Transport of N-nitrosamines through reverse osmosis membrane: Role of the molecular size and nitrogen atom

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Manuscripts

1   **Transport of *N*-nitrosamines through Reverse Osmosis Membrane:**

2   **Role of the Molecular Size and Nitrogen Atom**

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Abstract

Reliable and adequate removal of small and uncharged trace organic chemicals (TOrCs), particularly *N*-nitrosodimethylamine (NDMA) that is carcinogenic and known to occur in treated effluent, is essential for implementing direct potable water use. This study provides new insights to explain the low rejection of NDMA and other *N*-nitrosamines by reverse osmosis (RO) membranes by examining the role of the molecular size and polarity in their molecular structure. The results show that molecular weight is not a suitable molecular property for evaluating the rejection of small uncharged chemicals. In this study, NDMA and two other uncharged chemicals have similar MW (i.e., 72–74 g/mol), but their rejection by the ESPA2 RO membrane varied considerably from 30 to 88%. Instead, minimum projection area was identified to be a suitable molecular property, indicating that size exclusion plays a primary role in their rejection. It was also identified that chemicals with more nitrogen atoms in their chemical structure consistently showed lower rejection than their counterparts in molecular size. The results suggest that chemicals bearing more nitrogen atoms (e.g., NDMA) are more attracted onto amide or amine functional group of polyamide RO membrane possibly through hydrogen bonding interactions.

Keywords: *N*-nitrosodimethylamine; *N*-nitrosamine; potable reuse; polarity; reverse osmosis.

33   **INTRODUCTION**

34   *N*-nitrosamines are a group of trace organic chemical (TOrC) of significant concern in potable

35   reuse. Notable chemicals in this group include *N*-nitrosodimethylamine (NDMA), *N*-

36   nitrosomethylethylamine (NMEA), *N*-nitrosopyrrolidine (NPYR), and *N*-nitrosomorpholine

37   (NMOR). They are probable carcinogenic and are known to occur in secondary treated effluent

38   after chloramination.[1-3] Several water authorities around the world have issued standards or

39   guidelines to regulate their maximum concentration in water for potable reuse. For example, the

40   maximum concentration of NDMA in potable reuse water is set at 10 ng/L by the Australian

41   Water Recycling Guideline.[4] Unlike most high molecular weight or charged TOrCs, the rejection

42   of small and uncharged chemicals, particularly *N*-nitrosamines, by reverse osmosis (RO)

43   membranes varies widely and is often quite low.[5-8] In particular, since NDMA has a low

44   molecular weight (74 g/mol) and is uncharged in environmental water, NDMA rejection of less

45   than 50% has been reported for many RO membranes.[9] NDMA concentrations in RO permeate

46   higher than the guideline value of 10 ng/L have often been routinely reported in full scale potable

47   water reuse schemes.[7, 10] As a result, residual NDMA is further removed by advanced oxidation

48   process (AOP).[11] In the multi-barrier approach, AOP is expected to act as a redundant treatment

49   barrier to degrade contaminants that have inadvertently passed through RO treatment. Thus,

50   reliable and adequate NDMA removal by RO is essential to ensure public health protection in

51   potable water reuse.

52   A recent study by Fujioka[12] has demonstrated that high rejection of NDMA (e.g. >92%) can be

53   achieved by heat-treating RO membranes. However, economic feasibility of this approach has

54   not been ascertained especially, as NDMA rejection is coupled with a reduction in water

55 permeability. The trade-off relationship is likely associated with reduction in free-volume hole-

56 size, which could limit the transport of both solute (i.e., NDMA) and water molecules.[13, 14]

57 Nevertheless, the role of free-volume hole-size has not been fully understood from the viewpoint

58 of RO membrane properties due to analytical limitations at sub-nanometre scale.[15] In addition to

59 size exclusion, intermolecular interactions between uncharged chemicals and the functional

60 groups of the polyamide skin layer can play a role in determining their transport through RO

61 membrane matrix.[16-19] *N*-nitrosamines, which bear high electronegativity atoms (i.e., nitrogen

62 and oxygen atoms), are polar chemicals with have high partial negative charges. There has been

63 some evidence from the literature that dipolar interaction (e.g. hydrogen bonding) between small

64 and uncharged organic molecules and the membrane polyamide skin layer may their partitioning

65 to and transport through the skin layer.[18, 20]

66 New understanding of the interplay between size exclusion and intermolecular interaction in

67 governing the rejection of small and uncharged organic solutes has the potential to facilitate the

68 development of high NDMA rejection membranes. For example, the strong correlation between

69 minimum projection area and rejection confirms that the clearance between NDMA and the

70 membrane free-volume hole is an important parameter. As a result, membrane development may

71 focus on narrowing down the free-volume hole-diameter without considerably compromising

72 membrane permeability. Likewise, surface coating or modifying the membrane material

73 composition may also be explored to regulate intermolecular interaction, thus, enhancing the

74 rejection of NDMA as well as other small and uncharged organics of significant concern.

