

## Supporting Information

### Enhancing the antioxidant characteristics of phenolic acids by their conversion into cholinium salts

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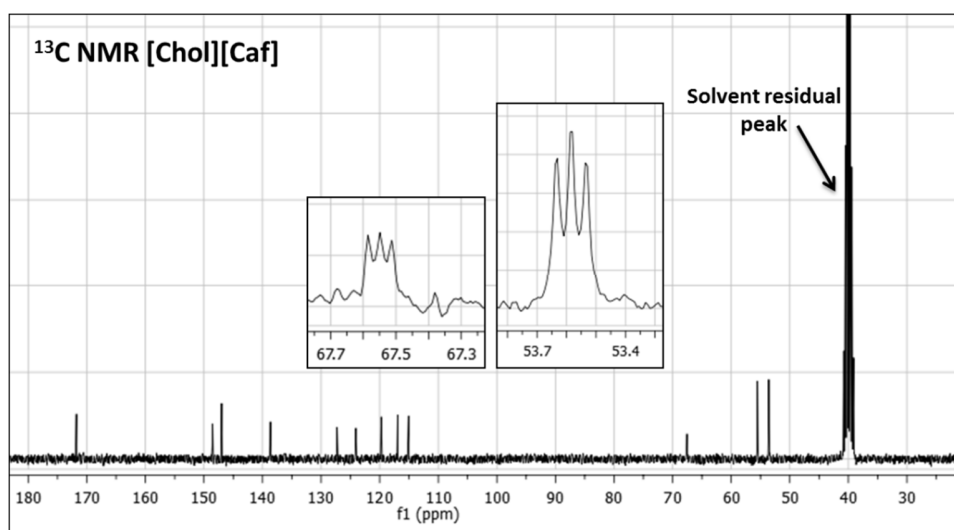
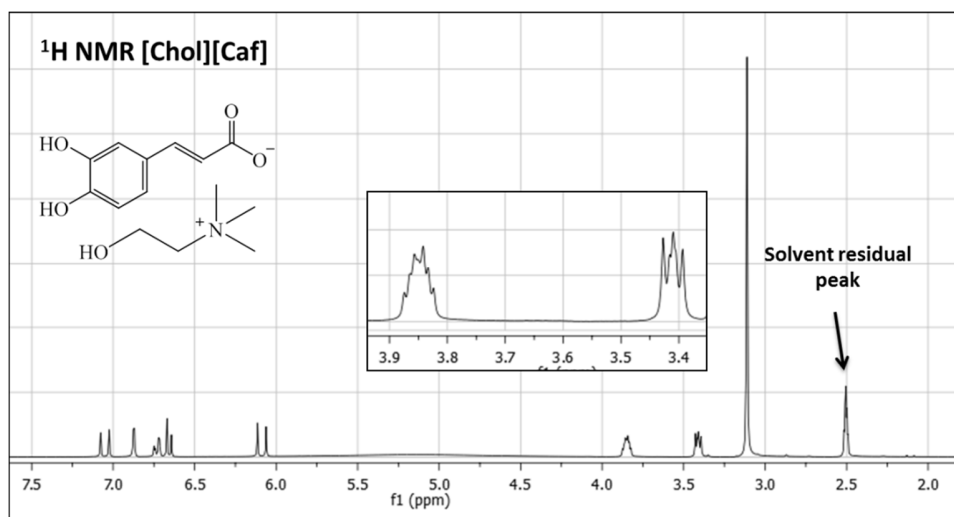
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## Synthesis and characterization of cholinium-based salts

