	97	MP
Zwitterion							
Norfloracin	C ₁₆ H ₁₈ FN ₃ O ₃	319.34	42.78	-0.98	5.58, 8.68	89	WA
Ciprofloxacin	C ₁₇ H ₁₈ FN ₃ O ₃	331.35	42.99	-0.87	5.56, 8.68	89	LKT
Enrofloxacin	C ₁₉ H ₂₂ FN ₃ O ₃	359.40	50.07	0.96	5.52, 6.66	96	ICN
Tetracycline	C ₂₂ H ₂₄ N ₂ O ₈	444.44	62.32	-3.50	8.19, 2.92	97	WA

*Chemical properties: The information was obtained from ChemAxon (<https://www.chemaxon.com/>).

**Suppliers: SA (Sigma-Aldrich Japan, Tokyo, Japan); US (Ultra Scientific, Kingstown, RI, USA); WK (Wako Pure Chemical Industries, Osaka, Japan); LKT (LKT Laboratories, St Paul, MN, USA); AA (Alfa Aesar, Ward Hill, MA, USA); ICN (ICN Biomedicals, Irvine, CA, USA); MP (MP Biomedicals, Santa Ana, CA, USA).

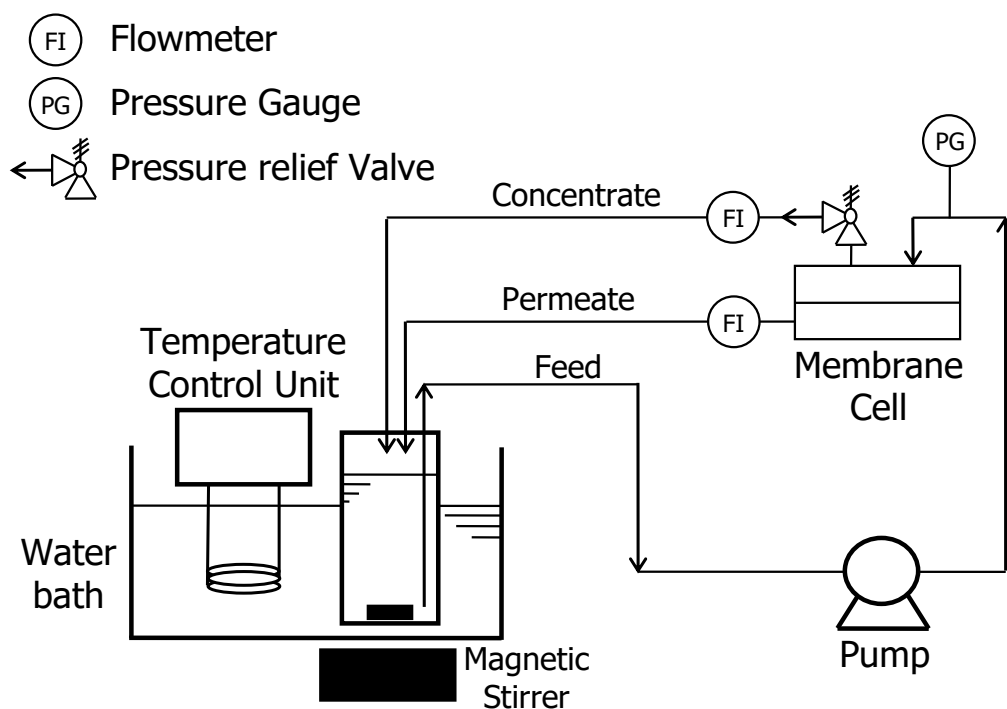


Fig. S1 – Schematic diagram of the cross-flow RO treatment system. A bench-scale RO treatment system was comprised of a stainless steel membrane cell (Iwai Pharma Tech, Tokyo, Japan), high-pressure pump (KP-12, FLOM, Tokyo, Japan), 2-L glass reservoir with a stainless steel heat exchanging coil connected to a temperature control unit (NCB-500, Tokyo Rikakikai, Tokyo, Japan). The membrane cell held a circular flat-sheet membrane coupon with effective surface area of 36.3 cm².

