Supplementary Table:

Comparison of residues lining the colchicine binding cavity in tubulin for colchicine and resveratrol analogues **3b** and **4a**.

	Colchicine	3b	4a
α-SUBUNIT	N101	-	-
	S178	S178	S178
	T179	T179	T179
	A180	A180	A180
	V181	V181	V181
	Y224	-	-
β-SUBUNIT	V238	-	-
	T239	-	-
	C241	C241	C241
	L242	L242	L242
	L248	L248	L248
	A250	A250	A250
	D251	D251	D251
	L252	-	-
	K254	K254	K254
	L255	L255	L255
	N258	N258	N258
	M259	M259	M259
	T314	-	T314
	V315	-	V315
	A316	A316	A316
	A317	A317	A317
	V318	V318	V318
	N350	-	N350
	V351	-	V351
	K352	K352	K352
	-	-	T353
	-	-	A354
	I378	I378	I378

Residues are numbered as in the PDB 1SA0 file. Residues common to all three binding sites are not highlighted. Those unique to colchicine are highlighted red, while those that are either unique to **4a** (T353, A354), or are common to **4a** and colchicine (T314, V315, N350, V351) are highlighted yellow.

All starting materials used in this study were of at least reagent grade and were purchased from Sigma Aldrich and TCI America. Intermediate **5** was prepared as previously reported by Ruan *et al.*[1] and analytical data is consistent with the reported data.

Analytical data:

Compound 5: Pale yellow solid; 61 % yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.78 (s, 3H), 3.90 (s, 3H), 3.92 (s, 3H), 6.63 (s, 1H), 6.91 (s, 1H), 6.97 (d, 2H, J = 7.9 Hz), 7.21 (d, 1H, J = 16.2 Hz), 7.50 (d, 2H, J =7.9 Hz), 7.95 (d, 1H, J = 16.2 Hz), 10.41 (s, 1H) ppm. ^{13}C-NMR (DMSO-*d6*): 55.8, 56.1, 101.2, 102.5, 109.8, 114.3, 129.4, 130.5, 131.4, 139.7, 162.5, 167.8, 193.5 ppm. HRMS (ESI): m/z calcd for $C_{18}H_{19}O_4$ [M-H] 299.1283; found 299.1298.

Compound 3a: White solid; 82 % yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.67 (s, 3H, -OCH_3), 3.81 (s, 3H, -OCH_3), 3.83 (s, 6H, -OCH_3), 6.96 (s, 2H, -ArH), 7.09 (d, J =8.4 Hz, 1H, ArH), 7.88-7.91(m, 4H, ArH) *ppm*. ^{13}C NMR (100 MHz, DMSO-d_6): 55.88, 5652, 60.59, 103.58, 107.54, 114.92, 118.89, 126.72, 130.22, 131.47, 138.56, 142.59, 153.65, 161.48 *ppm*. HRMS (ESI): m/z calcd for $C_{19}H_{20}NO_4$ [M-H] 326.1392; found 326.1395.

Compound 3b: White solid; 72 % yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.69 (s, 3H, -OCH_3), 3.86 (s, 9H, -OCH_3), 6.97 (s, 2H, -ArH), 7.09 (d, J =8.4 Hz, 1H, ArH), 7.39 (d, J =8.4 Hz, 1H, ArH), 7.51 (s, 1H, ArH), 7.84 (s, 1H, ArH), 9.42 (s, 1H, -OH). ^{13}C NMR (100 MHz, DMSO-d_6): 56.08, 56.52, 60.58, 103.52, 107.09, 112.39, 115.61, 118.88, 122.96, 130.37, 138.45, 143.00, 146.93, 150.50, 153.63 *ppm*. HRMS (ESI): m/z calcd for $C_{19}H_{20}NO_5$ [M-H] 342.1341; found 342.1347.

Compound 3c: yellow solid; 85 % yield.^{1}H NMR (400 MHz, DMSO-d_6): δ 3.79 (s, 3H, -OCH_3), 3.84(s, 3H, -OCH_3), 3.85(s, 3H, -OCH_3), 7.04 (t, J =15.2 Hz, 2H, ArH), 7.23 (dd, J =2, 8.8 Hz, 1H, ArH), 7.29 (s, 1H, ArH), 7.38 (dd, J =1.6, 8.4 Hz, 1H, ArH), 7.49 (s, 1H, ArH), 7.77(s, 1H, ArH), 9.38 (s, 1H, -OH) *ppm*. ^{13}C NMR (100 MHz, DMSO-d_6): 55.93, 55.96, 56.02, 56.13, 56.16, 56.23, 107.16, 108.79, 112.23, 112.34, 112.39, 115.41, 115.65, 118.94, 118.97, 119.08, 122.75, 127.20, 127.29, 141.15, 141.37, 146.90, 149.53, 149.91, 150.22 *ppm*. HRMS (ESI): m/z calcd for $C_{18}H_{18}NO_4$ [M-H] 312.1236; found 312.1243.