### *Cholinium caffeate*, [Chol][Caf]

(2-Hydroxyethyl) trimethylammonium (E)-3-(3,4-dihydroxyphenyl)acrylate

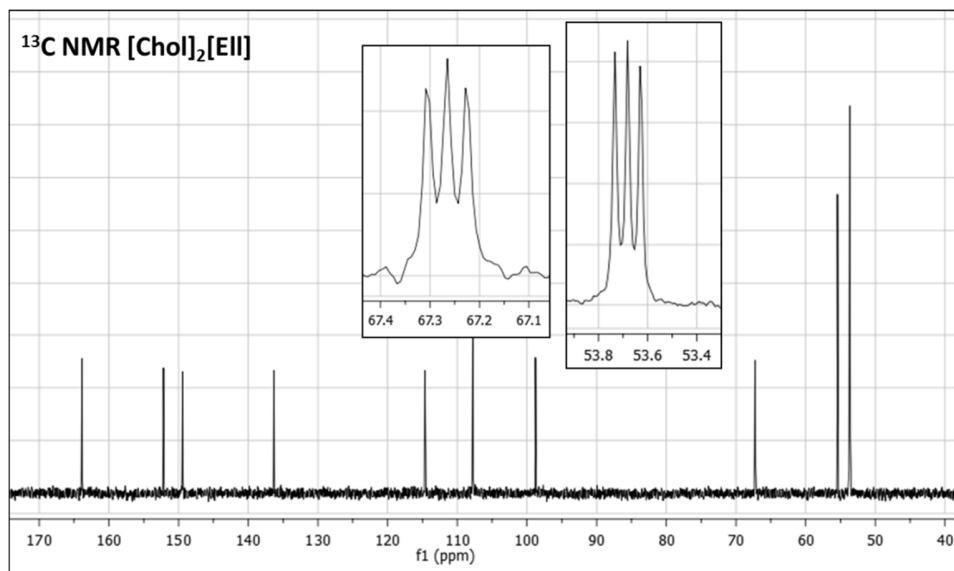
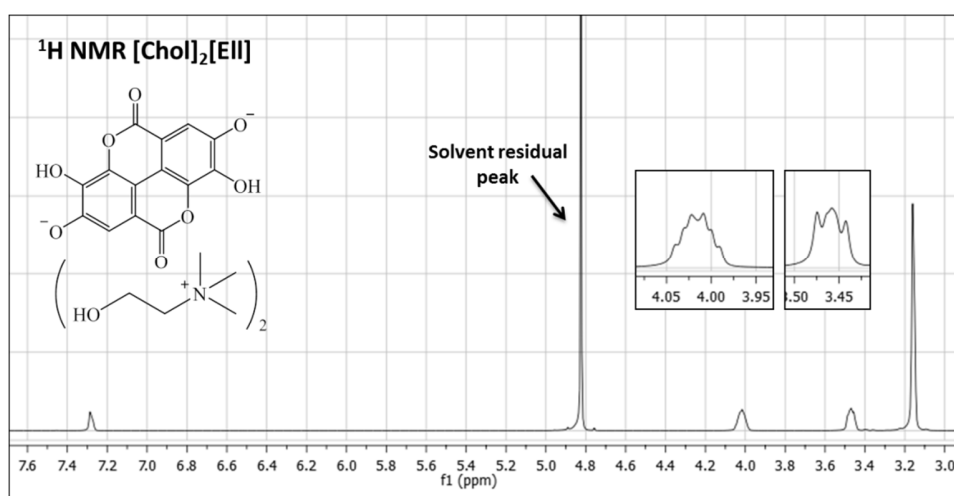
[Chol][Caf] was obtained as a white solid (99% yield).  $^1\text{H}$  NMR ( $d_6$ -DMSO, 300 MHz, [ppm]):  $\delta$  7.05 (d, 1H,  $J_{HH} = 15.7$  Hz, CHCHCOO), 6.87 (d, 1H,  $J_{HH} = 1.8$  Hz, H-2), 6.73 (dd, 1H,  $J_{HH} = 8.2$  Hz and  $J_{HH} = 1.8$  Hz, H-6), 6.66 (d, 1H,  $J_{HH} = 8.1$  Hz, H-5), 6.09 (d, 1H,  $J_{HH} = 15.7$  Hz, CHCHCOO), 3.90-3.80 (m, 2H, NCH<sub>2</sub>CH<sub>2</sub>OH), 3.46-3.36 (m, 2H, NCH<sub>2</sub>CH<sub>2</sub>OH), 3.11 (s, 9H, N(CH<sub>3</sub>)<sub>3</sub>).  $^{13}\text{C}$  NMR ( $d_6$ -DMSO, 75.47 MHz, [ppm]):  $\delta$  171.74 (COO), 148.47 (CHCHCOO), 146.94 (COH-4), 138.57 (COH-3), 127.32 (CHCHCOO), 124.17 (C-1), 119.74 (C-6), 116.88 (C-5), 114.98 (C-2), 67.55 (t,  $J_{CN} = 2.8$  Hz, NCH<sub>2</sub>CH<sub>2</sub>OH), 55.54 (NCH<sub>2</sub>CH<sub>2</sub>OH), 53.59 (t,  $J_{CN} = 3.8$  Hz, N(CH<sub>3</sub>)<sub>3</sub>). IR (Wavenumber, cm<sup>-1</sup>): 3024 (OH), 1635, 1589 (COO), 1512 (CH), 1373 (COO), 1265, 1157 (CN), 987, 864, 817, 694, 586. Elemental analysis (%): calculated/expected for C<sub>14</sub>H<sub>21</sub>NO<sub>5</sub>: C 59.35, H 7.47, N 4.94; found: C 60.63, H 7.33, N 4.87.



**Cholinium ellagate, [Chol]<sub>2</sub>[Ell]**

Di((2-hydroxyethyl) trimethylammonium) 3,8-dihydroxy-5,10-dioxo-5,10-dihydrochromeno[5,4,3-cde]chromene-2,7-bis(olate)

