

Supplementary information

Activity of New Synthetic (2-Chloroethylthio)-1,4-Naphthoquinones in Prostate Cancer Cells

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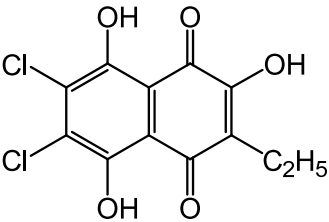
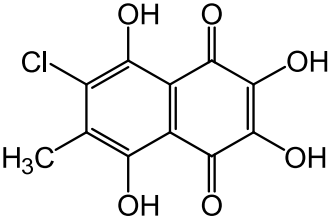
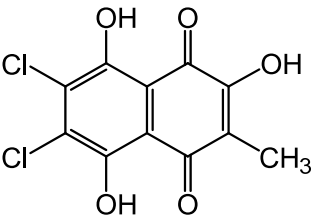
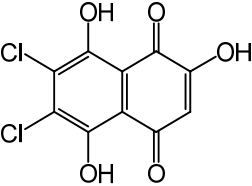
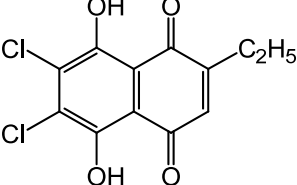
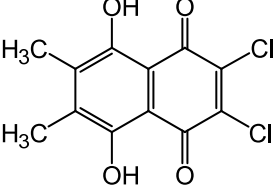
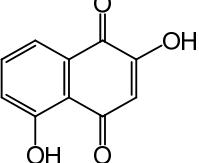
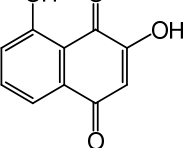
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CHEMISTRY	1
Table S1.1. Starting compounds used for the synthesis.....	1
Table S1.2. Synthesized compounds.	3
Table S1.3. Synthesized compounds.	6
Table S1.4. Synthesized compounds.	7
BIOLOGY	13
Cell culture conditions	13
Figure S1. Effects of 30 and 32 on cell viability in combination with platinum or taxane agents.....	13
Table S2. Molar ratios of the individual drugs used for drug combinational studies.....	14

CHEMISTRY

Table S1.1. Starting compounds used for the synthesis

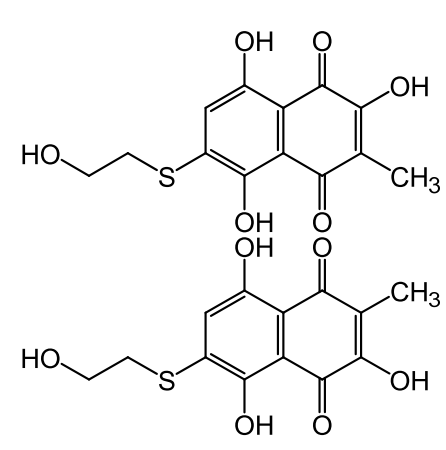
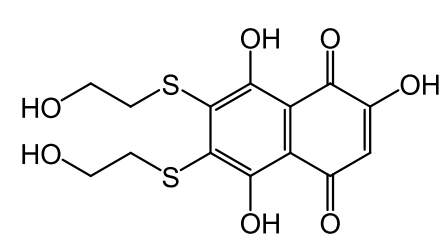
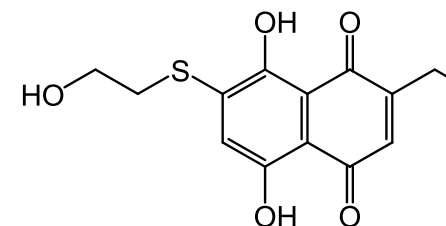
No	Formula	Spectral Information, References, Notes
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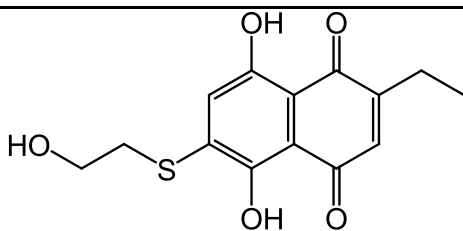
1		6,7-dichloro-2-ethyl-3,5,8-trihydroxy-1,4-naphthoquinone was synthesized as described in Anufriev, V.Ph.; Polonik, S.G.; Pokhilo, N.D.; Balanyova, N.N., Chemistry of naphthazarin derivatives. 11. Trisubstituted hydroquinone derivatives in the preparative synthesis of naphthazarins. <i>Russ. Chem. Bull. (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya)</i> 2003 , 52, 2247-2250.
2		6-chloro-2,3,5,8-tetrahydroxy-7-methyl-1,4-naphthoquinone was synthesized from methylchloromaleic anhydride and 1-hydroxy 2,3,4-trimethoxybenzene in a manner analogous to 6,7-dichloro-2-ethyl-3,5,8-trihydroxy-1,4-naphthoquinone (1) described by Anufriev, V.Ph.; Polonik, S.G.; Pokhilo, N.D.; Balanyova, N.N., Chemistry of naphthazarin derivatives. 11. Trisubstituted hydroquinone derivatives in the preparative synthesis of naphthazarins. <i>Russ. Chem. Bull. (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya)</i> 2003 , 52, 2247-2250.
3		6,7-dichloro-2,5,8-trihydroxy-3-methyl-1,4-naphthoquinone was synthesized from dichloromaleic anhydride and 1,2,4-trimethoxy-3-methylbenzene in a manner analogous to 6,7-dichloro-2-ethyl-3,5,8-trihydroxy-1,4-naphthoquinone (1) described by Anufriev, V.Ph.; Polonik, S.G.; Pokhilo, N.D.; Balanyova, N.N., Chemistry of naphthazarin derivatives. 11. Trisubstituted hydroquinone derivatives in the preparative synthesis of naphthazarins. <i>Russ. Chem. Bull. (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya)</i> 2003 , 52, 2247-2250.
4		6,7-dichloro-2,5,8-trihydroxy-1,4-naphthoquinone was synthesized as described in Anufriev, V.Ph.; Novikov, V.L.; Maximov O.B., Elyakov G.B., Levitsky D.O., Lebedev A.V., Sadretdinov, S.M.; Shvilkin, A.V.; Afonskaya, N.I.; Ruda, M.Ya.; Cherpachenko, N.M., Synthesis of some hydroxynaphthazarins and their cardioprotective effects under ischemia-reperfusion <i>in vivo</i> . <i>Bioorg. Med. Chem. Lett.</i> 1998 , 8, 587-592.
5		6,7-dichloro-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone was synthesized as described in Yakubovskaya, A.Ya.; Pokhilo, N.D.; Anufriev, V.F.; Anisimov, M.M., Synthesis and antimicrobial and antifungal activities of compounds of the naphthazarin series. <i>Pharmaceutical Chemistry Journal</i> 2009 , 43, 396-398.
6		2,3-dichloro-5,8-dihydroxy-6,7-dimethyl-1,4-naphthoquinone was synthesized as described in Anufriev, V.Ph.; Polonik, S.G.; Pokhilo, N.D.; Balanyova, N.N., Chemistry of naphthazarin derivatives. 11. Trisubstituted hydroquinone derivatives in the preparative synthesis of naphthazarins. <i>Russ. Chem. Bull. (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya)</i> 2003 , 52, 2247-2250.
7		2,5-dihydroxy-1,4-naphthoquinone was synthesized as described in Fieser, L.F.; Dunn, J.T., The addition of dienes to halogenated and hydroxylated naphthoquinones. <i>J. Am. Chem. Soc.</i> 1937 , 59, 1016-1021.
8		2,8-dihydroxy-1,4-naphthoquinone was synthesized as described in Fieser, L.F.; Dunn, J.T., The addition of dienes to halogenated and hydroxylated naphthoquinones. <i>J. Am. Chem. Soc.</i> 1937 , 59, 1016-1021.

