

1 **Supporting information for**

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3 **Title: Chiral mixed matrix membrane with (S,S)- Whelk-O®1 selector supported**
4 **on polyethersulfone/MCM-41**

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31 **S1. Validation of the LC method for evaluation of the membranes**

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33 The validation of the analytical method was performed according to parameters
34 established by *International Conference on Harmonization of Technical Requirements*
35 *for Registration of Pharmaceuticals for Human Use (ICH)* ¹.

36 **A. Validation with (R)-6MeX and (S)-6MeX enantiomers:**

37 Seven standard solutions with different concentrations of (R)- 6MeX and (S)- 6MeX
38 enantiomers were prepared for calibration curve (Table S1). Calibration curves is
39 presented in Figure S1 . The calibration curve was obtained by plotting the concentration
40 of the (R)- 6MeX and (S)- 6MeX enantiomers versus the area of the respective signals.
41 The value of the linear correlation coefficient (r^2) was 0.99778 and 0.99476, respectively.

42 Table S1 – Concentrations of standard solutions and the values obtained for the areas.

Concentrations of 6MeX ($\mu\text{mol L}^{-1}$)	Area (S)- 6MeX	Area (R)- 6MeX
5	6.3347 \pm 0.0310	7.0124 \pm 0.0073
10	9.8670 \pm 0.1066	11.3273 \pm 0.1104
25	25.2259 \pm 0.0219	29.6362 \pm 0.1063
50	51.1752 \pm 0.0577	61.0830 \pm 0.5818
75	77.4371 \pm 0.0890	74.9468 \pm 0.1967
100	92.2077 \pm 0.0512	113.1189 \pm 0.0946
125	106.5526 \pm 0.2277	123.5150 \pm 5.0332

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44 The linearity of the method was determined from analytical curves presented above, each
45 showing 7 concentrations between 5 and 125 $\mu\text{mol L}^{-1}$ of the 6MeX enantiomers diluted
46 in EtOH. Repeatability or precision was assessed using the calculation of relative standard
47 deviation (RSD):

$$RSD = \frac{SD}{MCD} \times 100$$

48

Eq.1

49 where, SD is the standard deviation and MCD, the mean concentration determined.

50 Accuracy was determined through concentration values determined experimentally,

51 compared to theoretical concentration, according to equation 2.

$$52 \quad Accuracy = \frac{MCD}{TC} \times 100 \quad Eq.2$$

53 where TC is the theoretical concentration.

54 To determine the intra-day and inter-day precision and accuracy, three standards solution

55 (different from the concentration of calibration levels) *n* of the pure enantiomers in

56 concentrations of 18, 65, and 85 $\mu\text{mol mL}^{-1}$, in triplicate, were analyzed (Table S2 and

57 Table S3). Accuracy was determined using experimentally determined concentration

58 values, compared to the theoretical concentration (Table S3).

59 Table S2 - Relative standard deviation (RSD) values for the concentrations of the (*R*)-
60 6MeX and (*S*)- 6MeX enantiomers determined for precision evaluation.

	TC ($\mu\text{mol L}^{-1}$)	Day 1 RSD (%)	Day 2 RSD (%)	Day 3 RSD (%)	Inter-days RSD (%)
<i>(S)</i> - 6MeX	18	0.4625	1.2674	0.6858	8.5365
	65	0.0483	0.1335	1.3313	4.1730
	85	0.5691	0.0475	0.0823	7.8565
<i>(R)</i> - 6MeX	18	0.3395	0.4972	0.5022	3.7084
	65	0.2585	0.2031	0.6158	6.2415
	85	0.1212	0.1886	0.9161	3.4871

61

62 Table S3 – Intra-day and inter-day accuracy assessment of (*R*)- 6MeX and (*S*)- 6MeX
63 enantiomers.

	TC ($\mu\text{mol L}^{-1}$)	Day 1 % de Rec.	Day 2 % de Rec.	Day 3 % de Rec.	Inter-days % de Rec.
<i>(S)</i> - 6MeX	18	91.9806	86.5883	88.9849	89.1846
	65	113.1920	106.6311	116.0136	111.9456
	85	97.4197	94.8712	97.4595	96.5835
<i>(R)</i> - 6MeX	18	116.4247	114.9777	116.1193	115.8406

65	94.5714	95.8898	94.5369	94.9994
85	95.0604	94.7815	114.8341	101.5587

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65 The RSD values determined between days were all below the value recommended
66 by the Standard, which is a maximum of 10%, so the method can be considered accurate.
67 The accuracy varied from 89 a 117%, being within the specifications established by ICH.