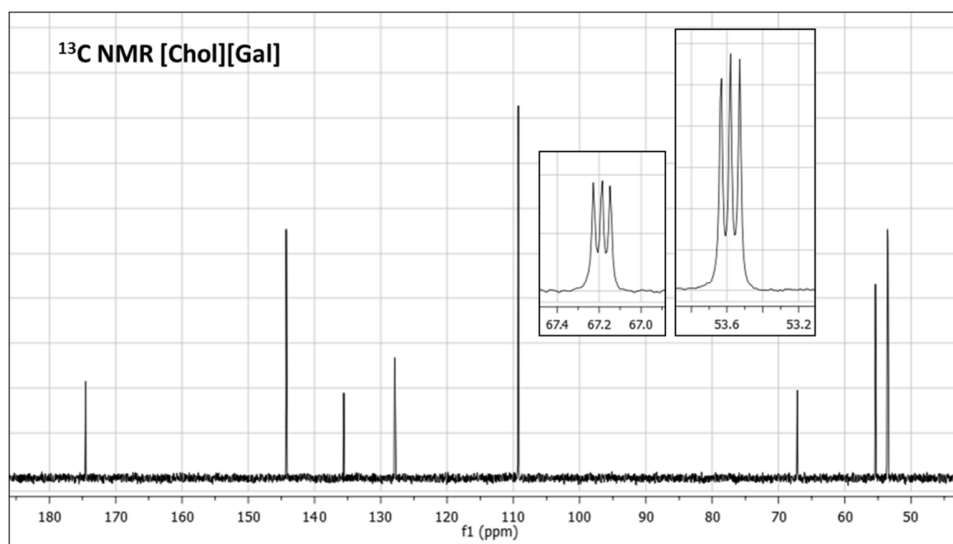
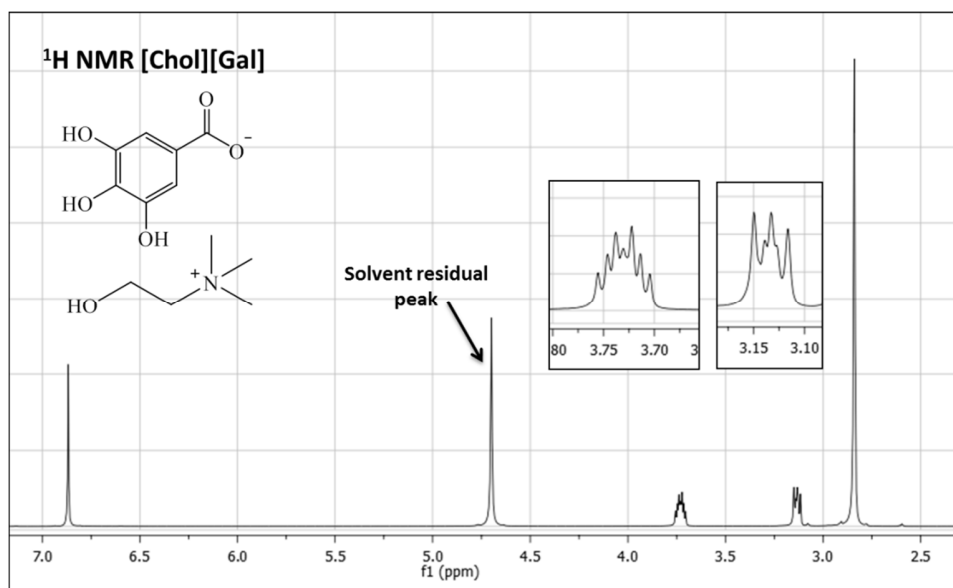
[Chol]<sub>2</sub>[Ell] was obtained as a light brown solid (80% yield). <sup>1</sup>H NMR (D<sub>2</sub>O, 300 MHz, [ppm]): δ 7.29 (s, 2H, (2x CHCO)), 4.07-3.97 (m, 4H, (2x (NCH<sub>2</sub>CH<sub>2</sub>OH))), 3.51-3.43 (m, 4H, (2x (NCH<sub>2</sub>CH<sub>2</sub>OH))), 3.16 (s, 18H, (2x (N(CH<sub>3</sub>)<sub>3</sub>))). <sup>13</sup>C NMR (D<sub>2</sub>O, 75.47 MHz, [ppm]): δ 163.91 (2x (CCO)), 152.19 (2x (CO)), 149.41 (2x (COH)), 136.37 (2x (COCO)), 114.72 (2x (COCO)), 107.82 (2x (CCO)), 98.84 (2x (C(C)<sub>3</sub>)), 67.27 (t, *J*<sub>CN</sub> = 2.9 Hz, 2x (NCH<sub>2</sub>CH<sub>2</sub>OH)), 55.44 (2x (NCH<sub>2</sub>CH<sub>2</sub>OH)), 53.69 (t, *J*<sub>CN</sub> = 3.9 Hz, 2x (N(CH<sub>3</sub>)<sub>3</sub>))). IR (Wavenumber, cm<sup>-1</sup>): 3101 (OH), 2869, 1681, 1573 (COO), 1481 (CH), 1311 (COO), 1172 (CN), 1064, 810, 740, 632. Elemental analysis (%): calculated/expected for C<sub>24</sub>H<sub>32</sub>N<sub>2</sub>O<sub>10</sub>: C 56.69, H 6.34, N 5.51; found: C 56.92, H 6.28, N 5.37.