9		2-hydroxy-5,6,7-trimethoxy-1,4-naphthoquinone was synthesized from 2-(3,4,5-trimethoxyphenyl)acetic acid as described in Kun, L.; Kun, Ya.; Lifang Zh.; Yuanyuan, L.; Qi W.; Ruili, L.; Dian, H., Anti-acute myeloid leukemia activity of 2-chloro-3-alkyl-1,4-naphthoquinone derivatives through inducing mtDNA damage and GSH depletion. <i>Bioorganic and Medicinal Chemistry</i> 2018 , 26, 4191–4200.
10		2,5,8-trihydroxy-7-methoxy-1,4-naphthoquinone was synthesized as described in Glazunov, V.P.; Tchizhova, A.Ya.; Shestak, O.P.; Sopel'nyak, G.I.; Anufriev, V.Ph., Chemistry of naphthazarin derivatives. 8. Determination of structures of substituted 2-hydroxy-6(7)-methoxynaphthazarins and 7(8)-hydroxypyranonaphthazarins by IR spectroscopy. <i>Russ. Chem. Bull.</i> (Translation of <i>Izvestiya Akademii Nauk, Seriya Khimicheskaya</i>) 2001 , 50, 95-100.
11		3,5-dihydroxy-6-methoxy-2-methyl-1,4-naphthoquinone (ancistroquinone B) was synthesized as described in Khmelevskaya, E.A.; Pelageev, D.N., A convenient synthetic approach to dioncoquinone B and related compounds. <i>Tetrahedron Lett.</i> 2019 , 60, 1022-1024.
12		3,5,6-trihydroxy-2-methyl-1,4-naphthoquinone (dioncoquinone B) was synthesized as described in Khmelevskaya, E.A.; Pelageev, D.N., A convenient synthetic approach to dioncoquinone B and related compounds. <i>Tetrahedron Lett.</i> 2019 , 60, 1022-1024.

Table S1.2. Synthesized compounds.

No	Formula	Spectral Information, References, Notes
13		2-Ethyl-3,5,8-trihydroxy-6,7-di(2-hydroxyethylthio)-1,4-naphthoquinone (13) (obtained from 6,7-dichloro-2-ethyl-3,5,8-trihydroxy-1,4-naphthoquinone (1)): dark violet solid; yield: 564 mg (73%); mp 142–146 °C. IR (CHCl₃) ν_{max} : 3419, 2937, 2878, 1601, 1382, 1365, 1330, 1279 cm ⁻¹ . ¹H NMR (CDCl₃, 300 MHz) : δ = 14.05 (s, 1 H, α -OH), 12.49 (s, 1 H, α -OH), 7.49 (br s, 1 H, β -OH), 3.71 (t, J = 5.0 Hz, 2 H), 3.67 (t, J = 5.0 Hz, 2 H), 3.47 (t, J = 5.0 Hz, 2 H), 3.34 (t, J = 5.0 Hz, 2 H), 2.63 (q, J = 7.3 Hz, 2 H), 1.15 (t, J = 7.3 Hz, 3 H). ¹³C NMR (CDCl₃, 75 MHz) : δ = 187.9, 181.2, 158.0, 157.9, 153.5, 143.8, 136.3, 127.0, 109.2, 108.8, 61.1, 60.6, 39.0, 38.7, 16.4, 12.5. HRMS (ESI) : m/z [M-H] ⁻ calcd for C ₁₆ H ₁₇ O ₇ S ₂ : 385.0421; found: 385.0424.
14		2,3,5,8-tetrahydroxy-6-(2-hydroxyethylthio)-7-methyl-1,4-naphthoquinone (14) (obtained from 6-chloro-2,3,5,8-tetrahydroxy-7-methyl-1,4-naphthoquinone (2)): dark red solid; yield: 393 mg (63%); mp 195-200°C. IR (KBr) : 3480, 3402, 1677, 1658, 1599, 1451, 1406,

	<p>1303, 1279, 1218 cm⁻¹. ¹H NMR (acetone-d₆, 300 MHz): δ = 13.08 (s, 1 H, α-OH), 12.68 (s, 1 H, α-OH), 9.03 (s, 2 H, β-OH), 3.86 (br s, 1 H, OH), 3.65 (t, <i>J</i> = 6.5 Hz, 2 H), 3.21 (t, <i>J</i> = 6.5 Hz, 2 H), 2.49 (s, 3 H, CH₃). ¹³C NMR (DMSO-d₆, 75 MHz): δ = 183.8, 183.4, 157.2, 155.0, 142.2, 141.7, 141.6, 135.1, 108.1, 107.1, 61.0, 36.8, 15.0. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₃H₁₁O₇S: 311.0231; found: 311.0232.</p>
<p>15a 15b</p> 	<p>mixture of 2,5,8-trihydroxy-6-(2-hydroxyethylthio)-3-methyl-1,4-naphthoquinone (15a) and 3,5,8-trihydroxy-6-(2-hydroxyethylthio)-2-methyl-1,4-naphthoquinone (15b) (obtained from 6,7-dichloro-2,5,8-trihydroxy-3-methyl-1,4-naphthoquinone (3)): Dark red solid; yield: 326 mg (55%); HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₃H₁₁O₆S: 295.0282; found: 295.0286. 15a ¹H NMR (CDCl₃, 300 MHz): δ = 13.71 (s, 1 H, α-OH), 11.67 (s, 1 H, α-OH), 6.95 (s, 1 H), 3.96 (t, <i>J</i> = 6.0 Hz, 2 H), 3.22 (t, <i>J</i> = 6.0 Hz, 2 H), 2.09 (s, 3 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 188.3, 179.1, 158.6, 155.6, 154.5, 145.6, 120.4, 119.5, 109.0, 107.1, 60.1, 33.9, 8.4. 15b ¹H NMR (CDCl₃, 300 MHz): δ = 12.92 (s, 1 H, α-OH), 12.16 (s, 1 H, α-OH), 7.08 (s, 1 H), 3.93 (t, <i>J</i> = 6.0 Hz, 2 H), 3.21 (t, <i>J</i> = 6.0 Hz, 2 H), 2.11 (s, 3 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 186.7, 181.2, 158.1, 156.2, 153.1, 139.8, 124.5, 122.4, 109.2, 107.6, 60.1, 33.7, 8.2.</p>
<p>16</p> 	<p>6,7-di(2-hydroxyethylthio)-2,5,8-trihydroxy-1,4-naphthoquinone (16) (obtained from 6,7-dichloro-2,5,8-trihydroxy-1,4-naphthoquinone (4)): dark violet solid; yield: 437 mg (61%); mp 187–189 °C. IR (KBr): 3525, 2917, 1663, 1607, 1545, 1467, 1408, 1387, 1357 cm⁻¹. ¹H NMR (DMSO-d₆, 300 MHz): δ = 13.91 (br s, 1 H, α-OH), 13.35 (br s, 1 H, α-OH), 12.27 (br s, 1 H, β-OH), 6.57 (s, 1 H), 5.65 (br s, 2 H, OH), 3.63–3.49 (m, 4 H), 2.75–2.63 (m, 4 H). ¹³C NMR (DMSO-d₆, 75 MHz): δ = 186.1, 178.1, 162.3, 160.1, 158.4, 138.2, 136.5, 111.4, 110.5, 109.6, 61.5, 61.3, 36.9, 36.8. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₄H₁₃O₇S₂: 357.0108; found: 357.0111.</p>
<p>17a 17b</p> 	<p>mixture of 2-ethyl-5,8-dihydroxy-7-(2-hydroxyethylthio)-1,4-naphthoquinone (17a) and 2-ethyl-5,8-dihydroxy-6-(2-hydroxyethylthio)-1,4-naphthoquinone (17b) (obtained from 6,7-dichloro-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone(5)): red solid; yield: 265 mg (45%); HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₄H₁₃O₅S: 293.0489; found: 293.0491.</p>