75 This study aimed to elucidate the influence of size exclusion and dipolar interactions on the

76 rejection of TOrCs including NDMA by polyamide-based RO membranes. Four *N*-nitrosamines,

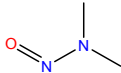77 including NDMA and NMEA, were used to demonstrate the importance of size exclusion. To
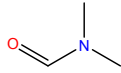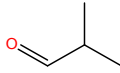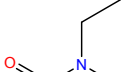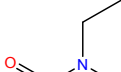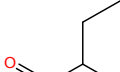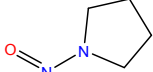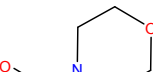
78   identify the importance of dipolar interactions, four other chemicals similar to NDMA or NMEA

79   in structure but have less or no nitrogen atoms were used with two RO membranes that have

80   different nitrogen content on their surface.

MATERIALS AND METHODS

81

Chemicals

82

83   All chemicals used for separation experiments were analytical grade. The four *N*-nitrosamines in

84   this study — namely NDMA, NMEA, NPYR, and NMOR **(Table 1)** — were from Ultra

85   Scientific (Kingstown, RI, USA). In addition, chemicals with similar backbone structure to the

86   two smallest *N*-nitrosamines (i.e. NDMA and NMEA) in terms of molecular weight but are

87   different in the number of nitrogen atoms in the molecule were also selected. For comparison

88   with NDMA, the selected chemicals were dimethylformamide (DMF) and isobutyraldehyde

89   (IBAL), which have one and two nitrogen atoms less than that of the corresponding *N*-

90   nitrosamine reference, respectively **(Table 1)**. Likewise, for comparison with NMEA, the

91   selected chemicals were *N*-Ethyl-*N*-methylformamide (NEMF) and 2-methylbutanal (MBTL),

92   which have one and two nitrogen atoms less than that of the corresponding *N*-nitrosamine

93   reference, respectively. All of the eight solutes are hydrophilic and neutral (uncharged) at the

94   experimental pH (pH 6 to 7) of this study **(Table S1)**.

95 **Table 1** – Structure and properties of the selected chemicals.

Group	Number of nitrogen atom	2	1	0
A	Name	NDMA	DMF	IBAL
	Structure			
	Molecular weight [g/mol]	74.1	73.1	72.1
	Minimum projection area[a, b] [Å^2]	19.4	20.2	22.9
B	Name	NMEA	NEMF	MBTL
	Structure			
	Molecular weight [g/mol]	88.1	87.1	86.1
	Minimum projection area[a, b] [Å^2]	22.1	24.0	25.4
C	Name	NPYR	N.A.	N.A.
	Structure			
	Molecular weight [g/mol]	100.1		
	Minimum projection area[a, b] [Å^2]	24.1		
D	Name	NMOR	N.A.	N.A.
	Structure			
	Molecular weight [g/mol]	116.1		
	Minimum projection area[a, b] [Å^2]	26.9		

96 [a] Marvin software (ChemAxon, Budapest, Hungary).

97 [b] Minimum projection area is the area of the compound projection with the minimum plane of its

98 circular disk, based on the van der Waals radius.

99 N.A.: Not available (not used).

Membrane treatment system and protocols

101 A pilot-scale cross-flow RO system with one 4-inch low pressure RO membrane element was

102 used **(Fig. S1 and Text S1a)**. The RO membrane elements selected in this study were ESPA2-

103 LD-4040 and LFC3-LD-4040 (Hydranautics/Nitto, CA, USA), both of which have been widely

104 used for water recycling applications. Both RO membrane elements have a large membrane

105 surface area (7.43 m^2 as opposed to < 0.01 m^2 in a typical lab scale study), which eliminates any

106 local variation in separation performance. Conductivity rejection by the ESPA2-LD-4040 RO