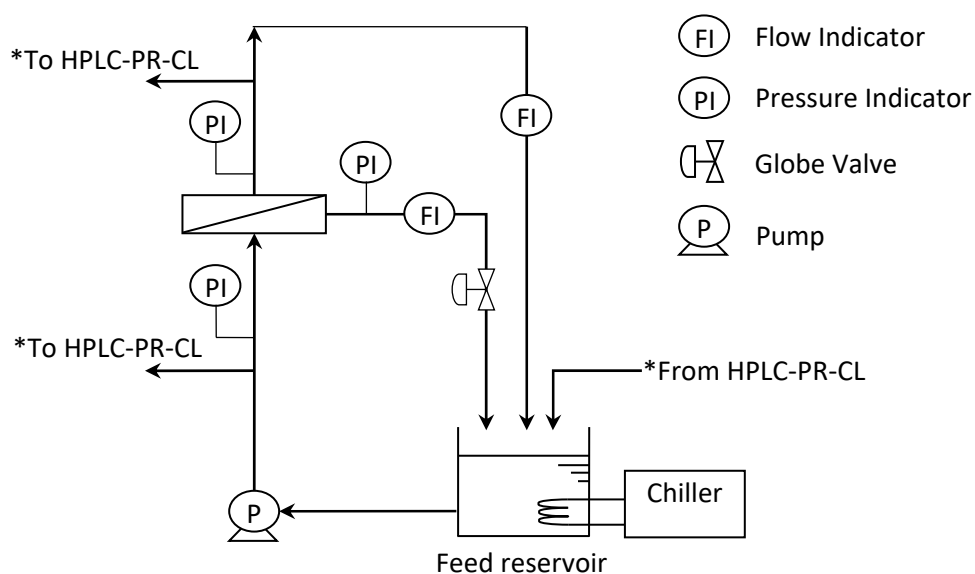


Fig. S2 – Schematic diagram of the pilot-scale RO treatment system. The system comprised of a 4-in. glass-fibre pressure vessel (ROPV, Nangang, China), 65-L stainless steel reservoir, a high-pressure pump (25NED15Z, Nikuni Co., Ltd., Kawasaki, Japan), digital flow meters (FDM, Keyence Co., Osaka, Japan), 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).

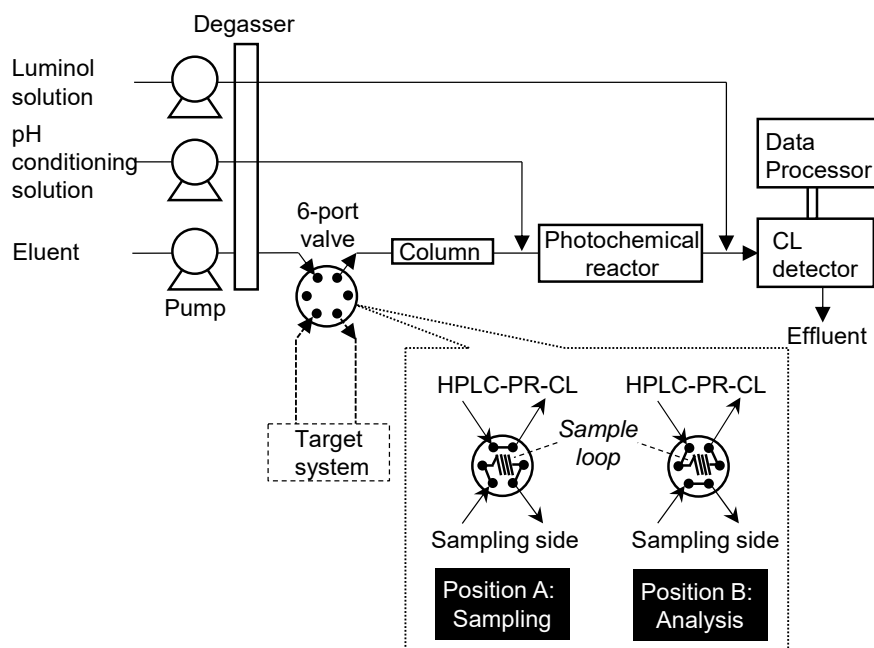


Fig. S3 – Schematic diagram of the online HPLC-PR-CL instrument with a 6-port valve. The online HPLC-PR-CL monitor was assembled with commercially available components: DGU-20A₃ degasser (Shimadzu), six-port valve (HV-2080-01, JASCO, Tokyo, Japan), valve controller (Nichiri Mfg. Co. Ltd., Chiba, Japan), 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.