17a

¹H NMR (CDCl₃, 300 MHz): δ = 12.75 (s, 1 H, α-OH), 12.64 (s, 1 H, α-OH), 7.07 (s, 1 H), 6.73 (s, 1 H), 3.92 (t, *J* = 6.0 Hz, 2 H), 3.12 (t, *J* = 6.0 Hz, 2 H), 2.72 (q, *J* = 7.5 Hz, 2 H), 1.91 (br s, 1H, OH), 1.25 (t, *J* = 7.5 Hz, 3 H).

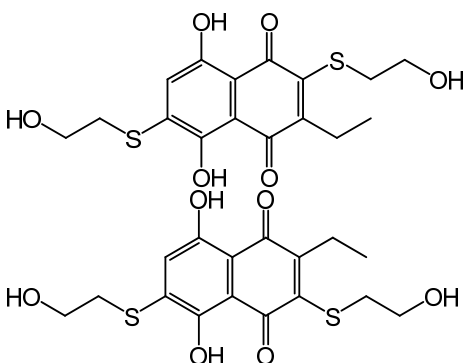
¹³C NMR (CDCl₃, 75 MHz): δ = 180.0, 179.7, 163.1, 162.7, 152.5, 147.0, 129.5, 127.0, 110.9, 109.4, 59.9, 33.5, 23.0, 12.6.

17b

¹H NMR (CDCl₃, 300 MHz): δ = 13.06 (s, 1 H, α-OH), 12.38 (s, 1 H, α-OH), 7.02 (s, 1 H), 6.72 (s, 1 H), 3.92 (t, *J* = 6.0 Hz, 2 H), 3.12 (t, *J* = 6.0 Hz, 2 H), 2.73 (q, *J* = 7.5 Hz, 2 H), 1.91 (br s, 1H, OH), 1.25 (t, *J* = 7.5 Hz, 3 H).

¹³C NMR (CDCl₃, 75 MHz): δ = 180.8, 179.4, 163.5, 161.8, 153.2, 149.4, 127.3, 126.7, 110.3, 109.9, 59.9, 33.5, 23.1, 12.6.

18a
18b



mixture of 3-ethyl-5,8-dihydroxy-2,6-di(2-hydroxyethylthio)-1,4-naphthoquinone (18a) and 2-ethyl-5,8-dihydroxy-3,6-di(2-hydroxyethylthio)-1,4-naphthoquinone (18b)

(obtained from 6,7-dichloro-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone(5)):

red solid;

yield: 200 mg (27%);

HRMS (ESI): *m/z* [M-H]⁻ calcd for C₁₆H₁₇O₆S₂: 369.0472; found: 369.0474.

18a

¹H NMR (CDCl₃, 300 MHz): δ = 13.23 (s, 1 H, α-OH), 13.08 (s, 1 H, α-OH), 6.82 (s, 1 H), 3.95 (t, *J* = 7.5 Hz, 2 H), 3.79 (t, *J* = 7.5 Hz, 2 H), 3.15 (t, *J* = 7.5 Hz, 2 H), 3.11 (t, *J* = 7.5 Hz, 2 H), 3.07 (q, *J* = 7.5 Hz, 2 H), 1.17 (t, *J* = 7.5 Hz, 3 H).

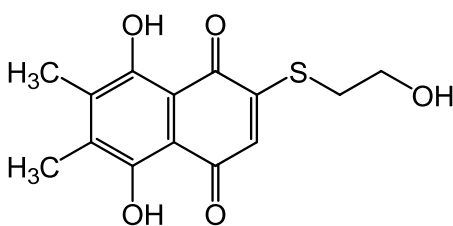
¹³C NMR (CDCl₃, 75 MHz): δ = 175.6, 174.5, 167.9, 165.7, 154.2, 148.8, 136.1, 125.8, 110.1, 109.7, 60.7, 59.3, 36.1, 31.5, 22.8, 13.7.

18b

¹H NMR (CDCl₃, 300 MHz): δ = 13.36 (s, 1 H, α-OH), 13.02 (s, 1 H, α-OH), 6.81 (s, 1 H), 3.93 (t, *J* = 7.5 Hz, 2 H), 3.75 (t, *J* = 7.5 Hz, 2 H), 3.17 (t, *J* = 7.5 Hz, 2 H), 3.13 (t, *J* = 7.5 Hz, 2 H), 3.06 (q, *J* = 7.5 Hz, 2 H), 1.16 (t, *J* = 7.5 Hz, 3 H).

¹³C NMR (CDCl₃, 75 MHz): δ = 175.2, 174.1, 167.3, 167.1, 151.5, 149.1, 139.4, 125.3, 110.4, 109.0, 60.6, 59.4, 36.1, 31.5, 22.8, 13.7.

19



5,8-dihydroxy-2-(2-hydroxyethylthio)-6,7-dimethyl-1,4-naphthoquinone (19) (obtained from 2,3-dichloro-5,8-dihydroxy-6,7-dimethyl-1,4-naphthoquinone (6)):

purple solid;

yield: 194 mg (33%);

mp 133-137°C.

IR (CHCl₃): 3662, 3610, 2929, 2883, 2857, 1715, 1600, 1552, 1432, 1391, 1302, 1261 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz): δ = 13.11 (s, 1 H, α-OH), 13.07 (s, 1 H, α-OH), 6.78 (s, 1 H), 3.97 (t, *J* = 6.0 Hz, 2 H), 3.15 (t, *J* = 6.0 Hz, 2 H), 2.25 (s, 3 H, Me), 2.24 (s, 3 H, Me).