107 membrane element is 98.5%, slightly lower than that of the LFC3-LD-4040 RO element (98.9%)

108   **(Table S2)**. The skin layer of polyamide ESPA2 RO membrane is formed via the cross-linking

109   of *m*-phenylenediamine and trimesoyl chloride monomers; thus, polyamide materials are present

110   in the top skin layer.[21] LFC3 RO membrane is prepared by coating a layer of polyvinyl alcohol

111   (PVA, $(C_2H_4O)_x$) onto a ready-made ESPA2 RO membrane sheet; thus, a major difference

112   between LFC3 and ESPA2 RO membranes is the presence of the PVA active skin layer. These

113   two RO membranes were evaluated to examine the influence of nitrogen content in the

114   membrane polymeric matrix on the rejection of nitrogen bearing chemicals.

115   The RO system was operated in a recirculation mode at a constant permeate flux of 20 L/m²h,

116   constant feed temperature of 20 °C, and the system recovery of 20%. Prior to each separation

117   experiment, the system was operated using a 50 L deionised water for at least one hour to

118   stabilise the filtration performance **(Text S1b)**. Thereafter, stock solution of each chemical was

119   added to obtain 700 ng/L of each *N*-nitrosamine or 14–20 mg/L for the other chemicals in the

120   feed solution.

121   *Analysis*

122   Concentrations of four *N*-nitrosamines were determined by high-performance liquid

123   chromatography-photochemical reaction-chemiluminescence.[22] Concentrations of DMF and

124   NEMF were determined through solid-phase extraction followed by gas chromatography (GC)

125   and mass spectrometry (MS). Concentrations of IBAL and MBTL were determined through

126   derivatisation followed by liquid phase extraction and GC-MS **(Text S1c)**. Chemical

127   composition of the face side as well as the side facing the supporting layer (herein called reverse

128   side) of the skin layer was evaluated using an X-ray photoelectron spectroscopy (XPS)

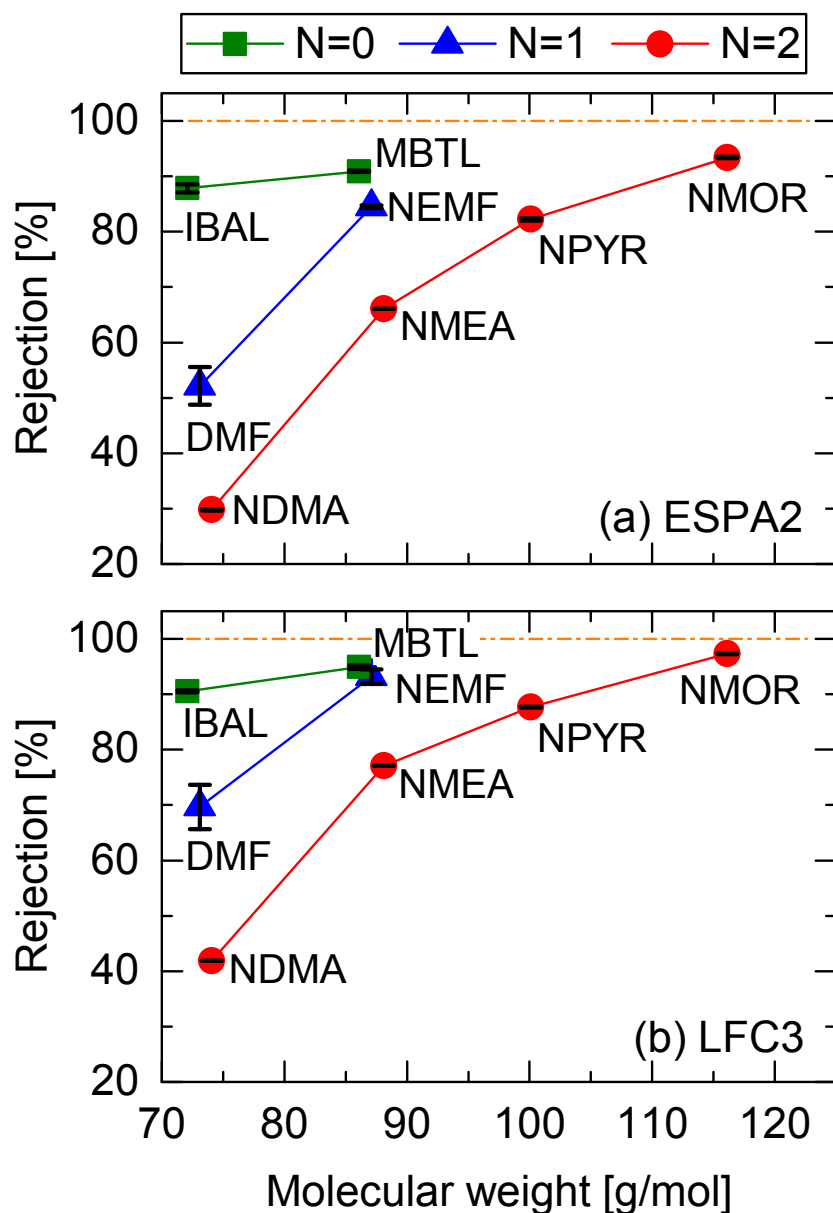129   (ESCA3200, Shimadzu, Tokyo, Japan) **(Text S1d)**.