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69 **B. Validation with (*R*)-NPX and (*S*)-NPX enantiomers:**

70 Seven standard solutions with different concentrations of (*R*)-NPX and (*S*)-NPX
71 enantiomers were prepared for calibration curve (Table S4). Calibration curves is
72 presented in Figure S2 . The calibration curve was obtained by plotting the concentration
73 of the (*R*)-NPX and (*S*)-NPX enantiomers versus the area of the respective signals. The
74 value of the linear correlation coefficient (r^2) was 0,99876 and 0,9946, respectively.

75 Table S4 – Concentrations of standard solutions and the values obtained for the areas.

Concentrations of NPX ($\mu\text{mol L}^{-1}$)	Area (<i>S</i>)-NPX	Area (<i>R</i>)-NPX
5	0.5624 \pm 0.0072	0.4896 \pm 0.0044
10	1.1229 \pm 0.0051	1.2456 \pm 0.0126
25	3.4171 \pm 0.0050	3.0025 \pm 0.0119
50	7.4636 \pm 0.0055	6.6345 \pm 0.0226
75	11.3792 \pm 0.1080	10.7693 \pm 0.0148
100	13.9502 \pm 0.0355	13.6395 \pm 0.0248
125	17.2481 \pm 0.0152	17.2430 \pm 0.0157

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77 The linearity of the method was determined from analytical curves presented above, each
78 showing 7 concentrations between 5 and 125 $\mu\text{mol L}^{-1}$ of the NPX enantiomers diluted in
79 EtOH. Repeatability or precision was assessed using the calculation of relative standard
80 deviation (RSD). Accuracy was determined through concentration values determined
81 experimentally, compared to theoretical concentration, according to equation 2.

82 To determine the intra-day and inter-day precision and accuracy, three standards solution
 83 (different from the concentration of calibration levels) *n* of the pure enantiomers in
 84 concentrations of 18, 65, and 85 $\mu\text{mol mL}^{-1}$, in triplicate, were analyzed (Table S5 and
 85 Table S6). Accuracy was determined using experimentally determined concentration
 86 values, compared to the theoretical concentration (Table S6).

87 Table S5 - Relative standard deviation (RSD) values for the concentrations of the (*R*)-
 88 NPX and (*S*)-NPX enantiomers determined for precision evaluation.

	TC ($\mu\text{mol L}^{-1}$)	Day 1 RSD (%)	Day 2 RSD (%)	Day 3 RSD (%)	Inter-days RSD (%)
<i>(S)</i> -NPX	18	0.4011	0.4089	0.9184	1.2430
	65	0.9576	0.0495	0.0381	7.4994
	85	0.1300	0.1372	0.0384	9.8909
<i>(R)</i> -NPX	18	1.3270	0.1759	0.2011	7.1999
	65	0.1719	0.1027	0.0204	6.1492
	85	0.2663	0.0317	0.0522	4.2578