¹³C NMR (CDCl₃, 75 MHz): δ = 173.8, 172.6, 169.8, 168.5, 149.3, 141.9, 139.6, 125.1, 109.3, 108.4, 59.8,

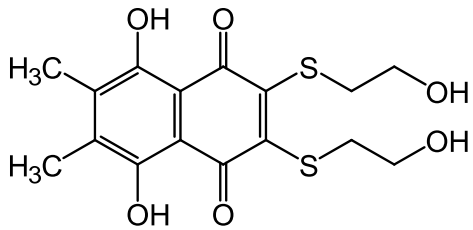
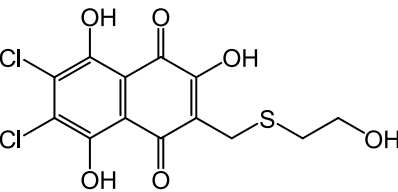
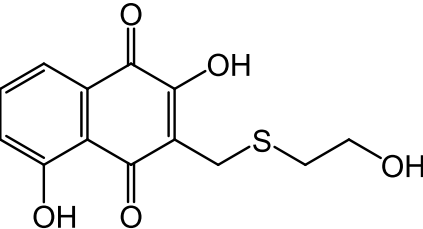
	33.5, 12.5, 12.3. HRMS (ESI): m/z [M-H] ⁻ calcd for C ₁₄ H ₁₃ O ₅ S: 293.0489; found: 293.0488.
<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">20</div>  </div>	5,8-dihydroxy-2,3-di(2-hydroxyethylthio)-6,7-dimethyl-1,4-naphthoquinone (20) (obtained from 2,3-dichloro-5,8-dihydroxy-6,7-dimethyl-1,4-naphthoquinone (6)): purple solid; yield: 356 mg (48%); mp 115-120°C. IR (CHCl₃): 2932, 2875, 1601, 1395, 1330, 1297, 1269 cm ⁻¹ . ¹H NMR (CDCl₃, 300 MHz): δ = 13.50 (s, 2 H, 2 α-OH), 3.72 (t, <i>J</i> = 4.7 Hz, 4 H), 3.43 (t, <i>J</i> = 4.7 Hz, 4 H), 2.23 (s, 6 H, Me). ¹³C NMR (CDCl₃, 75 MHz): δ = 172.7, 169.9, 144.3, 141.5, 109.6, 61.3, 38.7, 12.6. HRMS (ESI): m/z [M-H] ⁻ calcd for C ₁₆ H ₁₇ O ₆ S ₂ : 369.0472; found: 369.0475.

Table S1.3. Synthesized compounds.

No	Formula	Spectral Information, References, Notes
21		6,7-dichloro-2,5,8-trihydroxy-3-((2-hydroxyethylthio)methyl)-1,4-naphthoquinone (21) (obtained from 6,7-dichloro-2,5,8-trihydroxy-1,4-naphthoquinone (4)): red solid; yield: 347 mg (95%); mp 165-168°C. IR (KBr): 3415, 1608, 1402, 1277, 1217, 1178, 1135, 1114, 1054, 990 cm ⁻¹ . ¹H NMR (DMSO-d₆, 300 MHz): δ = 13.71 (br s, 1 H, α-OH), 13.51 (br s, 1 H, α-OH), 12.22 (br s, 1 H, β-OH), 5.62 (br s, 1 H, OH), 3.56 (s, 2 H), 3.54 (t, <i>J</i> = 6.8 Hz, 2 H), 2.62 (t, <i>J</i> = 6.8 Hz, 2 H). ¹³C NMR (DMSO-d₆, 75 MHz): δ = 186.7, 181.8, 157.5, 153.0, 152.8, 132.0, 129.7, 122.2, 110.8, 110.1, 60.9, 35.0, 23.2. HRMS (ESI): <i>m/z</i> [M-H] ⁻ calcd for C ₁₃ H ₉ Cl ₂ O ₆ S: 362.9502; found: 362.9503.
22		2,5-dihydroxy-3-((2-hydroxyethylthio)methyl)-1,4-naphthoquinone (22) (obtained from 2,5-dihydroxy-1,4-naphthoquinone (7)): yellow solid; yield: 260 mg (93%); mp 124-126 °C. IR (CHCl₃): 3393, 2930, 1661, 1622, 1603, 1459, 1388, 1332, 1294, 1277, 1241, 1228, 1220, 1206, 1166 cm ⁻¹ . ¹H NMR (CDCl₃, 300 MHz): δ = 12.28 (s, 1 H, α-OH), 7.68 (dd, <i>J</i> = 7.5, 1.0 Hz, 1 H), 7.65 (br s, 1 H, β-OH), 7.57 (t, <i>J</i> = 7.5 Hz, 1 H), 7.32 (dd, <i>J</i> = 7.5, 1.0 Hz, 1 H), 3.86 (t, <i>J</i> = 7.8 Hz, 2 H), 3.73 (s, 2 H), 2.81 (t, <i>J</i> = 7.8 Hz, 2 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 189.7, 180.5, 161.6, 153.7, 135.4, 129.3, 126.8, 120.6, 119.7, 114.3, 60.8, 35.6, 22.6. HRMS (ESI): <i>m/z</i> [M-H] ⁻ calcd for C ₁₃ H ₁₁ O ₅ S: 279.0333; found: 279.0336.

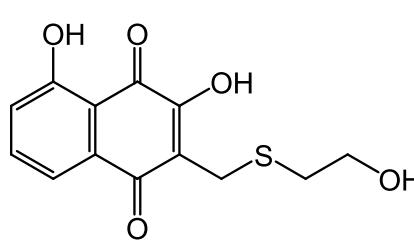
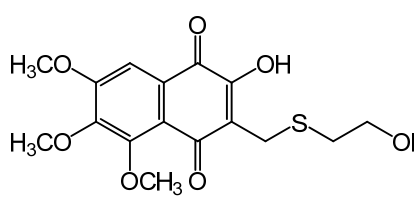
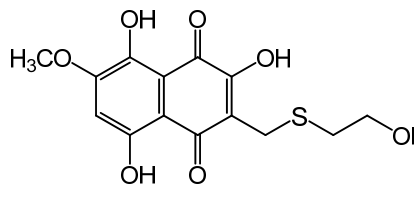
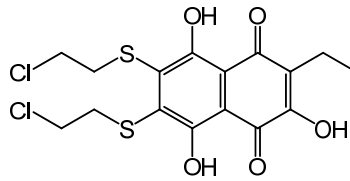
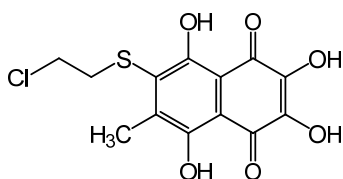
<p>23</p> 	<p>3,5-dihydroxy-2-((2-hydroxyethylthio)methyl)-1,4-naphthoquinone (23) (obtained from 2,8-dihydroxy-1,4-naphthoquinone (8)): yellow solid; yield: 266 mg (95%); mp 132-134 °C. IR (KBr): 3374, 2931, 1624, 1577, 1482, 1460, 1406, 1386, 1369, 1292, 1218, 1209, 1162, 1146, 1066 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ = 11.07 (s, 1 H, α-OH), 7.72-7.62 (m, 2 H), 7.60 (s, 1 H, β-OH), 7.23 (dd, <i>J</i> = 7.5, 2.0 Hz, 1 H), 3.85 (t, <i>J</i> = 5.6 Hz, 2 H), 3.82 (s, 2 H), 2.80 (t, <i>J</i> = 5.6 Hz, 2 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 184.4, 183.0, 161.5, 153.0, 137.9, 132.3, 123.6, 122.3, 120.0, 113.0, 60.8, 35.6, 23.0. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₃H₁₁O₅S: 279.0333; found: 279.0334.</p>
<p>24</p> 	<p>2-hydroxy-3-((2-hydroxyethylthio)methyl)-5,6,7-trimethoxy-1,4-naphthoquinone (24) (obtained from 2-hydroxy-5,6,7-trimethoxy-1,4-naphthoquinone (9)): yellow solid; yield: 322 mg (91%); mp 126-128°C. IR (KBr): 3413, 2941, 1659, 1574, 1484, 1468, 1454, 1416, 1373, 1328, 1251, 1215, 1200, 1142, 1100, 972 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ = 7.48 (s, 1 H), 7.40 (br s, 1 H, β-OH), 4.00 (s, 3 H), 3.98 (s, 3 H), 3.93 (s, 3 H), 3.84 (t, <i>J</i> = 5.8 Hz, 2 H), 3.70 (s, 2 H), 2.81 (t, <i>J</i> = 5.8 Hz, 2 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 182.6, 180.7, 156.7, 154.7, 151.6, 149.7, 126.3, 122.0, 119.7, 106.2, 61.6, 61.4, 60.7, 56.4, 35.7, 23.1. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₆H₁₇O₇S: 353.0700; found: 353.0703.</p>
<p>25</p> 	<p>3,5,8-trihydroxy-2-((2-hydroxyethylthio)methyl)-6-methoxy-1,4-naphthoquinone (25) (obtained from 2,5,8-trihydroxy-7-methoxy-1,4-naphthoquinone (10)): red solid; yield: 300 mg (92%); mp 195-198°C. IR (KBr): 3530, 1594, 1484, 1455, 1437, 1408, 1385, 1363, 1309, 1195, 1064, 1024 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ = 13.22 (s, 1 H, α-OH), 12.03 (s, 1 H, α-OH), 7.32 (s, 1 H, β-OH), 6.59 (s, 1 H), 3.99 (s, 3 H, OCH₃), 3.87 (t, <i>J</i> = 7.8 Hz, 2 H), 3.85 (s, 2 H), 2.80 (t, <i>J</i> = 7.8 Hz, 2 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 181.6, 177.2, 164.2, 157.1, 155.4, 152.9, 122.8, 110.3, 109.4, 108.8, 60.8, 56.8, 35.6, 23.0. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₄H₁₃O₇S: 325.0387; found: 325.0387.</p>