Compound 3d: White solid; 70 % yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (s, 3H, -OCH_3), 3.80 (s, 6H, -OCH_3), 3.87 (s, 6H, -OCH_3), 6.65 (s, 1H, -ArH), 7.01 (s, 2H, -ArH), 7.12 (d, J =2 Hz, 2H, ArH), 7.96 (s, 1H, -ArH) *ppm*. ^{13}C NMR (100 MHz, DMSO-d_6): 56.32, 57.05, 61.10, 103.39, 104.39, 107.97, 111.57, 118.82, 130.18, 136.34, 139.49, 143.29, 154.16, 161.49 *ppm*. HRMS (ESI): m/z calcd for $C_{20}H_{22}NO_5$ [M-H] 356.1498; found 356.1504.

Compound 3e: White solid; 75 % yield. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 3.81 (s, 6H, -OCH3), 6.71 (s, 1H, -ArH), 7.21 (s, 2H, -ArH), 8.04 (d, J =9.2 Hz, 2H, ArH), 8.25 (s, 1H, -ArH), 8.37 (d, J =8.8 Hz, 2H, ArH) *ppm*. ^{13}C NMR (100 MHz, DMSO-*d*6): 55.8, 99.5, 99.6, 105.4, 118.5, 124.5, 125.6, 125.8, 132.4, 136.5, 140.8, 147.1 *ppm*. HRMS (ESI): m/z calcd for $C_{17}H_{15}N_2O_4$ [M-H] 311.1032; found 311.1033.

Compound 3f: White solid; 70 % yield. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 3.79 (s, 6H, -OCH3), 3.81 (s, 3H, -OCH3), 3.71 (s, 6H, -OCH3), 6.62 (s, 1H, -ArH), 7.05-7.10 (m, 4H, ArH), 7.69 (d, J =8.8 Hz, 2H, ArH), 7.84 (s, 1H, -ArH) ppm. ^{13}C NMR (100 MHz, DMSO-*d*6): 55.1, 55.4, 55.6, 111.4, 114.5, 115.9, 118.8, 126.7, 134.2, 135.1, 138.6, 142.9, 147.1, 149.1 ppm. HRMS (ESI): m/z calcd for $C_{18}H_{18}NO_3$ [M-H] 296.1287; found 296.1290.

Compound 3g: White solid; 90 % yield. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 3.58 (s, 3H, -OCH3), 3.63 (s, 3H, -OCH3), 3.71 (s, 6H, -OCH3), 7.12 (s, 2H, -ArH), 7.15 (d, J =8.0 Hz, 2H, ArH), 7.21 (d, J =8.8 Hz, 2H, ArH), 7.36 (s, 1H, -ArH) ppm. ^{13}C NMR (100 MHz, DMSO-*d*6): 55.88, 55.2, 56.9, 101.5, 104.5, 114.9, 118.8, 126.7, 134.2, 135.1, 138.6, 142.9, 154.5, 155.8 ppm. HRMS (ESI): m/z calcd for $C_{19}H_{20}NO_4$ [M-H] 326.1392; found 326.1399.

Compound 3h: White solid; 72 % yield.^{1}H NMR (400 MHz, DMSO-*d*6): δ 3.71-3.75 (m, 6H, -OCH3), 3.84 (s, 6H, - OCH3), 3.87 (s, 6H, -OCH3), 7.00 (s, 2H, -ArH), 7.32 (s, 2H, ArH), 7.94 (s, 1H, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-*d*6): 60.5, 60.6, 103.6, 107.2, 109.4, 118.7, 129.4, 129.8, 138.8, 139.9, 142.8, 153.2, 153.6 ppm. HRMS (ESI): m/z calcd for $C_{21}H_{24}NO_6$ [M-H] 386.1604; found 386.1611.

Compound 4a: yellow solid; 90 % yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (s, 9H, -OCH_3), 3.75 (s, 3H, -OCH_3), 6.67 (s, 2H, -ArH), 6.72 (s, 1H, -ArH), 6.78 (d, J =8.4 Hz, 1H, ArH), 6.89 (d, J =8.4 Hz, 1H, ArH), 7.42 (S, 1H, ArH), 9.15 (S, 1H, -OH) *ppm*. ^{13}C NMR (100 MHz, DMSO-d_6): 55.86, 56.07, 56.35, 56.57, 60.53, 60.75, 106.20, 106.38, 110.00, 112.06, 116.65, 121.06, 123.51, 126.45, 128.59, 138.55, 144.67, 144.94, 146.46, 150.16, 153.92 *ppm*. HRMS (ESI): m/z calcd for $C_{19}H_{20}NO_5$ [M-H] 342.1341; found 342.1348.