### Cholinium gallate, [Chol][Gal]

(2-Hydroxyethyl) trimethylammonium 3,4,5-trihydroxybenzoate

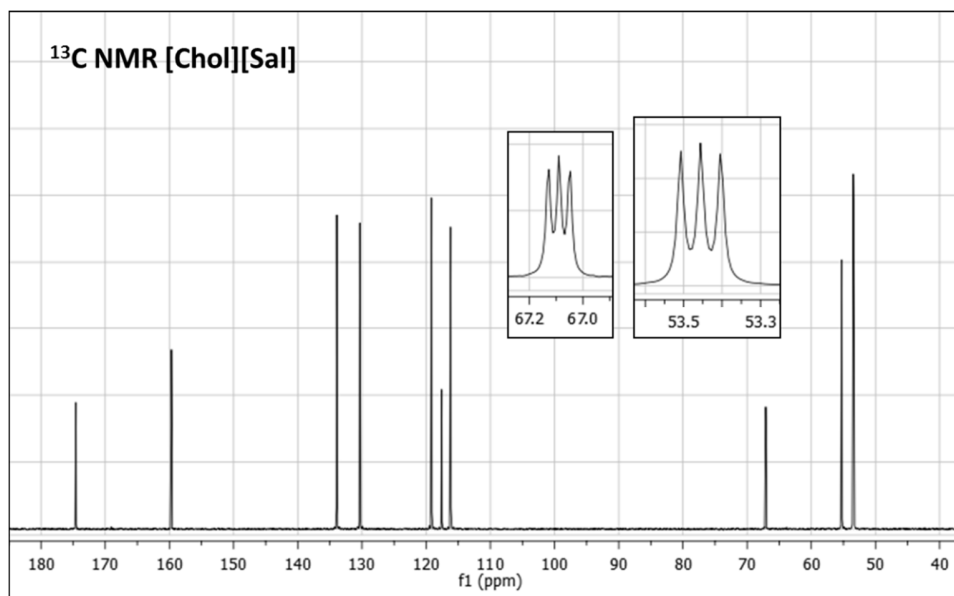
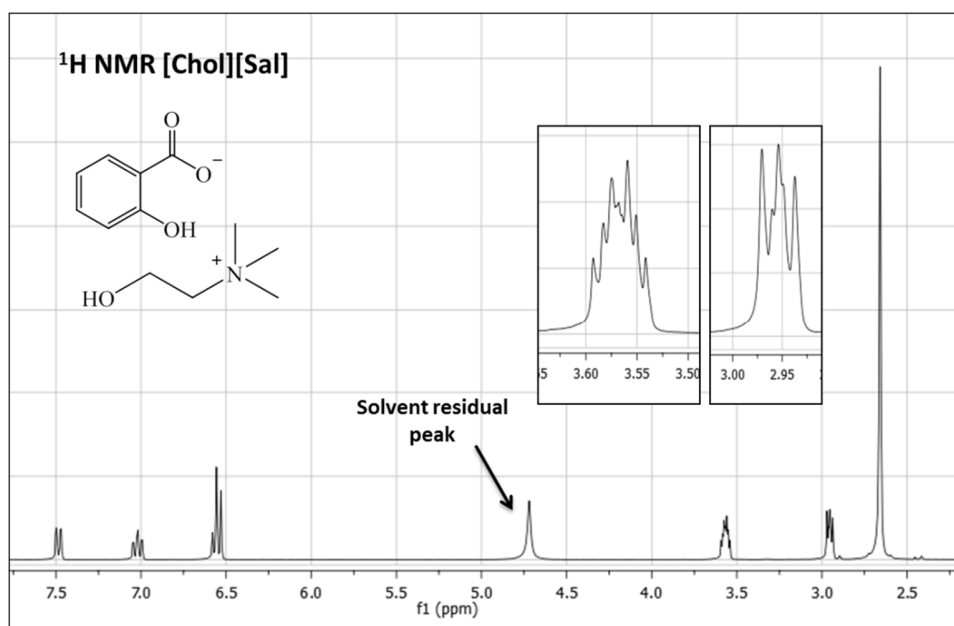
[Chol][Gal] was obtained as a white solid (87% yield).  $^1\text{H NMR}$  ( $\text{D}_2\text{O}$ , 300 MHz, [ppm]):  $\delta$  6.87 (s, 2H,  $\underline{\text{H}}\text{-2}$  and  $\underline{\text{H}}\text{-6}$ ), 3.79-3.67 (m, 2H,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 3.18-3.09 (m, 2H,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 2.84 (s, 9H,  $\text{N}(\text{CH}_3)_3$ ).  $^{13}\text{C NMR}$  ( $\text{D}_2\text{O}$ , 75.47 MHz, [ppm]):  $\delta$  174.73 ( $\underline{\text{C}}\text{OO}$ ), 144.28 ( $\underline{\text{C}}\text{-3}$  and  $\underline{\text{C}}\text{-5}$ ), 135.62 ( $\underline{\text{C}}\text{-4}$ ), 128.01 ( $\underline{\text{C}}\text{-1}$ ), 109.33 ( $\underline{\text{C}}\text{-2}$  and  $\underline{\text{C}}\text{-6}$ ), 67.30 (t,  $J_{\text{CN}} = 2.9$  Hz,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 55.49 ( $\text{NCH}_2\text{CH}_2\text{OH}$ ), 53.72 (t,  $J_{\text{CN}} = 3.9$  Hz,  $\text{N}(\text{CH}_3)_3$ ). IR (Wavenumber,  $\text{cm}^{-1}$ ): 3070 (OH), 2530, 1512 (COO), 1342 (COO), 1188 (CN), 1033, 941, 879, 756. Elemental analysis (%): calculated/expected for  $\text{C}_{12}\text{H}_{19}\text{NO}_6$ : C 52.74, H 7.01, N 5.13; found: C 53.75, H 7.03, N 5.06.