Table S1.4. Synthesized compounds.

No	Formula	Spectral Information, References, Notes
26		<p>6,7-di(2-chloroethylthio)-2-ethyl-3,5,8-trihydroxy-1,4-naphthoquinone (26) (obtained from 6,7-di(2-hydroxyethylthio)-2,5,8-trihydroxy-1,4-naphthoquinone (13)): dark violet solid; yield: 159 mg (75%); mp 126-128°C.</p>

27



IR (CHCl_3): 3418, 2977, 1617, 1600, 1365, 1331, 1280 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz): δ = 14.07 (s, 1 H, α -OH), 12.49 (s, 1 H, α -OH), 7.35 (s, 1 H, β -OH), 3.73-3.56 (m, 6 H), 3.50-3.43 (m, 2 H), 2.64 (q, J = 7.5 Hz, 2 H), 1.16 (t, J = 7.5 Hz, 3 H).

^{13}C NMR (CDCl_3 , 75 MHz): δ = 187.4, 180.5, 158.0, 157.8, 153.3, 143.2, 135.4, 126.9, 109.0, 108.6, 43.3, 43.1, 36.7, 36.5, 16.3, 12.4.

HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{16}\text{H}_{15}\text{Cl}_2\text{O}_5\text{S}_2$: 420.9743; found: 420.9744.

6-(2-Chloroethylthio)-2,3,5,8-tetrahydroxy-7-methyl-1,4-naphthoquinone (obtained from 2,3,5,8-tetrahydroxy-6-(2-hydroxyethylthio)-7-methyl-1,4-naphthoquinone (**14**)):

purple solid;

yield: 136 mg (82%);

mp 162-166°C.

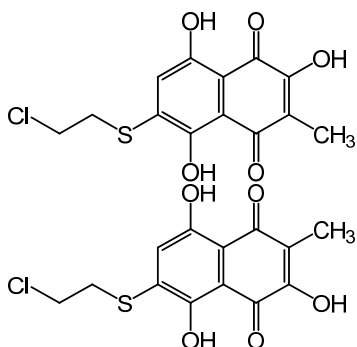
IR (CHCl_3): 3662, 3433, 1693, 1599, 1416, 1376, 1310, 1288 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz): δ = 12.69 (s, 1 H, α -OH), 12.23 (s, 1 H, α -OH), 6.70 (s, 2 H, β -OH), 3.60 (t, J = 7.5 Hz, 2 H), 3.41 (t, J = 7.5 Hz, 2 H), 2.54 (s, 3 H).

^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ = 183.3, 183.1, 156.5, 154.5, 142.3, 141.2, 141.2, 132.8, 108.0, 106.9, 43.9, 35.7, 14.5.

HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_{10}\text{ClO}_6\text{S}$: 328.9892; found: 328.9896.

28



mixture of 6-(2-chloroethylthio)-2,5,8-trihydroxy-3-methyl-1,4-naphthoquinone (28a) and 6-(2-chloroethylthio)-3,5,8-trihydroxy-2-methyl-1,4-naphthoquinone (28b)

(obtained from the mixture of 2,5,8-trihydroxy-6-(2-hydroxyethylthio)-3-methyl-1,4-naphthoquinone (**15a**) and 3,5,8-trihydroxy-6-(2-hydroxyethylthio)-2-methyl-1,4-naphthoquinone (**15b**)):

dark red solid;

yield: 134 mg (85%);

HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_{10}\text{ClO}_5\text{S}$: 312.9943; found: 312.9945.

6-(2-chloroethylthio)-2,5,8-trihydroxy-3-methyl-1,4-naphthoquinone (28a)

^1H NMR (CDCl_3 , 700 MHz): δ = 13.64 (s, 1 H, α -OH), 11.61 (s, 1 H, α -OH), 7.45 (s, 1 H, β -OH), 6.88 (s, 1 H), 3.75 (t, J = 7.5 Hz, 2 H), 3.37 (t, J = 7.5 Hz, 2 H), 2.08 (s, 3 H).

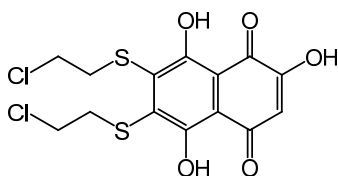
^{13}C NMR (CDCl_3 , 175 MHz): δ = 188.3, 179.3, 158.4, 155.4, 154.5, 144.3, 120.6, 119.4, 109.2, 107.4, 40.9, 32.7, 8.1.

6-(2-chloroethylthio)-3,5,8-trihydroxy-2-methyl-1,4-naphthoquinone (28b)

^1H NMR (CDCl_3 , 700 MHz): δ = 12.87 (s, 1 H, α -OH), 12.10 (s, 1 H, α -OH), 7.25 (s, 1 H, β -OH), 7.03 (s, 1 H), 3.73 (t, J = 7.5 Hz, 2 H), 3.36 (t, J = 7.5 Hz, 2 H), 2.10 (s, 3 H).

^{13}C NMR (CDCl_3 , 175 MHz): δ = 186.9, 181.3, 157.9, 155.9, 153.1, 138.5, 124.5, 122.4, 109.4, 107.9, 41.1, 32.9, 8.3.

29



6,7-di(2-chloroethylthio)-2,5,8-trihydroxy-1,4-naphthoquinone (obtained from 6,7-di(2-hydroxyethylthio)-2,5,8-trihydroxy-1,4-naphthoquinone (**16**)):

purple solid;

yield: 134 mg (68%);

mp 133–136 °C.