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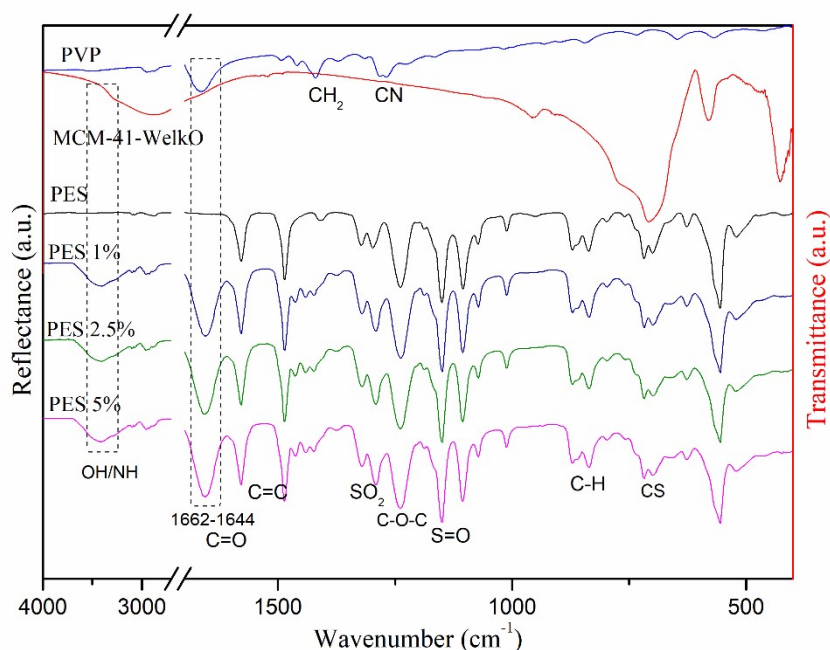
90 Table S6 – Intra-day and inter-day accuracy assessment of (*R*)-NPX and (*S*)-NPX
 91 enantiomers.

	TC ($\mu\text{mol L}^{-1}$)	Day 1 % de Rec.	Day 2 % de Rec.	Day 3 % de Rec.	Inter-days % de Rec.
<i>(S)</i> -NPX	18	75.6418	75.5530	77.2349	76.1432
	65	81.4935	92.0835	80.6976	84.7582
	85	82.7094	99.1206	85.3641	89.0647
<i>(R)</i> -NPX	18	81.7122	91.5098	80.3566	84.5262
	65	85.9899	94.3675	84.2131	88.1902
	85	86.0285	92.2024	85.4510	87.8939

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93 The RSD values determined between days were all below the value recommended
 94 by the Standard, which is a maximum of 10%, so the method can be considered accurate.
 95 The accuracy varied from 75 a 99%, being within the specifications established by ICH.

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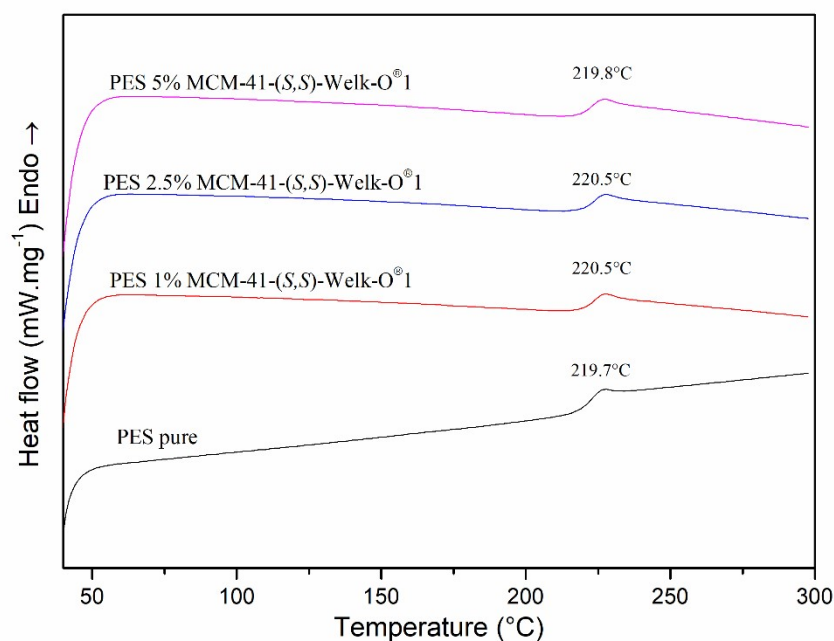


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98 **Figure S1.** The FTIR spectra of PES/MCM-41-(*S,S*)-Welk-O[®]1 1% (w/w); PES/MCM-
 99 41-(*S,S*)-Welk-O[®]1 2.5% (w/w); PES/MCM-41-(*S,S*)-Welk-O[®]1 5% (w/w); PES pure;
 100 MCM-41-(*S,S*)-Welk-O[®]1 and PVP.