### ***Cholinium salicylate*, [Chol][Sal]**

(2-Hydroxyethyl) trimethylammonium 2-hydroxybenzoate

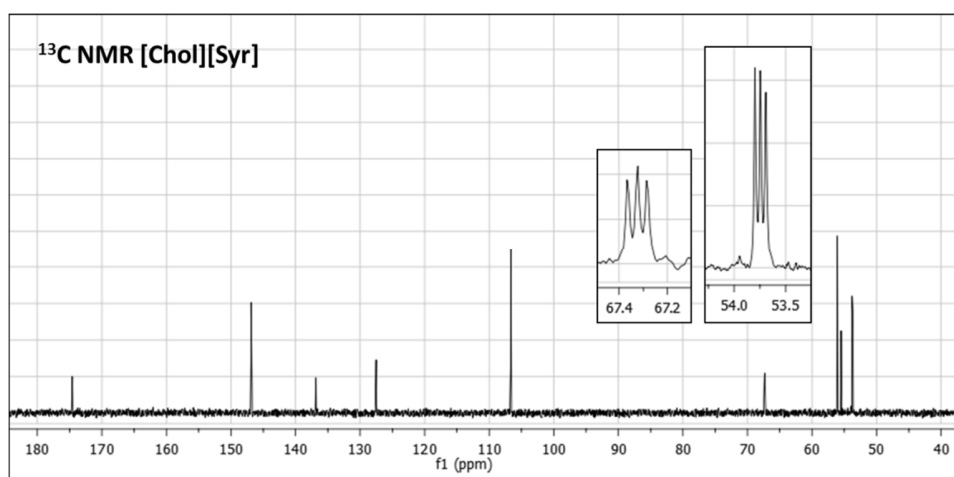
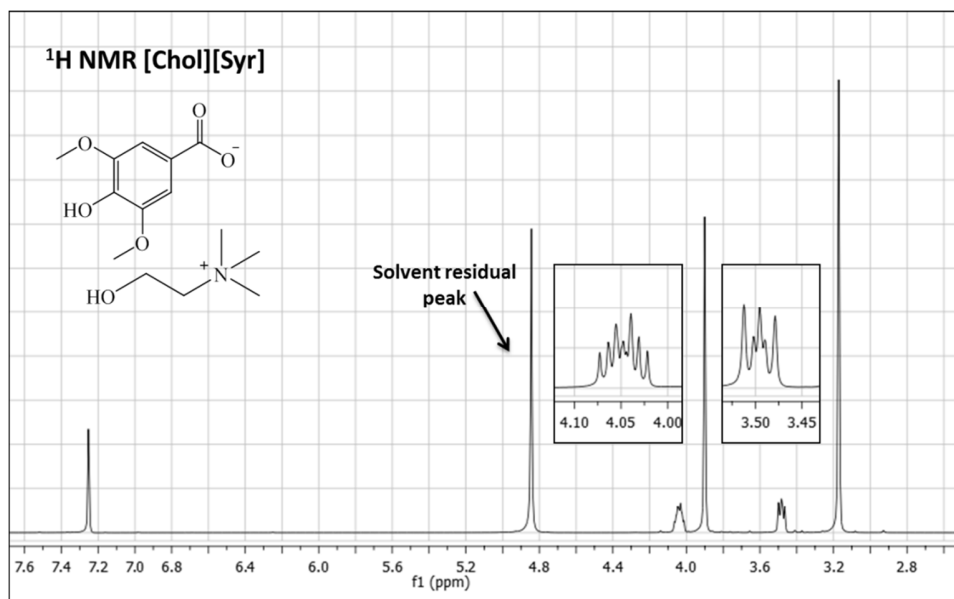
[Chol][Sal] was obtained as a viscous and light yellow liquid (93% yield), as described in literature.<sup>1</sup> <sup>1</sup>H NMR (D<sub>2</sub>O, 300 MHz, [ppm]): δ 7.48 (d, 1H,  $J_{HH} = 7.8$  Hz, H-6), 7.02 (t, 1H,  $J_{HH} = 7.8$  Hz, H-4), 6.56 (m, 2H, H-3 and H-5), 3.62-3.51 (m, 2H, NCH<sub>2</sub>CH<sub>2</sub>OH), 3.01-2.91 (m, 2H, NCH<sub>2</sub>CH<sub>2</sub>OH), 2.66 (s, 9H, N(CH<sub>3</sub>)<sub>3</sub>). <sup>13</sup>C NMR (D<sub>2</sub>O, 75.47 MHz, [ppm]): δ 175.44 (COO), 159.58 (COH-2), 133.96 (C-4), 130.45 (C-6), 119.35 (CCO-1), 118.00 (C-5), 116.26 (C-3), 67.09 (t,  $J_{CN} = 3.1$  Hz, NCH<sub>2</sub>CH<sub>2</sub>OH), 55.52 (NCH<sub>2</sub>CH<sub>2</sub>OH), 53.44 (t,  $J_{CN} = 3.9$  Hz, N(CH<sub>3</sub>)<sub>3</sub>). IR (Wavenumber, cm<sup>-1</sup>): 3271 (OH), 1627, 1581 (COO), 1450 (CH), 1380 (COO), 1134(CN), 1087,956, 856, 810, 763, 702, 663. Elemental analysis (%): calculated/expected for C<sub>12</sub>H<sub>19</sub>NO<sub>4</sub>: C 59.73, H 7.94, N 5.81; found: C 57.40, H 8.19, N 5.38.