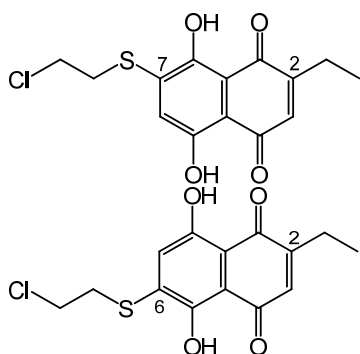
IR (CHCl₃): 3518, 3413, 2953, 1659, 1605, 1534, 1442, 1403, 1384, 1343, 1269, 1194, 1106 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz): δ = 13.84 (s, 1 H, α-OH), 12.52 (s, 1 H, α-OH), 7.41 (s, 1 H, β-OH), 6.43 (s, 1 H), 3.75–3.61 (m, 6 H), 3.48 (t, *J* = 7.5 Hz, 2 H).

¹³C NMR (CDCl₃, 75 MHz): δ = 185.6, 177.2, 160.8, 159.8, 157.0, 137.9, 135.8, 111.0, 109.1, 108.7, 43.5, 43.3, 36.9, 36.5.

HRMS (ESI): *m/z* [M-H]⁻ calcd for C₁₄H₁₁Cl₂O₅S₂: 392.9430; found: 392.9431.

30



Equimolar mixture of 7-(2-chloroethylthio)-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone (30a) and 6-(2-chloroethylthio)-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone (30b)

(obtained from the mixture of 2-ethyl-5,8-dihydroxy-7-(2-hydroxyethylthio)-1,4-naphthoquinone (**17a**) and 2-ethyl-5,8-dihydroxy-6-(2-hydroxyethylthio)-1,4-naphthoquinone (**17b**)):

red solid; yield:

134 mg (86%);

HRMS (ESI): *m/z* [M-H]⁻ calcd for C₁₄H₁₂ClO₄S: 311.0150; found: 311.0151.

7-(2-chloroethylthio)-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone (30a)

¹H NMR (CDCl₃, 300 MHz): δ = 12.73 (s, 1 H, α-OH), 12.62 (s, 1 H, α-OH), 7.07 (s, 1 H), 6.68 (s, 1 H), 3.76 (t, *J* = 7.5 Hz, 2 H), 3.28 (t, *J* = 7.5 Hz, 2 H), 2.71 (q, *J* = 7.5 Hz, 2 H), 1.25 (t, *J* = 7.5 Hz, 3 H).

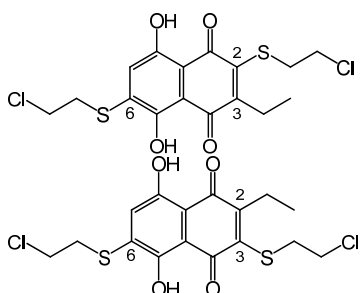
¹³C NMR (CDCl₃, 75 MHz): δ = 179.1, 179.0, 163.8, 163.3, 151.2, 147.3, 129.6, 126.6, 110.8, 109.3, 40.4, 32.4, 22.9, 12.5.

6-(2-chloroethylthio)-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone (30b)

¹H NMR (CDCl₃, 300 MHz): δ = 13.03 (s, 1 H, α-OH), 12.36 (s, 1 H, α-OH), 7.01 (s, 1 H), 6.66 (s, 1 H), 3.76 (t, *J* = 7.5 Hz, 2 H), 3.28 (t, *J* = 7.5 Hz, 2 H), 2.73 (q, *J* = 7.5 Hz, 2 H), 1.26 (t, *J* = 7.5 Hz, 3 H).

¹³C NMR (CDCl₃, 75 MHz): δ = 180.1, 178.5, 164.1, 162.4, 152.0, 149.6, 127.5, 126.2, 110.1, 109.9, 40.4, 32.4, 23.1, 12.5.

31



Equimolar mixture of 2,6-di(2-chloroethylthio)-3-ethyl-5,8-dihydroxy-1,4-naphthoquinone (31a) and 3,6-di(2-chloroethylthio)-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone (31b)

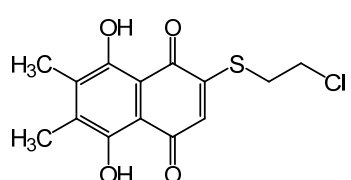
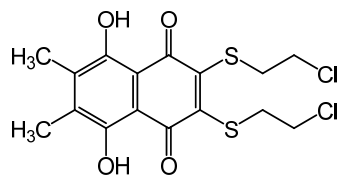
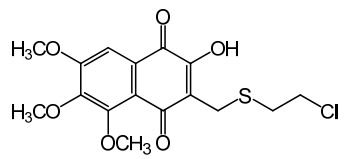
(obtained from the mixture of 3-ethyl-5,8-dihydroxy-2,6-di(2-hydroxyethylthio)-1,4-naphthoquinone (**18a**) and 2-ethyl-5,8-dihydroxy-3,6-di(2-hydroxyethylthio)-1,4-naphthoquinone (**18b**)):

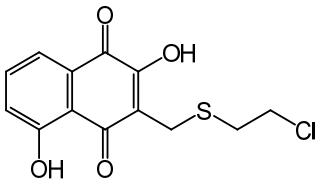
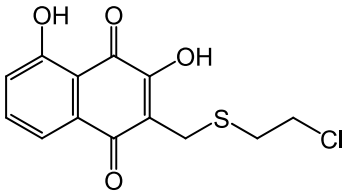
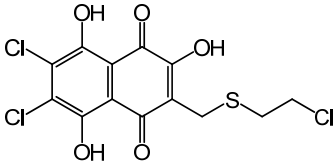
dark red solid;

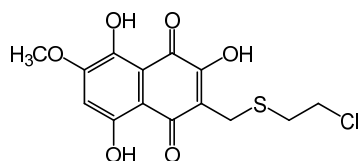
yield: 141 mg (69%);

HRMS (ESI): *m/z* [M-H]⁻ calcd for C₁₆H₁₅Cl₂O₄S₂: 404.9794; found: 404.9792.