RESULTS AND DISCUSSION

Elemental composition of RO skin layer

Three organic elements detected here include: oxygen (O), nitrogen (N), and carbon (C) **(Fig. S2)**. The face side of ESPA2 RO membrane had the elemental composition of O (15%), N (12%), and C (72%). The reverse side of ESPA2 membrane showed similar elemental composition at O (15%), N (11%), and C (74%), which will be same for the reverse side of LFC3 membrane. Almost identical elemental composition between the face side and reverse side indicate that the intermolecular interaction occurs at similar levels during the transport of chemicals through the skin layer. In contrast, the face side of LFC3 RO membrane had a low N content of only 6%.

Rejection of TOrCs

The rejection of four *N*-nitrosamines by the ESPA2 RO membrane increased according to the increase in their molecular weight **(Fig. 1a)**. However, when other chemicals with similar molecular structure but difference in the number of nitrogen atoms are also considered, the correlation between rejection and molecular weight was no longer valid. The three chemicals in group A (namely NDMA, DMF, and IBAL) have similar molecular weight (72–74 g/mol) and structure **(Table 1)** but markedly different rejection (30, 52, and 88%, respectively) **(Fig. 1a)**. Likewise, the three chemicals in group B (namely NMEA, NEMF, and MBTL) also have similar molecular weight (86–88 g/mol) and structure **(Table 1)**, yet their rejection also varied over a wide range. Similarly, the rejection of the selected chemicals by LFC3 RO membrane was not correlated with their molecular weight **(Fig. 1b)**.

Fig. 1 – Rejection of the selected chemicals with and without nitrogen (N) atoms in deionised water by (a) ESPA2 and (b) LFC3 RO membranes as a function of molecular weight (Permeate flux = 20 L/m²h, feed temperature = 20 °C, and transmembrane pressure = 0.41 and 0.50 MPa for the ESPA2 and LFC3 RO membranes, respectively; error bars represent one standard deviation of two replicate samples).

Further analysis indicated that the minimum projection area (MPA) of the selected chemicals instead of molecular weight was better correlated with their rejections for both RO membranes **(Fig. 2)**. MPA represents the minimum projection cross-sectional area of a chemical **(Fig. S3)**.

159   Another physical parameter (Van der Waals volume) showed a relatively high correlation **(Fig.**

160   **S4)**, because of the basis similar to minimum projected area, which is based on the van der

161   Waals radius. In contrast, the molecular length of the selected chemicals did not correlate with

162   their rejections **(Fig. S5)**. Results associated with MPA indicate that the 2-dimensional molecular

163   property can be a more relevant parameter that governs the rejection of small and uncharged

164   chemicals. In fact, a strong correlation between MPA and TOrCs has also been reported with

165   nanofiltration (NF) and cellulose triacetate RO membranes elsewhere.[23, 24] The transport of

166   TOrCs through RO membrane occurs via three major steps: (a) approach to the face side of the

167   membrane surface and penetration into the membrane structure; (b) diffuse through the skin

168   layer; and (c) exit from the membrane structure and departing from the reverse side to the

169   supporting layer.[25] After sorption (or partitioning) of uncharged chemicals into the membrane

