Supporting Information

Facile antibacterial materials with turbine-like structure for *P. aeruginosa* infected scald wounds healing

Tao Qin[a], Lixia Guo[b], Haipeng Diao[c] and Liheng Feng[a]**

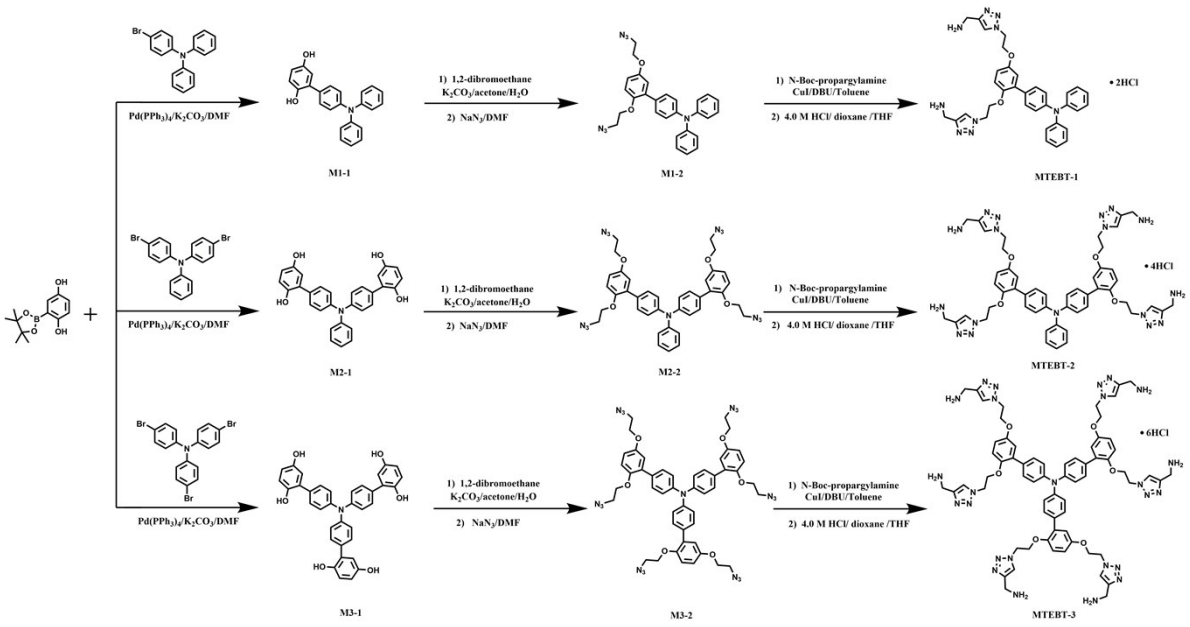
[a]School of Chemistry and Chemical Engineering, Shanxi University, Taiyuan, 030006, P. R. China. E-mail: lhfeng@sxu.edu.cn (L.H. Feng)

[b]School of Pharmacy, Shanxi Medical University, Taiyuan 030001, PR China.

[c]School of Basic Medical Sciences, Shanxi Medical University, Taiyuan 030001, PR China. E-mail: diaohp@sxmu.edu.cn (H.P. Diao)

Synthesis of MTEBT-n (n=1, 2, 3)

The synthesis routes of these compounds are shown in Scheme S1, and the detailed synthesis steps are shown as follow.