101 The bands at 1080 cm⁻¹ and 808 cm⁻¹ can be attributed to the asymmetric and
 102 symmetrical stretching, respectively, of the vibration of $\nu(\text{Si-O-Si})$ ² and 466 cm⁻¹
 103 corresponds to angular deformation $\nu(\text{Si-O-Si})$ ³. The band in the region around 3473
 104 cm⁻¹ corresponds to the stretching vibration of the $\nu(\text{O-H})$ bond of H₂O molecules
 105 adsorbed on the silica matrix. At 1644 cm⁻¹ it corresponds to the absorption of the
 106 carbonyl group of the secondary amide and the band in the region around 1550 cm⁻¹
 107 corresponds to the asymmetric axial deformation referring to the nitroaromatic groups (-
 108 NO₂) of the selector (*S,S*)-1-(3,5-dinitrobenzamido)-tetrahydrophenanthrene. This
 109 proves the presence of the selector in the mesoporous material.

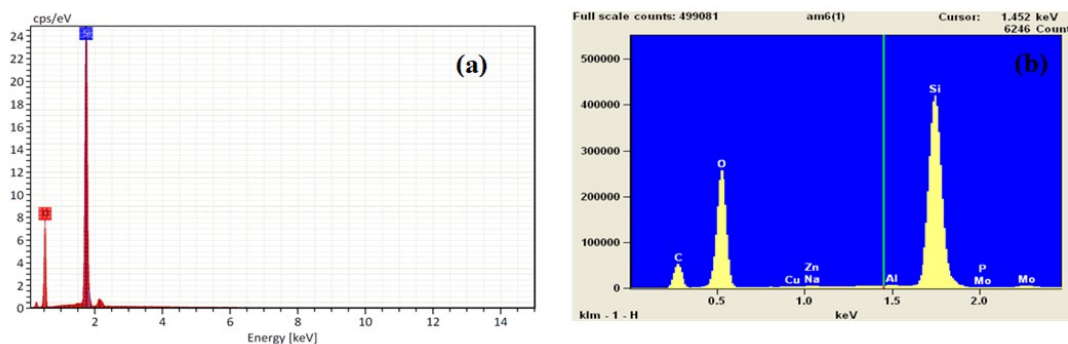
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111
 112 **Figure S2.** The DSC curves of PES/MCM-41-(S,S)-Welk-O®1 1% (w/w);
 113 PES/MCM-41-(S,S)-Welk-O®1 2.5% (w/w); PES/MCM-41-(S,S)-Welk-O®1 5% (w/w);
 114 PES pure.