170   polymeric matrix, their diffusion can be influenced by the clearance between the chemical and
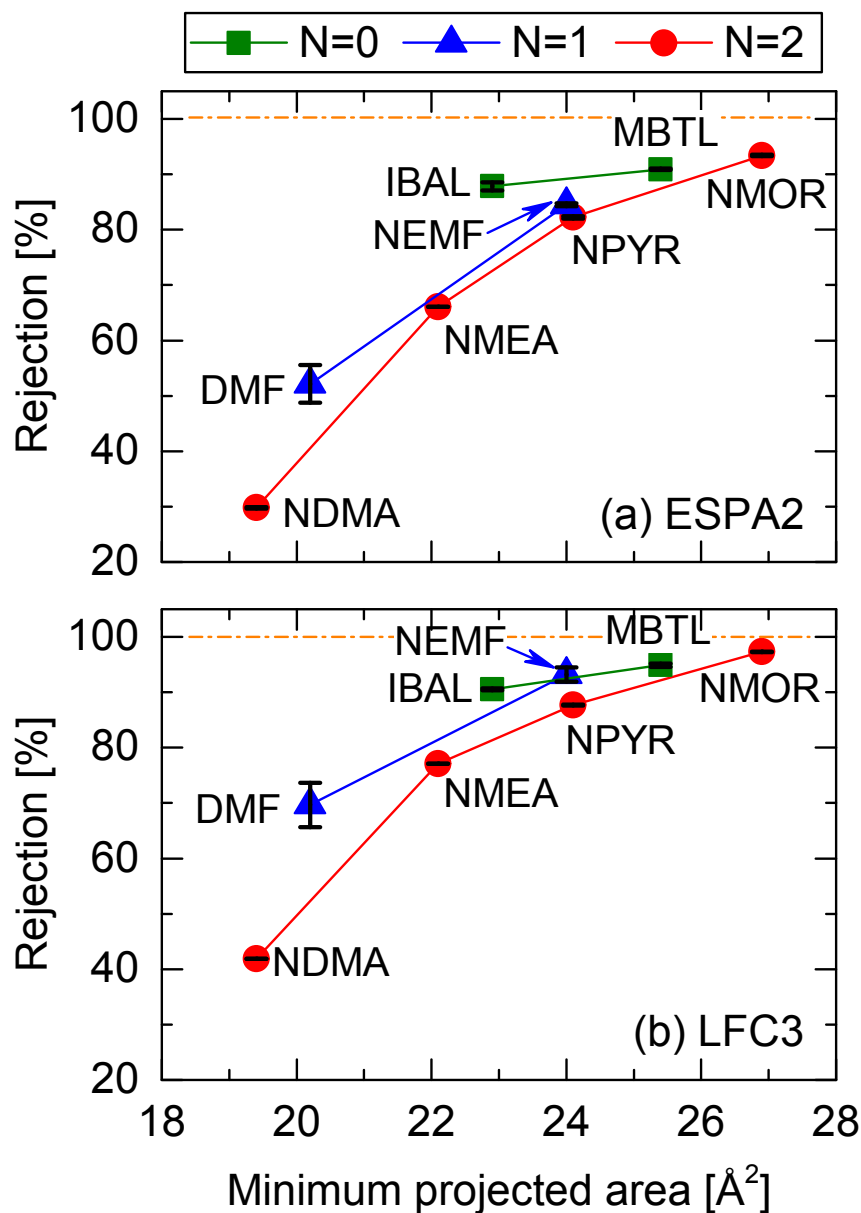
171   free-volume hole-size of the membrane active skin layer.

172

Fig. 2 – Rejection of the selected chemicals with and without nitrogen (N) atoms in deionised
water by (a) ESPA2 and (b) LFC3 RO membranes as a function of MPA (Permeate flux = 20
L/m²h and feed temperature = 20 °C; error bars represent one standard deviation of two replicate
samples).

Assuming that the chemical can rotate at any directions, the minimum clearance is attained with

two dimensional area (e.g. MPA), which can determine whether the chemical passes through the

free-volume hole. MPA of NDMA (MPA = 19 Å²) and other selected chemicals (20–27 Å²) was

180   comparable to the mean cross-sectional area of free-volume holes of ESPA2 RO membrane (24

181    $Å^2$), which was determined by approximating free-volume holes as uniform sphere-like voids

182   using positron annihilation technique.[21] The clearance between solute dimensions and membrane

183   free-volume holes can govern the transport of chemicals not only during the entry to the

184   membrane matrix but also during their diffusion through the skin layer, because free-volume

185   holes are composed small network and large aggregate holes that are more likely to provide

186   hinder solute transport depending on the level of clearance.[26, 27] This clearance may explain the

187   overall trend of high rejections by LFC3 RO membrane; free-volume hole-size in the membrane

188   matrix could have been reduced by the coating process compared to that of the ESPA2 RO

189   membrane.