Scheme S1 The synthesis routes of MTEBT-*n*

Synthesis of M1-1. 2,5-Dihydroxyphenylboronic acid pinacolate (0.354 g, 1.50 mmol), 4-bromotriphenylamine (0.324 g, 1.0 mmol), and $Pd(PPh_3)_4$ (0.116 g, 0.100 mmol) were added to a 100 mL round bottom flask. Then 10.0 mL DMF and 5.0 mL K_2CO_3 (2.0 M) were added. The resulting mixture was stirred under nitrogen atmosphere at 100 ℃ for 20 h. Afterward, the mixture was washed with ethyl acetate and water. The organic solvent was collected and dried with anhydrous sodium sulfate. After ethyl acetate was removed under vacuum, the crude product was purified with silica-gel column chromatography (ethyl acetate: dichloromethane = 1:20, v/v) to give 0.323 g of 4-(2,5-dihydroxybenzene)triphenylamine (M1-1) in 91.39% yield as purple black solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 -7.26 (m, 6H), 7.14 (d, 6H), 7.06 (t, 2H), 6.85 (d, 1H), 6.76-6.68 (m, 2H), 4.92 (s, 1H), 4.51 (s, 1H). ^{13}C NMR (100MHz, $CDCl_3$) δ: 115.04, 116.07, 116.43, 117.09, 123.18, 123.39, 124.25, 127.86, 129.93, 130.32, 133.54, 146.01, 147.15, 147.59, 150.12, 150.48; HRMS-ESI for $C_{24}H_{19}NO_2$ (m/z) 353.1403 $[M]^+$.

Synthesis of M2-1. This compound was synthesized following the same method described above for M1-1, using 2, 5-dihydroxyphenylboronic acid pinacolate (0.708 g, 3.00 mmol), 4,4'-dibromotriphenylamine (0.403 g, 1.00 mmol), $Pd(PPh_3)_4$ (0.116 g, 0.100 mmol), 15.0 mL DMF, and 5.00 mL K_2CO_3 (2.0 M). After drying, the crude product was purified with silica-gel column chromatography (ethyl acetate: dichloromethane=1:6, v/v) to give 0.424 g of 4, 4'-(bis(2,5-dihydroxy benzene)) triphenylamine (M2-1) in 91.87% yield as purple black solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (d, 6H), 7.25-7.17 (m, 6H), 7.11 (t, 1H), 6.85 (d, 2H), 6.76 (s, 2H), 6.74 (s, 1H), 6.72 (s, 1H), 4.92 (s, 2H), 4.59 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 115.14, 116.11, 116.58, 117.26, 123.39, 123.57, 124.37, 127.97, 130.02, 130.48, 133.68, 146.06, 147.20, 147.71, 150.19, 150.56; HRMS-ESI for $C_{30}H_{23}NO_4$ (m/z) 461.1619 $[M]^+$.

Synthesis of M3-1. This compound was synthesized following the same method described above for M1-1, using 2,5-dihydroxyphenylboronic acid pinacolate (1.92 g, 8.00 mmol), tri(4-bromobenzene)amine (0.960 g, 2.00 mmol), $Pd(PPh_3)_4$ (0.116 g, 0.100 mmol), 35.0 mL DMF, and 10.0 mL K_2CO_3 (2.0 M). After drying, the crude product was purified with silica-gel column chromatography (ethyl acetate: dichloromethane = 1:4, v/v) to give 0.860 g of 4-(tri(2,5-dihydroxybenzene))-triphenylamine (M3-1) in 75.4% yield as purple black solid. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 8.77 (d, 6H), 7.51 (d, 6H), 7.09 (d, 6H), 6.74 (d, 3H), 6.69 (d, 3H), 6.56 (d, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 115.24, 116.19, 116.67, 117.55, 123.48, 123.79, 124.52, 128.11, 130.12, 130.61, 133.73, 146.25, 147.33, 147.84, 150.36, 150.89; HRMS-ESI for $C_{36}H_{27}NO_6$ (m/z) 569.1821 $[M]^+$.

Synthesis of M1-2. M1-1 (0.786 g, 2.34 mmol), 1,2-dibromoethane (4.40g, 23.4 mmol), and K_2CO_3 (9.70 g, 70.2 mmol) were added to a 50 mL round bottom flask. Then 20.0 mL acetone and 5.0 mL water were added. The resulting mixture was stirred at 66 °C for 3 days. Afterward, the solvent was removed and the mixture was and washed with dichloromethane and water. The organic solvent was collected and dried with anhydrous sodium sulfate. After dichloromethane was removed under vacuum, the crude product was purified with silica-gel

column chromatography (dichloromethane: petroleum ether = 1:2, v/v) to give 0.482 g of 4-((2,5-bis(2-bromoethoxy))benzene)triphenylamine in 36.23% yield as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, 2H), 7.29 (s, 1H), 7.27 (s, 2H), 7.25 (s, 1H), 7.12 (d, 6H), 7.03 (t, 2H), 6.94 (d, 2H), 6.82 (d, 1H), 4.29 (t, 2H), 4.18 (t, 2H), 3.64 (t, 2H), 3.53 (t, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.95, 29.23, 68.54, 69.63, 114.03, 115.42, 117.38, 123.14, 123.27, 124.69, 129.25, 130.30, 131.72, 132.18, 146.66, 147.24, 149.58, 152.98; HRMS-ESI for $C_{28}H_{25}Br_2NO_2$(m/z) 567.0226 $[M]^+$.