2,6-di(2-chloroethylthio)-3-ethyl-5,8-dihydroxy-

	<p>1,4-naphthoquinone (31a) ¹H NMR (CDCl₃, 300 MHz): δ = 13.21 (s, 1 H, α-OH), 13.06 (s, 1 H, α-OH), 6.77 (s, 1 H), 3.76 (t, <i>J</i> = 7.5 Hz, 2 H), 3.65 (t, <i>J</i> = 7.5 Hz, 2 H), 3.45 (t, <i>J</i> = 7.5 Hz, 2 H), 3.31 (t, <i>J</i> = 7.5 Hz, 2 H), 3.06 (q, <i>J</i> = 7.5 Hz, 2 H), 1.17 (t, <i>J</i> = 7.5 Hz, 3 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 174.8, 173.8, 168.6, 166.2, 153.3, 149.1, 136.8, 125.4, 109.9, 109.6, 43.4, 40.5, 36.0, 32.5, 22.6, 13.5.</p> <p>3,6-di(2-chloroethylthio)-2-ethyl-5,8-dihydroxy-1,4-naphthoquinone (31b) ¹H NMR (CDCl₃, 300 MHz): δ = 13.34 (s, 1 H, α-OH), 13.00 (s, 1 H, α-OH), 6.76 (s, 1 H), 3.76 (t, <i>J</i> = 7.5 Hz, 2 H), 3.65 (t, <i>J</i> = 7.5 Hz, 2 H), 3.51 (t, <i>J</i> = 7.5 Hz, 2 H), 3.31 (t, <i>J</i> = 7.5 Hz, 2 H), 3.03 (q, <i>J</i> = 7.5 Hz, 2 H), 1.16 (t, <i>J</i> = 7.5 Hz, 3 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 174.5, 173.2, 167.9, 167.7, 150.4, 149.3, 139.6, 124.8, 110.3, 108.9, 43.5, 40.5, 36.0, 32.5, 22.4, 13.3.</p>
<p>32</p> 	<p>2-(2-Chloroethylthio)-5,8-dihydroxy-6,7-dimethyl-1,4-naphthoquinone (obtained from 5,8-dihydroxy-2-(2-hydroxyethylthio)-6,7-dimethyl-1,4-naphthoquinone (19)): purple solid; yield: 120 mg (77%); mp 125-127°C. IR (CHCl₃): 2927, 2856, 1733, 1715, 1601, 1555, 1457, 1391, 1300, 1267 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ = 13.09 (s, 1 H, α-OH), 13.07 (s, 1 H, α-OH), 6.79 (s, 1 H), 3.75 (t, <i>J</i> = 7.5 Hz, 2 H), 3.31 (t, <i>J</i> = 7.5 Hz, 2 H), 2.54 (s, 3 H). ¹³C NMR (CDCl₃, 75 MHz): δ = 172.6, 171.5, 171.1, 170.3, 147.8, 142.5, 140.3, 124.8, 109.7, 108.7, 40.8, 32.6, 12.7, 12.5. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₄H₁₂ClO₄S: 311.0150; found: 311.0152.</p>
<p>33</p> 	<p>2,3-di(2-chloroethylthio)-5,8-dihydroxy-6,7-dimethyl-1,4-naphthoquinone (obtained from 5,8-dihydroxy-2,3-di(2-hydroxyethylthio)-6,7-dimethyl-1,4-naphthoquinone (20)): purple solid; yield: 132 mg (65%); mp 132-136°C. IR (CHCl₃): 2928, 2856, 1600, 1445, 1392, 1379, 1297, 1270 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ = 13.51 (s, 2 H, 2 α-OH), 3.72 (t, <i>J</i> = 7.4 Hz, 4 H), 3.59 (t, <i>J</i> = 7.4 Hz, 4 H), 2.26 (s, 6 H, Me). ¹³C NMR (CDCl₃, 75 MHz): δ = 171.9, 170.1, 143.0, 141.3, 109.4, 43.5, 36.6, 12.5. HRMS (ESI): <i>m/z</i> [M-H]⁻ calcd for C₁₆H₁₅Cl₂O₄S₂: 406.3246; found: 406.3250.</p>
<p>34</p> 	<p>3-((2-chloroethylthio)methyl)-2-hydroxy-5,6,7-trimethoxy-1,4-naphthoquinone (obtained from 2-hydroxy-3-((2-hydroxyethylthio)methyl)-5,6,7-trimethoxy-1,4-naphthoquinone (24)): yellow solid; yield: 158 mg (85%); mp 129-132°C. IR (CHCl₃): 3410, 3001, 1704, 1655, 1578, 1483, 1466, 1418, 1374, 1334, 1294, 1143, 1102 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ = 7.48 (s, 1 H), 7.28 (br s, 1 H, β-OH), 4.00 (s, 3 H), 3.98 (s, 3 H), 3.93</p>

		<p>(s, 3 H), 3.72 (t, $J = 7.8$ Hz, 2 H), 3.69 (s, 2 H), 2.92 (t, $J = 7.8$ Hz, 2 H).</p> <p>^{13}C NMR (CDCl_3, 75 MHz): $\delta = 182.3, 180.7, 156.7, 154.8, 151.5, 149.8, 126.2, 121.8, 119.7, 106.2, 61.7, 61.4, 56.5, 42.9, 34.4, 23.5$.</p> <p>HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{16}\text{H}_{17}\text{ClO}_6\text{S}$: 371.0361; found: 371.0364.</p>
35		<p>3-((2-chloroethylthio)methyl)-2,5-dihydroxy-1,4-naphthoquinone (obtained from 2,5-dihydroxy-3-((2-hydroxyethylthio)methyl)-1,4-naphthoquinone (22)): yellow solid;</p> <p>yield: 114 mg (76%);</p> <p>mp 116-118 °C.</p> <p>IR (CHCl_3): 3391, 3010, 1660, 1623, 1459, 1415, 1387, 1332, 1294, 1277, 1191, 1167, 1070 cm^{-1}.</p> <p>^1H NMR (CDCl_3, 300 MHz): $\delta = 12.27$ (s, 1 H, α-OH), 7.68 (dd, $J = 7.5, 1.0$ Hz, 1 H), 7.65 (br s, 1 H, β-OH), 7.57 (t, $J = 7.5$ Hz, 1 H), 7.32 (dd, $J = 7.5, 1.0$ Hz, 1 H), 3.73 (t, $J = 7.8$ Hz, 2 H), 3.71 (s, 2 H), 2.93 (t, $J = 7.8$ Hz, 2 H).</p> <p>^{13}C NMR (CDCl_3, 75 MHz): $\delta = 189.6, 180.3, 161.6, 153.6, 135.4, 129.3, 126.7, 120.6, 119.7, 114.2, 42.8, 34.4, 22.9$.</p> <p>HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_{10}\text{ClO}_4\text{S}$: 296.9996; found: 296.9994.</p>
36		<p>2-((2-chloroethylthio)methyl)-3,5-dihydroxy-1,4-naphthoquinone (obtained from 3,5-dihydroxy-2-((2-hydroxyethylthio)methyl)-1,4-naphthoquinone (23)): yellow solid;</p> <p>yield: 117 mg (78%);</p> <p>mp 119-121 °C.</p> <p>IR (CHCl_3): 3412, 3003, 1653, 1630, 1577, 1461, 1417, 1367, 1318, 1277, 1170 cm^{-1}.</p> <p>^1H NMR (CDCl_3, 500 MHz): $\delta = 11.05$ (s, 1 H, α-OH), 7.70-7.64 (m, 2 H), 7.52 (s, 1 H, β-OH), 7.23 (dd, $J = 8.0, 1.5$ Hz, 1 H), 3.72 (t, $J = 7.6$ Hz, 2 H), 3.71 (s, 2 H), 2.93 (t, $J = 7.6$ Hz, 2 H).</p> <p>^{13}C NMR (CDCl_3, 125 MHz): $\delta = 184.3, 182.8, 161.5, 152.8, 138.0, 132.3, 123.6, 122.1, 120.0, 113.0, 42.8, 34.4, 23.4$.</p> <p>HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_{10}\text{ClO}_4\text{S}$: 296.9994; found: 296.9994.</p>
37		<p>6,7-dichloro-2-((2-chloroethylthio)methyl)-3,5,8-trihydroxy-1,4-naphthoquinone (obtained from 6,7-dichloro-2,5,8-trihydroxy-3-((2-hydroxyethylthio)methyl)-1,4-naphthoquinone (21)): red solid;</p> <p>yield: 139 mg (72%);</p> <p>mp 143-147 °C.</p> <p>IR (CHCl_3): 3410, 3010, 1657, 1630, 1610, 1553, 1432, 1402, 1323, 1271, 1226, 1212, 1204, 1180, 1113 cm^{-1}.</p> <p>^1H NMR (CDCl_3, 500 MHz): $\delta = 13.34$ (s, 1 H, α-OH), 12.01 (s, 1 H, α-OH), 7.55 (s, 1 H, β-OH), 3.74 (s, 2 H), 3.72 (t, $J = 7.8$ Hz, 2 H), 2.94 (t, $J = 7.8$ Hz, 2 H).</p> <p>^{13}C NMR (CDCl_3, 125 MHz): $\delta = 186.3, 180.7, 154.7$ (2C), 153.7, 135.7, 131.7, 122.5, 108.9, 108.8, 42.7, 34.6, 23.0.</p> <p>HRMS (ESI): m/z $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_8\text{Cl}_3\text{O}_5\text{S}$: 380.9163; found: 380.9165.</p>



2-((2-chloroethylthio)methyl)-3,5,8-trihydroxy-6-methoxy-1,4-naphthoquinone (obtained from 3,5,8-trihydroxy-2-((2-hydroxyethylthio)methyl)-6-methoxy-1,4-naphthoquinone (**25**)):

red solid;

yield: 128 mg (74%);

mp 176-179 °C.