190   It is noted that the rejection of chemicals with one or no nitrogen atoms in structure by ESPA2

191   RO membrane was generally higher than their corresponding N-nitrosamines (N = 2) **(Fig. 2a)**.

192   Hydrogen bonding between these nitrogen bearing chemicals and functional groups of

193   polyamide membrane can be the cause of this observed variation. In the polyamide skin layer,

194   hydrogen atom on the amide (CO-NH-) or free amine (NH$_2$-) functional groups can act as a

195   hydrogen bond donor, because N in the amide or amine functional group strips electron density

196   from the proton, which causes its partial positive charge (δ^+) **(Fig. S6)**. Although keto group

197   (=O) in all of the chemicals is a hydrogen bond acceptor with partial negative charge (δ^-),

198   nitrogen atoms in nitrogen bearing chemicals (e.g., NDMA) are also hydrogen bond acceptors,

199   which increases the number of hydrogen bonding pairs. In contrast, both IBAL and MBTL do

200   not have any nitrogen atom in their molecular structure; thus, the number of hydrogen bonding

201   pair is less than NDMA and NMEA. The increased number of hydrogen bonds may enhance the

202   diffusion of nitrogen bearing chemicals, enhancing their permeation to the permeate.

203   A similar trend but with discernible difference in individual rejection values between *N*-

204   nitrosamines and other chemicals with less nitrogen atoms was also observed for the LFC3 RO

205   membrane **(Fig. 2b)**. The LFC3 RO membrane has a lower nitrogen content on the face side due

206   to the PVA coating layer **(Table S1)** comparing to the ESPA2. However, hydroxyl groups (-OH)

207   of the PVA layer can also act as a hydrogen bond donor and form hydrogen bonding with N-

208   bearing chemicals. Indeed, the hydrogen bond donating potential of the hydroxyl group is higher

209   than that of the amide group of the original polyamide layer **(Fig. S6)**. Thus, hydrogen bonding

210   between the selected chemicals and PVA layer can be stronger than that between the chemicals

211   and polyamide chains. This implies that two nitrogen bearing chemicals that have two hydrogen

212   acceptor sites (i.e., *N*-nitrosamines) can have more hydrogen bonding with the PVA layer (i.e.

213   LFC3 membrane), causing the discrepancy in their rejection trend with one or no nitrogen

214   bearing chemicals (one hydrogen acceptor site) **(Fig. 2b)**. These results in this study suggest

215   hydrogen bonding as a potential cause of the low rejection of nitrogen bearing chemicals

216   including *N*-nitrosamines. It is noted that the tests in this study were conducted using deionised

217   water, whereas in water recycling the rejection of these chemicals may vary due to the presence

218   of dissolved ions and hydrogen bond disruptors such as urea. To confirm the importance of

219   hydrogen bonding, further investigation with many other chemicals with different partial positive

220   or negative charges and different water matrix is necessary.

221   ***Implications for future RO membranes***

222   This study showed MPA is a more appropriate parameter than molecular weight for describing

223   the rejection of small and uncharged chemicals. In addition, this study identified for the first time

224   that the permeation of nitrogen atom-containing chemicals through polyamide RO membrane

225   can be enhanced by the number of hydrogen bond pairs. Based on the importance in size

226   exclusion mechanisms identified in this study, the restriction of free-volume hole-size can

227   primarily reduce the number of NDMA molecules entering the free-volume holes, enhancing

228   NDMA rejection. However, free-volume hole-size restriction can also inhibit the entry of water

229   molecules, consequently reducing water permeability. The effect of hydrogen bonding identified

230   in this study suggests that the reduction of electron donor in RO membrane matrix has the

231   potential to reduce the permeation of NDMA molecules. Hydrogen bond donor can be removed

232   or reduced by changing membrane polymer materials, however, the change in polymer materials

233   can also change the membrane structure including free-volume hole-size. Provision of surface

234   coating layer without hydrogen bonding donor also has the potential of enhanced NDMA

235   rejection.

SUPPORTING INFORMATION

237   Additional text, tables and figures.

ACKNOWLEDGEMENT

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328

330   **TOC**

331

Decreasing number of N atom in the molecule

Increasing rejection due to intermolecular interaction

$C_2H_6N_2O$ C_3H_7NO C_4H_8O

RO membrane