Next, ((2,5-bis(2-bromoethoxy)) benzene)triphenylamine (0.0908 g, 0.160 mmol), NaN_3 (0.0832 g, 1.28 mmol), and 5.0 mL DMF were added to a 25 mL round bottom flask. The resulting mixture was stirred at 100 °C for overnight. Afterward, the mixture was added into water, and washed with dichloromethane. The organic solvent was collected and dried with anhydrous sodium sulfate. After dichloromethane was removed under vacuum, 4-((2,5-bis(2-azidoethoxy))benzene)triphenylamine (M1-2) was obtained as a pale yellow solid (0.0755 g, 96.0 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, 2H), 7.28 (s, 1H), 7.26 (s, 2H), 7.24 (s, 1H), 7.17-7.07 (m, 6H), 7.01 (d, 2H), 6.93 (d, 2H), 6.83 (d, 1H), 4.18-4.12 (m, 2H), 4.05-3.99 (m, 2H), 3.59 (t, 2H), 3.49 (t, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.01, 51.12, 68.46, 69.72, 114.54, 115.73, 117.54, 123.28, 125.01, 129.33, 130.48, 131.95, 132.18, 146.81, 147.52, 149.96, 153.17; HRMS-ESI for $C_{28}H_{25}N_7O_2$(m/z) 491.2062 $[M]^+$.

Synthesis of M2-2. This compound was synthesized following the same method described above for M1-2. In the first reaction, using M2-1 (0.56 g, 1.21 mmol), 1,2-dibromoethane (4.55 g, 24.2 mmol), K_2CO_3 (10.03 g, 72.60 mmol), 20.0 mL acetone, and 5.0 mL water. Afterwards, the crude product was purified with silica-gel column chromatography (dichloromethane: petroleum ether = 1:1, v/v) to give 0.488 g of 4,4'-(bis(2,5-bis(2-bromoethoxy)) benzene)triphenylamine in 45.19% yield as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, 4H), 7.30 (t, 2H), 7.24-7.11 (m, 6H), 7.06 (t, 1H), 6.97 (d, 2H), 6.91 (s, 2H), 6.86-6.79 (m, 2H), 4.30 (t, 4H), 4.19 (t, 4H), 3.64 (t, 4H), 3.54 (t, 4H). ^{13}C NMR (100

MHz, $CDCl_3$) δ: 29.33, 29.46, 68.67, 69.71, 114.17, 115.62, 117.54, 123.21, 123.40, 124.86, 129.35, 130.35, 131.81, 132.43, 146.86, 147.53, 149.84, 153.14; HRMS-ESI for $C_{38}H_{35}Br_4NO_4$ (m/z) 888.9286 $[M]^+$.

Subsequently, using 4,4'-(bis(2,5-bis(2-bromoethoxy))benzene) triphenylamine (0.0889 g, 0.100 mmol), NaN_3 (0.104 g, 1.60 mmol), and 5.00 mL DMF. 4,4'-(bis(2,5- bis(2-azide ethoxy))benzene) triphenylamine (M2-2) was obtained as a pale yellow solid (0.0619 g, 83.9 % yield). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45 (d, 4H), 7.29 (d, 2H), 7.17 (t, 6H), 7.04 (t, 1H), 6.97 (d, 2H), 6.92 (d, 2H), 6.83 (d, 2H), 4.20-4.12 (m, 4H), 4.07-3.99 (m, 4H), 3.63-3.55 (m, 4H), 3.54-3.45 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.10, 51.34, 68.58, 69.83, 114.62, 115.81, 117.76, 123.45, 125.06, 129.51, 130.67, 132.03, 132.33, 146.98, 147.84, 150.02, 153.29; HRMS-ESI for $C_{38}H_{35}N_{13}O_4$ (m/z) 737.2916 $[M]^+$.