Compound 4b: brown solid; 74 % yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.91 (s, 3H, -OCH_3), 3.94(s, 6H, -OCH_3), 7.03 (d, J =13.2 Hz, 2H, ArH), 7.14 (s, 1H, ArH), 7.24 (d, J =2, 8.4Hz, 1H, ArH), 7.30 (s, 1H, ArH), 7.31 (s, 1H, ArH), 7.35 (d, J =10.4

Hz, 1H, ArH) *ppm*. ^{13}C NMR (100 MHz, DMSO-d_6): 55.95, 56.07, 108.69, 108.74, 109.18, 110.59, 110.61, 111.26, 115.06, 115.19, 118.44, 118.75, 122.02, 122.12, 127.47, 127.66, 140.15, 140.24, 145.66, 148.25, 149.23, 149.76 *ppm*. HRMS (ESI): m/z calcd for $C_{18}H_{18}NO_4$ [M-H] 312.1236; found 312.1243.

Compound 7a: pale yellow solid; 60 % yield. ^{1}H NMR (DMSO-d_6): δ 3.71 (s, 3H, -OCH3), 3.75 (s, 3H, -OCH3), 3.82 (s, 3H, -OCH3), 3.85 (s, 6H, -OCH3), 3.89 (s, 3H, -OCH3), 6.61 (s, 1H, ArH), 6.94 (d, J=8.4 Hz, 2H), 7.00 (S, 3H, ArH), 7.08 (d, J=16 Hz, 2H), 7.28 (d, J=16 Hz, 2H), 7.49 (d, J=8.4 Hz, 1H), 7.98 (s, 1H, ArH) ppm. ^{13}C-NMR (DMSO-*d6*): δ 55.1, 55.3, 55.8, 56.1, 56.4, 98.2, 101.5, 104.7, 108.1, 110.5, 115.4, 117.6, 114.2, 121.4, 127.6, 131.7, 134.2, 159.7, 160.7, 162.8 166.7 ppm. HRMS (ESI): m/z calcd for $C_{29}H_{30}NO_6$ [M-H] 488.2073; found 488.2077.

Compound 7b: pale yellow solid; 74 % yield. ^{1}H NMR (DMSO-d_6): δ 3.74 (s, 3H, -OCH3), 3.81 (s, 6H, -OCH3), 3.84 (s, 3H, -OCH3), 3.89 (s, 3H, -OCH3), 6.60 (s, 1H, ArH), 6.93 (d, *J* =8.4 Hz, 2H), 6.97 (s, 1H, ArH), 7.03-7.07 (m, 2H), 7.28 (m, 2H), 7.33 (s, 1H, ArH), 7.47 (d, *J* =8.4 Hz, 2H), 7.89 (s, 1H, ArH) ppm. ^{13}C-NMR (DMSO-*d6*): δ 55.3, 55.4, 56.2, 56.4, 56.8, 56.9, 97.5, 100.8, 104.7, 108.4, 111.5, 111.8, 114.5, 124.7, 129.5, 131.4, 134.8, 138.4, 147.5, 149.6, 158.7, 163.8, 164.5 ppm. HRMS (ESI): m/z calcd for $C_{27}H_{26}NO_4$ [M-H] 428.1862; found 428.1869.

Compound 7c: White solid; 79 % yield. ^{1}H NMR (DMSO-d_6): δ 3.75 (s, 3H, -OCH3), 3.81 (s, 9H, -OCH3), 3.89 (s, 3H, -OCH3), 6.61 (d, *J* =7.2 Hz, 2H), 6.87 (d, *J* =1.6 Hz, 2H), 6.94 (d, *J* =8.8 Hz, 2H), 6.98 (d, J=1.2 Hz, 1H), 7.07 (d, 1H, *J* =16.0 Hz, ArH), 7.27 (d, 1H, *J* =16.0 Hz, ArH),7.49 (d, 1H, *J* =8.4 Hz, ArH), 8.03 (s, 1H, ArH) ppm. ^{13}C-NMR (DMSO-*d6*): δ 55.2, 55.8, 55.9, 99.5, 100.5, 101.7, 109.5, 118.6, 120.5, 114.2, 127.4, 131.4, 136.3, 158.5, 160.7, 161.5 ppm. HRMS (ESI): m/z calcd for $C_{28}H_{28}NO_5$ [M-H] 458.1967; found 458.1974.