***Cholinium syringate*, [Chol][Syr]**

(2-Hydroxyethyl) trimethylammonium 4-hydroxy-3,5-dimethoxybenzoate

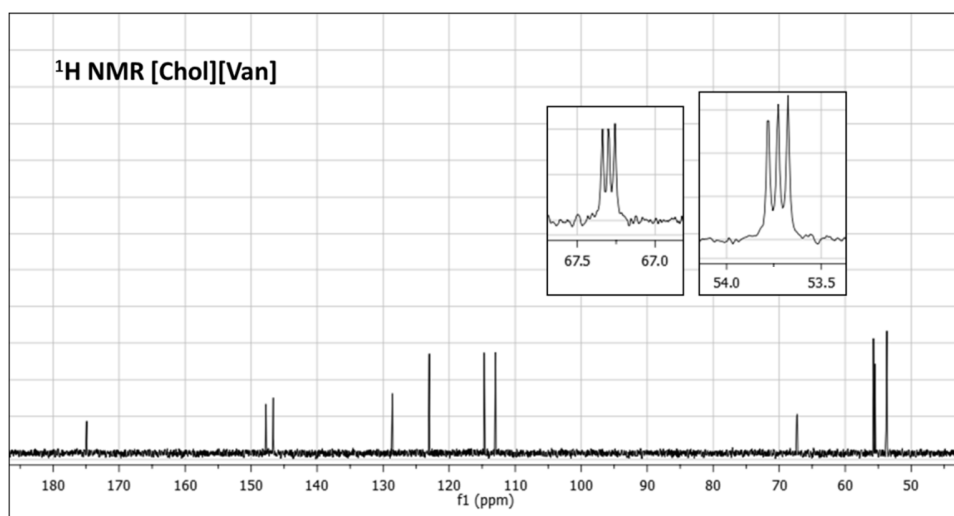
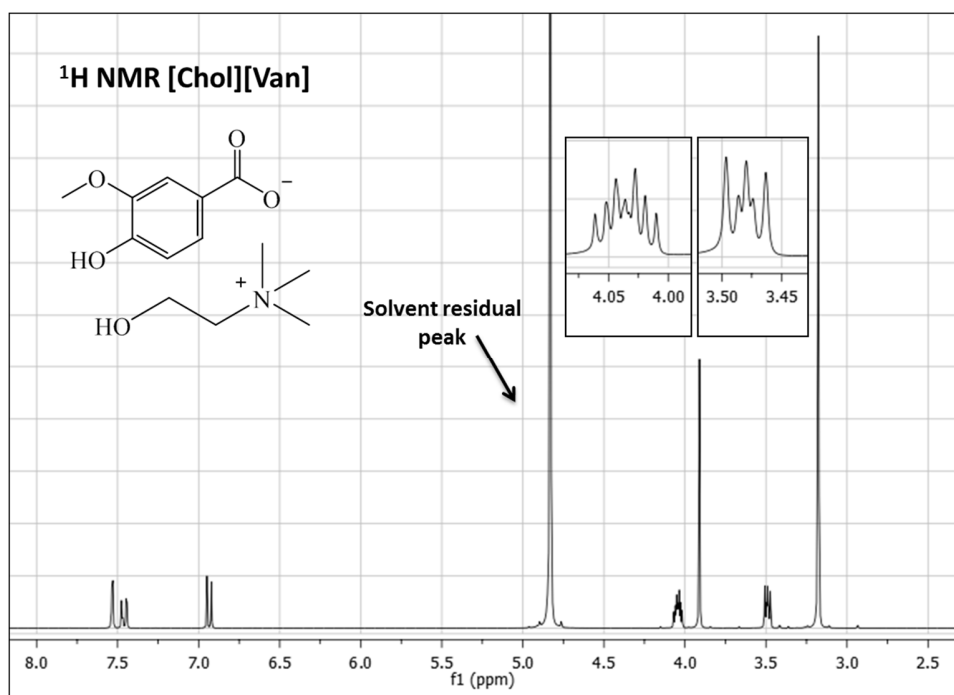
[Chol][Syr] was obtained as a white solid (98% yield).  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ , 300 MHz, [ppm]):  $\delta$  7.25 (s, 2H, H-2 and H-6), 4.09-4.01 (m, 2H,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 3.90 (s, 6H,  $2\times(\text{OCH}_3)$ ), 3.53-3.46 (m, 2H,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 3.17 (s, 9H,  $\text{N}(\text{CH}_3)_3$ ).  $^{13}\text{C}$  NMR ( $\text{D}_2\text{O}$ , 75.47 MHz, [ppm]):  $\delta$  174.59 (COO), 146.88 (COH-4), 136.85 ( $2\times(\text{COCH}_3)$ ), 127.51 (CCOO-1), 106.66 (C-6), 67.33 (t,  $J_{\text{CN}} = 3.0$  Hz,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 56.09 ( $\text{NCH}_2\text{CH}_2\text{OH}$ ), 55.51 ( $2\times(\text{OCH}_3)$ ), 53.75 (t,  $J_{\text{CN}} = 4.0$  Hz,  $\text{N}(\text{CH}_3)_3$ ). IR (Wavenumber,  $\text{cm}^{-1}$ ): 3085 (OH), 1558 (COO), 1465 (CH), 1357 (COO), 1188 (CN), 1095, 956, 879, 786, 725. Elemental analysis (%): calculated/expected for  $\text{C}_{14}\text{H}_{23}\text{NO}_6$ : C 55.80, H 7.69, N 4.65; found: C 55.13, H 7.69, N 4.49.