Synthesis of M3-2. This compound was synthesized following the same method described above for M1-2. In the first reaction, using M3-1 (2.59 g, 4.55 mmol), 1,2-dibromoethane (25.6 g, 136.5 mmol), and K_2CO_3 (12.6 g, 91.0 mmol), 50.0 mL acetone, and 10.0 mL water. Afterwards, the crude product was purified with silica-gel column chromatography (dichloromethane: petroleum ether=2:1, v/v) to give 2.55 g of 4-(tri(2,5-bis (2-bromoethoxy)) benzene)triphenylamine in 46.3% yield as white solid. ^1H NMR (600 MHz, $CDCl_3$) δ: 7.55 (d, 6H), 7.25 (d, 6H), 7.02 (d, 3H), 6.95 (d, 3H), 6.86 (d, 3H), 4.32 (t, 6H), 4.23 (t, 6H), 3.67 (t, 6H), 3.58 (t, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 29.39, 29.54, 68.89, 69.87, 114.25, 115.86, 117.63, 123.42, 123.55, 124.94, 129.62, 130.47, 131.93, 132.58, 146.98, 147.72, 150.04, 153.31; HRMS-ESI for $C_{48}H_{45}Br_6NO_6$ (m/z) 1210.8293 $[M]^+$.

Subsequently, using 4-(tri(2,5-bis(2-bromoethoxy))benzene)triphenylamine (0.130 g, 0.110 mmol), NaN_3 (0.210 g, 3.30 mmol), and 5.00 mL DMF. 4-(tri(2,5-bis (2-azide ethoxy))benzene)triphenylamine (M3-2) was obtained as a pale yellow solid (0.110 g, 99.0% yield). ^1H NMR (600 MHz, $CDCl_3$) δ:7.49 (s, 6H), 7.24 (s, 6H), 7.01 (s, 3H), 6.94 (s, 3H), 6.86 (s, 3H), 4.19 (s, 6H), 4.07 (s, 6H), 3.63 (s, 6H), 3.53 (s, 6H). ^{13}C NMR (150 MHz,

$CDCl_3$) δ: 51.26, 51.42, 68.70, 69.94, 114.76, 115.94, 117.83, 123.57, 125.18, 129.69, 130.89, 132.12, 132.47, 147.14, 147.98, 150.26, 153.43; HRMS-ESI for $C_{48}H_{45}N_{19}O_6$ (m/z) 983.3765 $[M]^+$.

Synthesis of MTEBT-1. M1-2 (0.208 g, 0.420 mmol) and N-Boc-aminopropyne (0.652 g, 4.20 mmol) were added to a 50 mL round bottom flask with 10.0 mL toluene. Then, cuprous iodide (0.0476 g, 0.250 mmol) was added after 10 min, and DBU (1,8-Diazabicyclo[5.4.0]undec-7-ene, 0.256 g, 1.68 mmol) was added after another 10 min. The resulting mixture was stirred at 60 °C for overnight under N_2 atmosphere. Afterward, the organic solvent was removed under vacuum, the crude product was purified with silica-gel column chromatography (methanol: dichloromethane = 1:30, v/v) to give 0.315 g of 4-((2,5-bis(2- (4- (N- tertbutyloxy- carbonyl methyleneamino)1H- 1,2,3- triazole) ethoxy)) benzene) triphenyl- amine in 93.41% yield as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (s, 1H), 7.32- 7.26 (m, 6H), 7.25 (s, 1H), 7.16-7.12 (m, 4H), 7.11-7.02 (m, 4H), 6.84 (d, 1H), 6.79 (d, 1H), 6.73 (d, 1H), 4.74 (s, 2H), 4.62 (s, 2H), 4.40 (s, 2H), 4.33 (s, 2H), 4.27 (s, 2H), 4.23 (s, 2H), 1.41 (s, 9H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.33, 34.27, 34.34, 49.82, 66.87, 68.08, 79.59, 114.38, 115.53, 117.06, 123.15, 125.09, 125.59, 130.29, 130.82, 131.01, 131.86, 140.63, 140.91, 146.72, 149.72, 152.89, 153.17; HRMS-ESI for $C_{44}H_{51}N_9O_6$ (m/z) 801.3983 $[M]^+$.