IR (CHCl₃): 3523, 3411, 2942, 1602, 1478, 1436, 1413, 1396, 1354, 1323, 1304, 1274, 1217, 1210, 1196, 1178 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz): δ = 13.20 (s, 1 H, α-OH), 12.02 (s, 1 H, α-OH), 7.30 (s, 1 H, β-OH), 6.59 (s, 1 H), 3.98 (s, 3 H, OCH₃), 3.75 (s, 2 H), 3.73 (t, *J* = 7.8 Hz, 2 H), 2.93 (t, *J* = 7.8 Hz, 2 H).

¹³C NMR (CDCl₃, 75 MHz): δ = 181.5, 177.1, 164.0, 157.0, 155.4, 152.9, 122.8, 110.3, 109.4, 108.8, 56.7, 42.8, 34.4, 23.1.

HRMS (ESI): *m/z* [M-H]⁻ calcd for C₁₄H₁₂ClO₆S: 343.0048; found: 343.0051.

BIOLOGY

Cell culture conditions

Cells were incubated at 37°C in a humidified atmosphere with 5% (v/v) CO₂. Cells were continuously kept in culture for a maximum of 3 months, and were routinely inspected microscopically for stable phenotype and regularly checked for contamination with mycoplasma.

PC-3, DU145, LNCaP, 22Rv1 and PNT2 cells were cultured in 10% FBS/RPMI medium (RPMI medium supplemented with GlutamaxTM-I (Invitrogen, Paisley, UK) containing 10% fetal bovine serum (FBS, Invitrogen) and 1% penicillin/streptomycin (Invitrogen)). MRC-9, HEK 293 and VCaP cells were cultured in 10% FBS/DMEM medium (DMEM medium supplemented with GlutamaxTM-I (Invitrogen) containing 10% FBS and 1% penicillin/streptomycin (Invitrogen)). RWPE-1 cells were cultured in Clonetics[®] EGMTM-2 SingleQuots[®] medium (Lonza, Walkersville, MD, USA) containing 10% FBS. HUVEC cells (passage 11) were cultured in Clonetics[®] EGMTM-2 SingleQuots[®] medium (Lonza, Walkersville, MD, USA) containing 10% FBS.

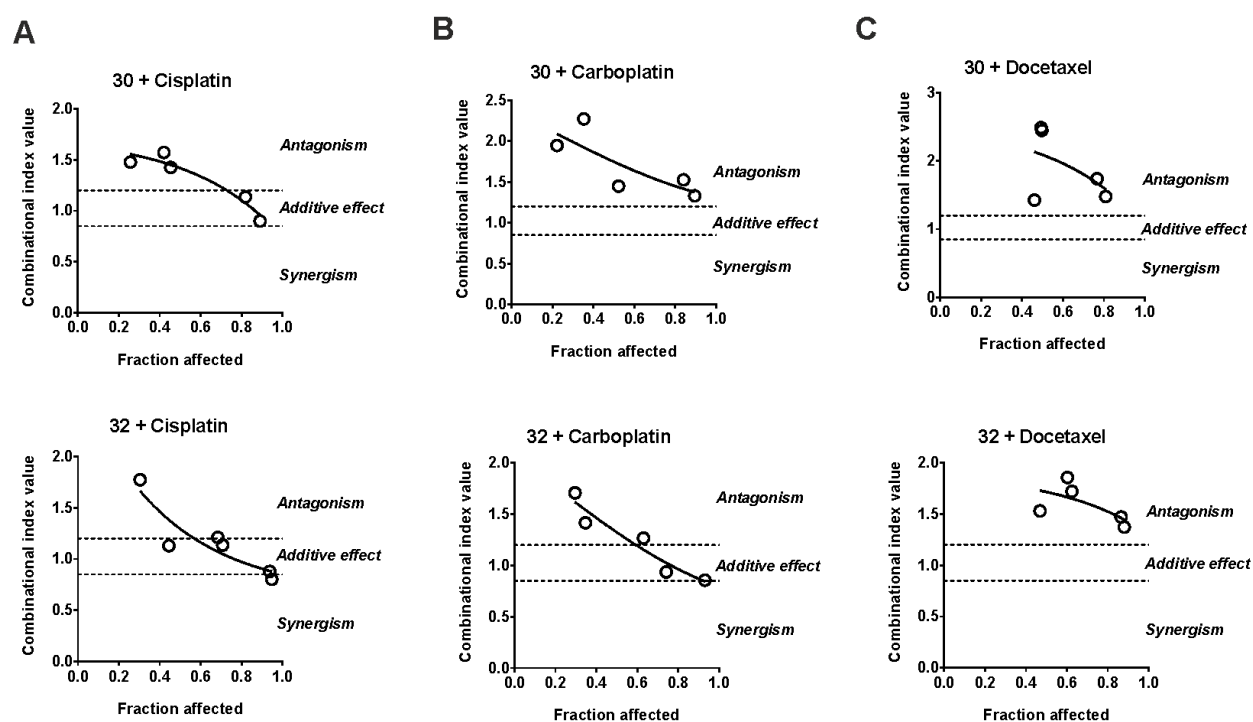


Figure S1. Effects of **30** and **32** on cell viability in combination with platinum or taxane agents.

22Rv1 cells were co-treated with indicated drug combinations for 48 h and the viability was evaluated using MTT viability assay and analyzed using Chou-Talalay method. Combinational index (CI) values were calculated using CompuSyn 1.0 software.

Table S2. Molar ratios of the individual drugs used for drug combinational studies.

Figure 3H	30 : Olaparib	0.6 : 100
	32 : Olaparib	0.4 : 100
Figure 4A	30 : SB203580	0.5 : 200
	30 : SCH772984	0.5 : 4
	30 : PD98059	0.5 : 200
	30 : GSK-690396	0.5 : 40
	30 : GSK-SP600125	0.5 : 100
Figure 4C	32 : SB203580	0.5 : 200
	32 : SCH772984	0.5 : 4
	32 : PD98059	0.5 : 200
	32 : GSK-690396	0.5 : 40
	32 : GSK-SP600125	0.5 : 100
Figure 5B	30 : Enzalutamide	0.6 : 100
	32 : Enzalutamide	0.4 : 100
Figure S1	30 : Cisplatin	0.6 : 10
	30 : Carboplatin	0.6 : 150
	30 : Docetaxel	0.6 : 0.02
	32 : Cisplatin	0.4 : 10
	32 : Carboplatin	0.4 : 150
	32 : Docetaxel	0.4 : 0.02