***Cholinium vanillate*, [Chol][Van]**

(2-Hydroxyethyl) trimethylammonium 4-hydroxy-3-methoxybenzoate

[Chol][Van] was obtained as a light brown solid (83% yield).  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ , 300 MHz, [ppm]):  $\delta$  7.53 (d, 1H,  $J_{\text{HH}}=2.0$  Hz, H-2), 7.46 (dd, 1H,  $J_{\text{HH}}=2.0$  Hz and  $J_{\text{HH}}=8.3$  Hz, H-6), 6.94 (d, 1H,  $J_{\text{HH}}=8.3$  Hz, H-5), 4.07-3.99 (m, 2H,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 3.91 (s, 3H,  $\text{OCH}_3$ ), 3.51-3.45 (m, 2H,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 3.18 (s, 9H,  $\text{N}(\text{CH}_3)_3$ ).  $^{13}\text{C}$  NMR ( $\text{D}_2\text{O}$ , 75.47 MHz, [ppm]):  $\delta$  175.02 ( $\text{COO}$ ), 148.17 ( $\text{COH-4}$ ), 146.78 ( $\text{COCH}_3\text{-3}$ ), 128.40 ( $\text{CCOO-1}$ ), 123.08 (C-6), 114.81 (C-5), 113.04 (C-2), 67.30 (t,  $J_{\text{CN}} = 3.1$  Hz,  $\text{NCH}_2\text{CH}_2\text{OH}$ ), 55.77 ( $\text{NCH}_2\text{CH}_2\text{OH}$ ), 55.51 ( $\text{OCH}_3$ ), 53.7, (t,  $J_{\text{CN}} = 3.9$  Hz,  $\text{N}(\text{CH}_3)_3$ ). IR (Wavenumber,  $\text{cm}^{-1}$ ): 3008 (OH), 2854, 1542 ( $\text{COO}$ ), 1373 ( $\text{COO}$ ), 1203 (CN), 1080, 1018, 956, 771, 632. Elemental analysis (%): calculated/expected for  $\text{C}_{13}\text{H}_{21}\text{NO}_5$ : C 57.55, H 7.80, N 5.16; found: C 58.59, H 7.85, N 5.07.



Due to the quadrupole moment of the  $^{14}\text{N}$  nucleus,  $^{13}\text{C}$ - $^{14}\text{N}$  couplings were observed in the  $^{13}\text{C}$  NMR spectrum of the all synthesized cholinium salts. Additionally, the methylenic protons located in  $\alpha$  to the N in the 2-hydroxyethyl chain appear as a characteristic multiplet because of the coupling with the neighbor  $\beta$ -CH<sub>2</sub>. According to literature,<sup>2-3</sup> the form of this multiplet suggests that the conformation of the cation at room temperature is preferentially *anti* in all synthesized compounds.

**Table S1.** Calibration curves used to determine the water solubility of the cholinium-based salts and of the respective acids.

	$\lambda_{max}/\text{nm}$	Calibration curve	$R^2$
[Chol][Van]	251	$y = 32.491x$	0.9996
Vanillic acid	256	$y = 54.32x$	0.9991
[Chol][Caf]	286	$y = 49.622x$	0.9991
Caffeic acid	290	$y = 78.35x$	0.9984
[Chol][Syr]	261	$y = 28.063x$	0.9941
Syringic acid	265	$y = 43.311x$	0.9905
[Chol][Gal]	259	$y = 30.338x$	0.9995
Gallic acid	265	$y = 44.072x$	0.9994
[Chol] <sub>2</sub> [Ell]	253	$y = 85.698x$	0.9944
Salicylic acid	297	$y = 25.392x$	0.9995



**Table S2.** Equations derived from the graphical representation of scavenging activity against the sample concentration.

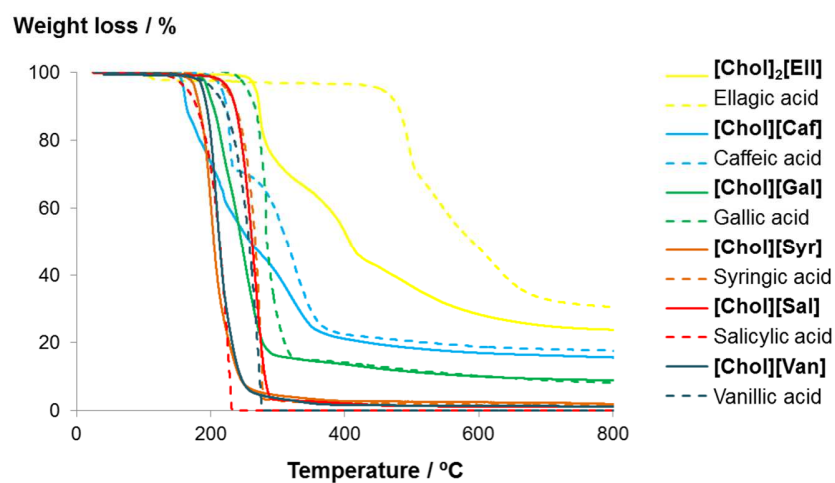
	AA(%) = m C( $\mu\text{g.mL}^{-1}$ )					
	30 min		90 min		120 min	
	M	R <sup>2</sup>	m	R <sup>2</sup>	m	R <sup>2</sup>
[Chol][Van]	2.2428	0.9814	2.7814	0.9448	3.1143	0.9665
	2.1885	0.9901	2.8179	0.9595	3.0804	0.9739
	2.2022	0.9911	2.8668	0.9709	3.1624	0.9766
Vanillic acid	---	---	0.6053	0.9572	0.6252	0.9535
	---	---	0.5958	0.9367	0.6112	0.9148
	---	---	0.5927	0.9683	0.6282	0.9604
[Chol][Caf]	17.281	0.9588	19.356	0.9778	20.181	0.9835
	16.783	0.9229	18.393	0.9261	19.133	0.9277
	17.162	0.9810	18.864	0.9897	19.625	0.9930
Caffeic acid	23.246	0.9947	24.533	0.9883	24.957	0.9961
	23.401	0.9902	24.624	0.9916	25.244	0.9918
	23.020	0.9704	24.389	0.9754	25.104	0.9762
[Chol][Syr]	19.805	0.9673	21.002	0.9753	21.280	0.9829
	18.943	0.9794	20.092	0.9828	20.277	0.9852
	18.616	0.9716	19.827	0.9753	19.948	0.9806
Syringic acid	24.921	0.9682	24.291	0.9385	24.673	0.9463
	24.396	0.9463	23.863	0.9609	24.246	0.9628
	24.150	0.9690	24.280	0.9327	24.638	0.9417
[Chol][Gal]	45.135	0.9894	46.089	0.9894	45.609	0.9869
	44.955	0.9929	45.495	0.9942	45.181	0.9923
	46.470	0.9901	47.372	0.9921	47.189	0.9929
Gallic acid	70.385	0.9727	69.687	0.9740	66.356	0.9608
	70.851	0.9658	70.008	0.9879	66.394	0.9917
	69.939	0.9862	69.943	0.9850	67.292	0.9733
[Chol] <sub>2</sub> [Ell]	40.483	0.9657	41.062	0.9672	42.196	0.9703
	38.881	0.9789	39.668	0.9831	40.658	0.9818
	38.655	0.9828	39.196	0.9894	40.638	0.9890
Ellagic acid	63.337	0.9901	65.223	0.9905	65.571	0.9895
	61.032	0.9869	62.850	0.9869	61.858	0.9854
	61.933	0.9909	63.979	0.9913	62.752	0.9890
Ascorbic acid	19.715	0.9738	19.370	0.9782	19.378	0.9795
	19.577	0.9761	19.062	0.9733	19.024	0.9736
	19.310	0.9705	19.083	0.9711	19.243	0.9698