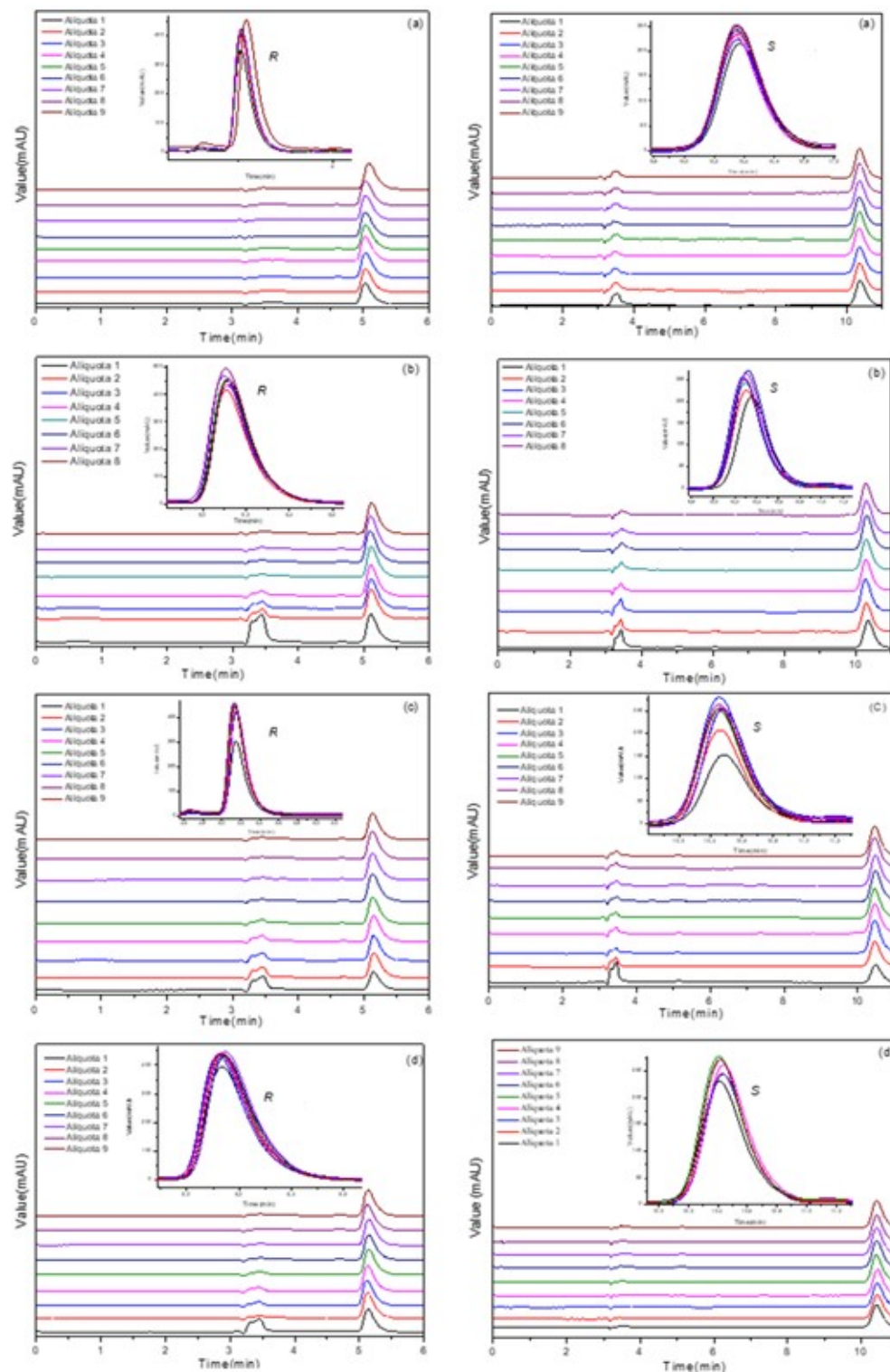
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116 It is observed that there was no variation in the T_g value for the pure PES
 117 membranes and with different contents of MCM-41-(S,S)-Welk-O®1 mesoporous
 118 material. Therefore, this event was observed in all of them with values ranging from 219.7
 119 to 220.5 °C.