4-((2,5-bis(2-(4-(N-tert-butyloxycarbonylmethyleneamino)1H-1,2,3-triazole)ethoxy)) -benzene)tri-phenylamine (0.107 g, 0.130 mmol) was added to a 50 mL round bottom flask. Then, 2 mL THF and 1 mL 1, 4-dioxane containing 4 M of HCl were added. The resulting mixture was stirred at room temperature for 36 h. Afterward, the solvent was removed and the crude product was recrystallized with chloroform and n-hexane to obtain 0.0735 g of 4-(2,5-bis(2-(4-(methylamine hydrochloride)1H-1,2,3-triazole)- ethoxy))benzene) triphenylamine (MTEBT-1) in 83.81% yield as a pale yellow solid. ^{1}H NMR (400 MHz, DMS-d_6) δ: 8.46 (s, 6H), 8.30 (s, 1H), 8.09 (s, 1H), 7.47-7.12 (m, 6H), 7.11-6.96 (m, 5H), 6.96-6.56 (m, 6H), 4.76

(d, 4H), 4.35 (d, 4H), 4.10 (s, 2H), 3.96 (s, 2H); ^{13}C NMR (150MHz, DMSO-d_6) δ: 34.18, 34.32, 49.74, 67.16, 67.93, 114.56, 115.32, 116.96, 122.78, 123.72, 124.61, 125.25, 125.55, 130.14, 130.67, 131.00, 131.71, 140.50, 140.80, 146.64, 147.53, 149.65, 152.85; HRMS-ESI for $C_{34}H_{37}Cl_2N_9O_2$ (m/z) 301.6523 $[M-2Cl]^{2+}$。

Synthesis of MTEBT-2. This compound was synthesized following the same method described above for MTEBT-1. In the first reaction, using M2-2 (0.130 g, 0.180 mmol)，N-Boc-aminopropyne (0.559 g, 3.60 mmol), cuprous iodide (0.0209 g, 0.110 mmol), DBU (0.110 g, 0.720 mmol). Afterward, the crude product was purified with silica-gel column chromatography (methanol: dichloromethane = 1:30, v/v) to give 0.219 g of 4,4'-(2(2,5-(2-(4-(N-tert-butyl oxygen carbonyl methylene amine)1H-1,2,3-triazole) ethoxy)) phenyl) triphenylamine in 89.72% yield as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (s, 2H), 7.41 (s, 2H), 7.32 (d, 6H), 7.20 (d, 2H), 7.16-7.07 (m, 5H), 6.86 (d, 2H), 6.81 (d, 2H), 6.74 (d, 2H), 4.74 (s, 4H), 4.63 (s, 4H), 4.40 (d, 4H), 4.34 (s, 4H), 4.28 (d, 4H), 4.24 (s, 4H), 1.41 (s, 18H), 1.36 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.38, 34.23, 34.38, 49.86, 66.93, 68.12, 79.62, 114.53, 115.76, 117.21, 123.34, 125.31, 125.82, 130.45, 130.93, 131.06, 132.09, 140.72, 140.98, 146.82, 149.83, 152.96, 153.24; HRMS-ESI for $C_{70}H_{87}N_{17}O_{12}$ (m/z) 1357.6708 $[M]^+$.

Subsequently, using 4,4'-(2(2,5-(2-(4-(N-tert-butyl oxygen carbonyl methylene amine) 1H -1,2,3 - triazole) ethoxy)) phenyl) triphenylamine (0.108 g, 0.0800 mmol), 4 mL THF, and 2 mL 1, 4-dioxane containing 4 M of HCl. Afterward, the crude product was precipitated with 10 mL ethyl ether, filtered and then washed three times with ethyl ether. 4,4'-(bis(2,5-bis(2-(4-(methyleneamine hydrochlori-de)1H-1,2,3- triazole)ethoxy)) benzene)triphenylamine (MTEBT-2，0.058g) was obtained in 65.67% yield as a rownish yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.50 (s, 12H), 8.30 (s, 2H), 8.12 (s, 2H), 7.35 (d, 6H), 7.08 (d, 9H), 6.92 (s, 4H), 4.79 (s, 4H), 4.75 (s, 4H), 4.39 (s, 4H), 4.33 (s, 4H), 4.12 (s, 4H), 4.01 (s, 4H); ^{13}C