**Table S3.** IC<sub>50</sub> (μg.mL<sup>-1</sup>) values determined for the cholinium-based salts under study and for the respective acids, as well as the respective standard deviations (std), after 30, 90 and 120 minutes of exposure to DPPH.

	(IC <sub>50</sub> ± std) / (μg.mL <sup>-1</sup> )		
	30 min	90 min	120 min
[Chol][Van]	22.61 ± 0.29	17.72 ± 0.27	16.03 ± 0.21
Vanillic acid <sup>a</sup>	---	83.63 ± 0.91	80.46 ± 1.18
[Chol][Caf]	2.93 ± 0.04	2.65 ± 0.07	2.55 ± 0.07
Caffeic acid	2.15 ± 0.02	2.04 ± 0.01	1.99 ± 0.01
[Chol][Syr]	2.62 ± 0.08	2.46 ± 0.07	2.44 ± 0.08
Syringic acid	2.04 ± 0.03	2.07 ± 0.02	2.04 ± 0.02
[Chol][Gal]	1.10 ± 0.02	1.08 ± 0.02	1.09 ± 0.03
Gallic acid	0.71 ± 0.01	0.72 ± 2.00 × 10 <sup>-3</sup>	0.75 ± 0.01
[Chol] <sub>2</sub> [Ell]	1.27 ± 0.03	1.25 ± 0.03	1.22 ± 0.03
Ellagic acid	0.81 ± 0.01	0.78 ± 0.01	0.79 ± 0.02
Ascorbic acid <sup>b</sup>	2.56 ± 0.027	2.61 ± 0.023	2.60 ± 0.024

<sup>a</sup>This acid presents a slow kinetic behaviour, which is in agreement with the literature;<sup>4</sup>

<sup>b</sup>This value is in accordance with literature.<sup>5</sup>



**Figure S1.** TGA curves of the synthesized cholinium-based salts and of the respective acidic species.

**Table S4.** EC<sub>50</sub> values (mg.L<sup>-1</sup>) for the antioxidant cholinium salts under study and for the corresponding acids, after 5, 15 and 30 minutes of exposure to the luminescent marine bacteria *Vibrio fischeri*, with the respective 95% confidence limits (in brackets).

	EC <sub>50</sub> / (mg.L <sup>-1</sup> ) (lower limit; upper limit)		
	5 min	15 min	30 min
[Chol][Van]	904.6 (433.5 - 1375.7)	1136.2 (570.8 - 1701.5)	1000.6 (470.7 - 1530.5)
Vanillic acid	26.7 (25.8 - 27.6)	27.1 (26.8 - 27.5)	27.5 (26.5 - 28.4)
[Chol][Caf]	1012.6 (978.5 - 1046.7)	931.1 (899.3 - 962.9)	856.3 (817.0 - 895.7)
[Chol][Syr]	622.3 (534.5 - 710.0)	605.4 (519.0 - 691.8)	568.5 (481.8 - 655.2)
Syringic acid	32.2 (27.2 - 37.2)	30.9 (26.2 - 35.6)	32.5 (28.8 - 36.1)
[Chol][Gal]	3723.0 (2575.9 - 4870.2)	2009.2 (1672.8 - 2345.6)	1725.4 (1465.7 - 1985.2)
Gallic acid	32.1 (31.2 - 33.0)	32.3 (32.0 - 32.5)	32.1 (32.0 - 32.2)
[Chol][Sal]	333.1 (198.1 - 468.2)	262.1 (150.3 - 373.8)	221.1 (129.1 - 313.0)
Salicylic acid	15.5 (11.8 - 19.2)	15.3 (11.2 - 19.3)	15.2 (10.7 - 19.8)

Due to the reduced water solubility of both ellagic and caffeic acids, it was not possible to determinate their EC<sub>50</sub> values. Moreover, the EC<sub>50</sub> value of [Chol]<sub>2</sub>[Ell] was not assessed due to the formation of a precipitate when the cholinium salt solution was in contact with the osmotic solution used in the Microtox<sup>®</sup> tests.

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