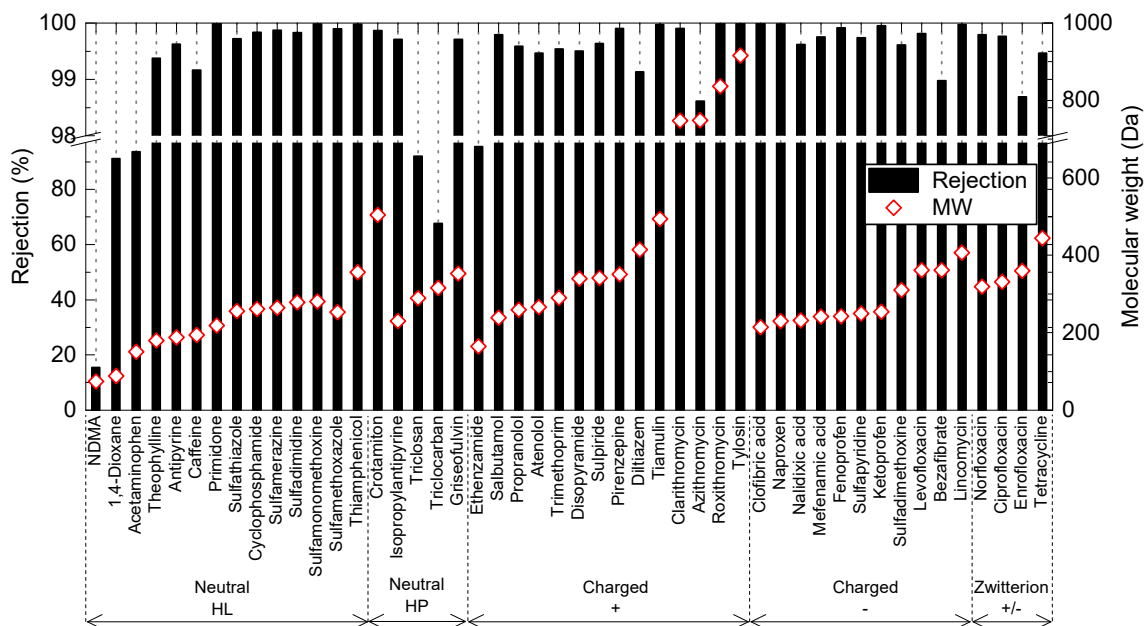


Fig. S4 – Rejection of TOrCs by ESPA2 RO membrane at the pilot scale (permeate flux = 20 L/m²h, feed temperature = 20–22°C).

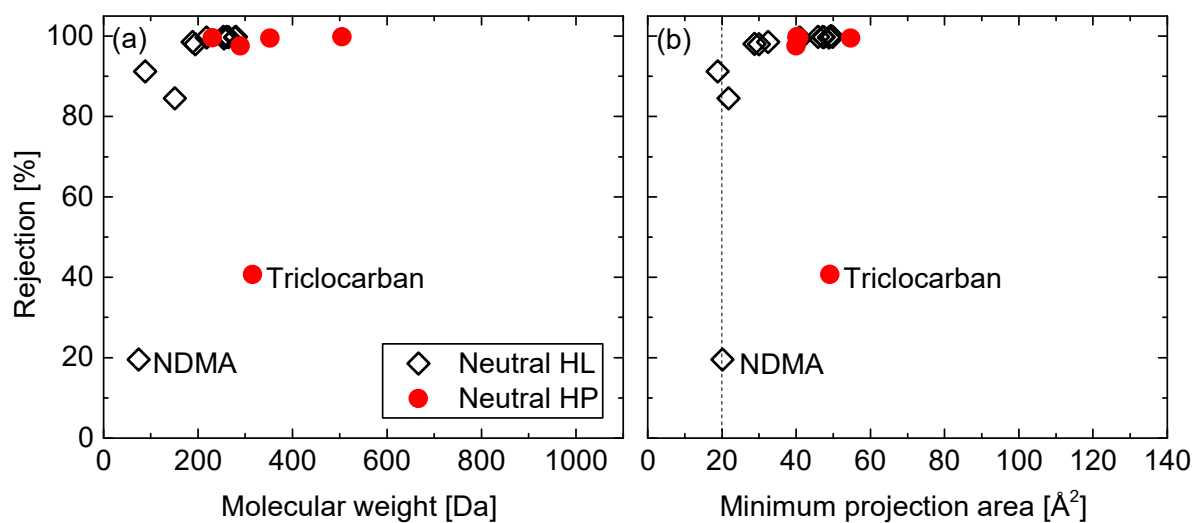


Fig. S5 – Rejection of NDMA, 1,4-dioxane and 17 neutral TOrCs by ESPA2 RO membrane as a function of their (a) molecular weight and (b) minimum projection area at the pilot scale treatment of UF-treated wastewater (permeate flux = 20 L/m²h, feed temperature = 29–30 °C).