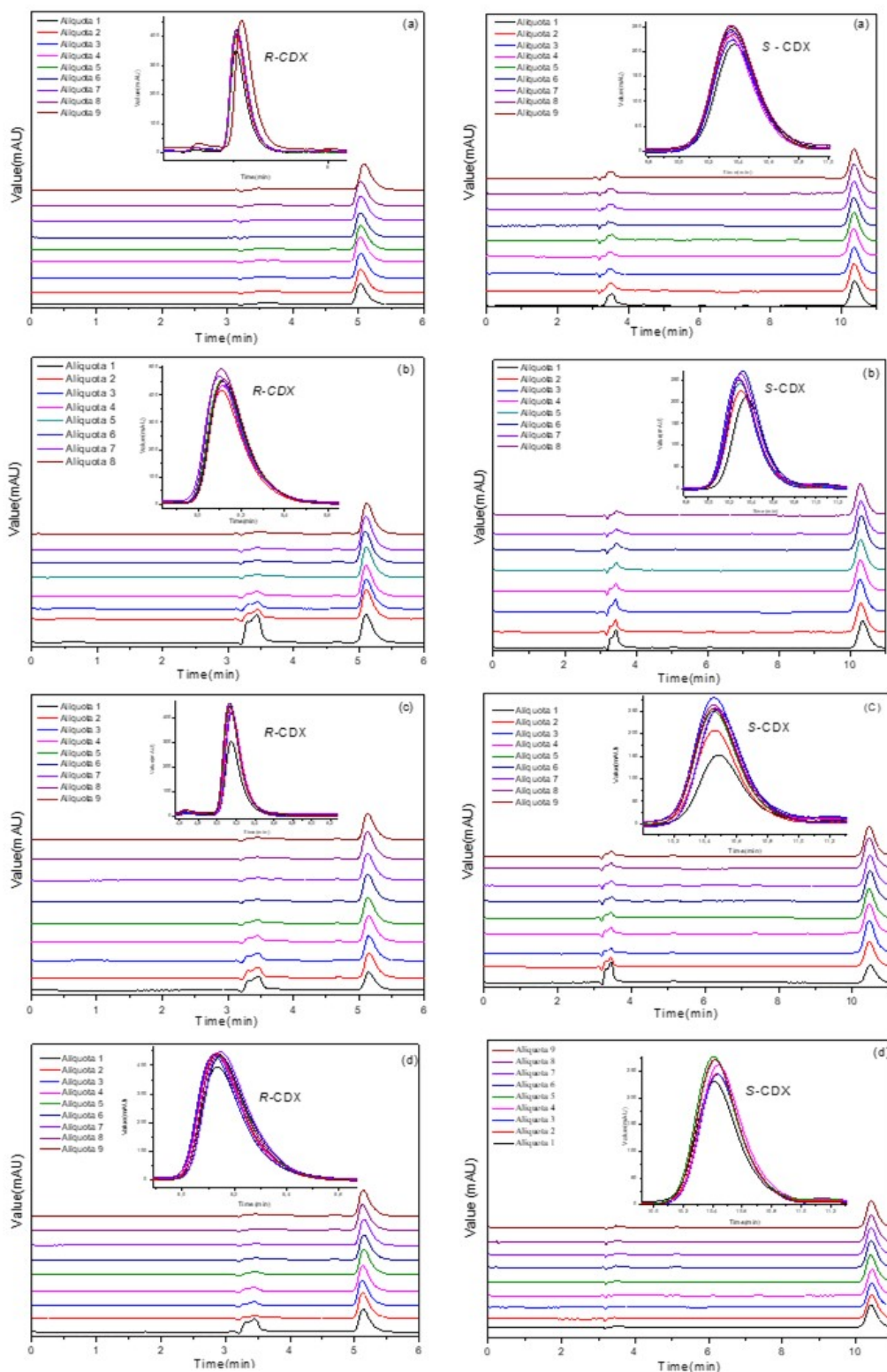
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121 **Figure S3.** EDS images from SEM-EDS analyzes obtained of the mesoporous materials:
 122 (a) MCM-41 and (c) MCM-41-(S,S)-Welk-O®1.



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125 **Figure S4.** LC chromatograms of aliquots removed at certain time intervals during the
 126 filtration of (*R*)- 6MeX and (*S*)- 6MeX through the membrane (a) PES pure, (b)
 127 PES/MCM-41-(*S,S*)-Welk-O[®]1 1% (w/w), (c) PES/MCM-41-(*S,S*)-Welk-O[®]1 2.5%
 128 (w/w) and (d) PES/MCM-41-(*S,S*)-Welk-O[®]1 5% (w/w). Column (*S,S*)-Welk-O[®]1 (25
 129 cm, 4,6 mm i.d., 5 mm particle size, 100 Å pore size) from Regis[®] Technologies; Mobile
 130 phase ACN:MeOH (50:50 v/v); flow rate: 1mL min⁻¹; detection wavelength 254 nm.



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132 **Figure S5.** LC chromatograms of aliquots removed at certain time intervals during the
 133 filtration of (*R*)-NPX and (*S*)-NPX through the membrane (a) PES pure, (b) PES/MCM-
 134 41-(*S,S*)-Welk-O[®]1 1% (w/w), (c) PES/MCM-41-(*S,S*)-Welk-O[®]1 2.5% (w/w) and (d)
 135 PES/MCM-41-(*S,S*)-Welk-O[®]1 5% (w/w). Column (*S,S*)-Welk-O[®]1 (25 cm, 4,6 mm
 136 i.d., 5 mm particle size, 100 Å pore size) from Regis[®] Technologies; Mobile phase EtOH,
 137 0.1%HAc; flow rate: 1mL min⁻¹; detection wavelength 254 nm.

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