Compound 7d: yellow solid; 81 % yield. ^{1}H NMR (DMSO-d_6): δ 3.73 (s, 3H, -OCH3), 3.81 (s, 3H, -OCH3), 3.84 (s, 3H, -OCH3), 6.23 (s, 1H, ArH), 6.79 (d, *J* = 8.6 Hz, 2H), 6.83 (s, 2H, ArH), 7.12 (d, 1H, *J* =16.0 Hz, ArH), 7.28 (d, 1H, *J* = 8.0 Hz, ArH), 7.36-7.47 (m, 6H, ArH), 7.77 (d, 2H, *J* = 8.4 Hz, ArH), 8.04 (s, 1H, ArH). ^{13}C-NMR (DMSO-*d6*): δ 55.1, 55.6, 55.8, 87.4, 111.2, 114.7, 117.8, 118.4, 118.9, 124.8, 126.6, 127.6, 128.2, 129.5, 129.8, 131.9, 135.4, 138.5, 144.4, 158.5, 158.8, 158.9 ppm. HRMS (ESI): m/z calcd for $C_{26}H_{23}N_2O_5$ [M-H] 443.1607; found 443.1604.

Compound 7e: yellow solid; 66 % yield. ^{1}H NMR (DMSO-d_6): δ 3.75 (s, 3H, -OCH_3), 3.81 (s, 6H, -OCH_3), 3.89 (s, 3H, -OCH_3), 6.60 (s, 1H, ArH), 6.91-7.07 (m, 6H, ArH), 7.22 (d, 1H, *J* = 16.4 Hz, ArH), 7.45 (d, 2H, ArH ,*J* = 8.4 Hz), 7.68 (d, 2H, ArH and *J* = 8 Hz), 7.83 (s, 1H, ArH) *ppm*. ^{13}C-NMR (DMSO-d_6): δ 55.6, 55.9, 55.9, 56.1, 98.2, 102.2, 114.7, 115.5, 117.2, 117.6, 123.7, 126.1, 128.5, 129.6, 129.7, 129.9, 131.6, 133.8, 138.9, 139.4, 158.9, 159.7, 161.6 *ppm*. HRMS (ESI): m/z calcd for $C_{27}H_{26}NO_4$ [M-H] 428.1862; found 428.1868.

Compound 7f: yellow solid; 60 % yield. ^{1}H NMR (DMSO-d_6): δ 3.78 (s, 3H, -OCH3), 3.86 (s, 3H, -OCH3), 3.88 (s, 3H, -OCH3), 6.18 (s, 1H, ArH), 6.75 (d, *J* =8.6 Hz, 2H), 6.83 (s, 2H, ArH), 7.12 (d, 1H, *J* =16.0 Hz, ArH), 7.28 (d, 1H, *J* =16.0 Hz, ArH), 7.43-7.50 (m, 6H, ArH), 7.77 (d, 2H, *J* = 8.4 Hz, ArH), 8.01 (s, 1H, ArH). ^{13}C-NMR (DMSO-*d6*): δ 55.7, 55.2, 56.4, 99.1, 101.2, 114.7, 117.3, 117.9, 118.9, 124.8, 126.6, 127.6, 128.2, 129.5, 129.8, 131.9, 135.4, 138.5, 140.2, 158.6, 158.8, 162.4 ppm. HRMS (ESI): m/z calcd for $C_{27}H_{23}F_3NO_3$ [M-H] 466.1630; found 466.1628.

Compound 7g: pale yellow solid; 78 % yield. ^{1}H NMR (DMSO-d_6): δ 3.74 (s, 3H, -OCH3), 3.82 (s, 3H, -OCH3), 3.89 (s, 3H, -OCH3), 6.13 (s, 1H, ArH), 6.93 (d, J=8.8 Hz, 2H), 6.98 (s, 2H, ArH), 7.08 (d, 1H, *J* =16.4 Hz, ArH), 7.22 (d, 1H, *J* =16.4 Hz, ArH), 7.45-7.51 (m, 6H, ArH), 7.76 (d, 2H, *J* = 7.2 Hz, ArH), 7.98 (s, 1H, ArH). ^{13}C-NMR (DMSO-*d6*): δ 55.5, 55.9, 56.1, 98.2, 102.2, 114.7, 115.5, 117.1, 117.59, 123.6, 126.0, 128.4, 129.5, 129.6, 129.9, 131.9, 133.8, 138.9, 139.4, 158.8, 159.6, 161.6 ppm. HRMS (ESI): m/z calcd for $C_{26}H_{24}NO_3$ [M-H] 398.1756; found 398.1760.

[1] B.-F. Ruan, X. Lu, J.-F. Tang, Y. Wei, X.-L. Wang, Y.-B. Zhang, L.-S. Wang and H.-L. Zhu, *Bioorganic & Medicinal Chemistry*, 2011, 19, 2688-2695.