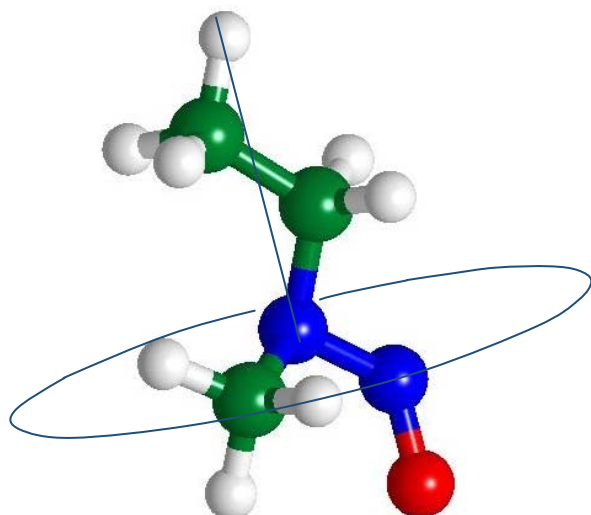


Fig. S6 – Schematic figure of minimum projection area of NMEA. The line perpendicular to the circular disk represents the center axis of the minimum projection area. Minimum projection area is calculated based on the van der Waals radius after the molecular orientation for the projection is fine-tuned by a numerical optimizer (projection optimization).

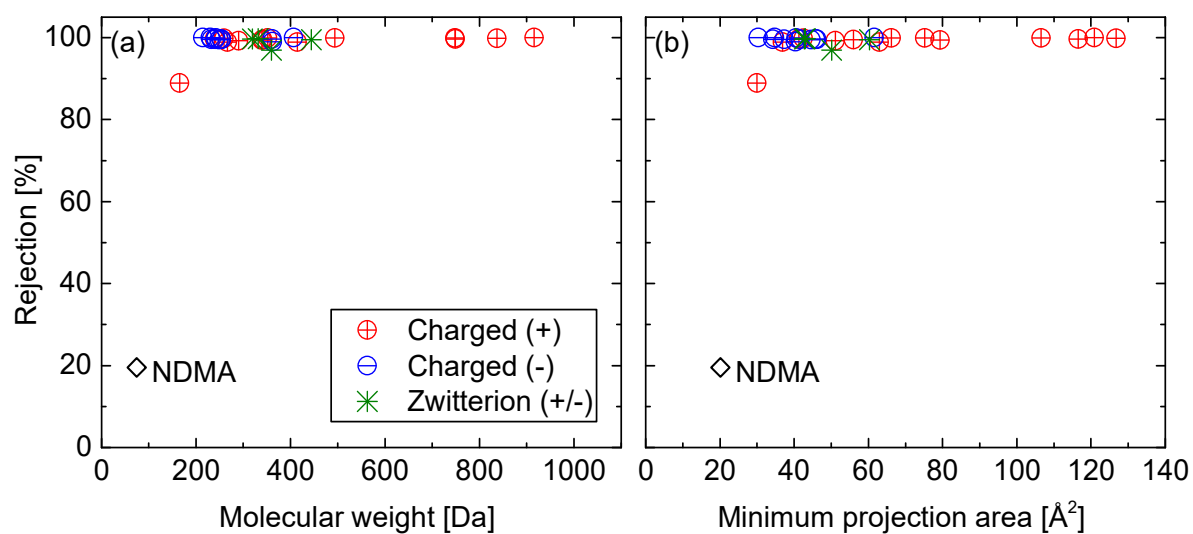


Fig. S7 – Rejection of NDMA and 29 charged TOxCs by ESPA2 RO membrane as a function of their (a) molecular weight and (b) minimum projection area at the pilot scale treatment of UF-treated wastewater (permeate flux = 20 L/m²h, feed temperature = 29–30 °C).