NMR (150MHz, DMSO-d_6) δ: 34.21, 34.33, 49.74, 67.16, 67.97, 114.55, 115.35, 117.03, 123.23, 125.20, 125.51, 130.28, 130.80, 130.97, 132.03, 140.53, 140.75, 146.44, 149.67, 152.87; HRMS-ESI for $C_{50}H_{59}Cl_4N_{17}O_4$ (m/z) 240.3729 $[M-4Cl]^{4+}$。

Synthesis of MTEBT-3. This compound was synthesized following the same method described above for MTEBT-1. In the first reaction, using M3-2 (0.100 g, 0.100 mmol)，N-Boc-aminopropyne (0.470 g, 3.00 mmol), cuprous iodide (0.011 g, 0.0600 mmol), DBU (0.060 g, 0.400 mmol). Afterward, the crude product was purified with silica-gel column chromatography (methanol: dichloromethane = 1:30, v/v) to give 0.170 g of 4,4'-(2(2,5-(2-(4-(N-tert-butyl oxygen carbonyl methylene amine)1H-1,2,3-triazole) ethoxy)) phenyl) triphenylamine in 90.0% yield as yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.74 (s, 6H), 7.44 (s, 6H), 7.35 (s, 6H), 7.21 (s, 6H), 6.90 (s, 3H), 6.82 (d, 3H), 6.77 (s, 3H), 4.74 (s, 6H), 4.64 (s, 6H), 4.40 (s, 6H), 4.36 (s, 6H), 4.26 (s, 12H), 1.42 (s, 27H), 1.35 (s, 27H)。^{13}C NMR (150 MHz, $CDCl_3$) δ: 28.42, 34.26, 34.40, 49.90, 66.96, 68.17, 79.73, 114.59, 115.82, 117.26, 121.33, 123.77, 125.37, 125.88, 130.53, 130.97, 131.15, 132.16, 140.83, 141.03, 145.58, 146.85, 149.87, 153.00, 153.31; HRMS-ESI for $C_{96}H_{123}N_{25}O_{18}$ (m/z) 1914.9523 $[M]^+$.

Subsequently, using 4-(tris(2,5-bis(2-(4-(N-tert-butyloxycarbonylmethyl- eneamino)1H-1,2,3-triazole)ethoxy))benzene)triphenylamine (0.110 g, 0.0600 mmol), 4 mL THF, and 2 mL 1, 4-dioxane containing 4 M of HCl. Afterward, the crude product was precipitated with 10 mL ethyl ether, filtered and washed three times with ethyl ether. 4-(tris(2,5-bis(2-(4-(methyleneamine hydrochloride)1H-1,2,3-triazole) ethoxy))benzene) triphenylamine (MTEBT-3, 0.0620 g) was obtained in 67.4% yield as a rownish yellow solid. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 8.60 (d, 18H), 8.34 (s, 3H), 8.18 (s, 3H), 7.42 (d, 6H), 7.09 (d, 6H), 7.03 (d, 3H), 6.96 (s, 3H), 6.89 (d, 3H), 4.80 (s, 6H), 4.76 (s, 6H), 4.39 (s, 6H), 4.34 (s, 6H), 4.11 (d, 6H), 4.02 (d, 6H); ^{13}C NMR (150MHz, DMSO-d_6) δ: 34.24, 34.33, 49.77, 67.20, 68.11, 114.59, 115.47, 117.12, 121.24, 123.72, 125.30, 125.64, 130.75, 130.96, 131.03, 132.33,

140.66, 140.83, 145.56, 146.31, 149.69, 152.90; HRMS-ESI for $C_{66}H_{81}Cl_6N_{25}O_6$ (m/z) 219.9433 $[M-6Cl]^{6+}$。

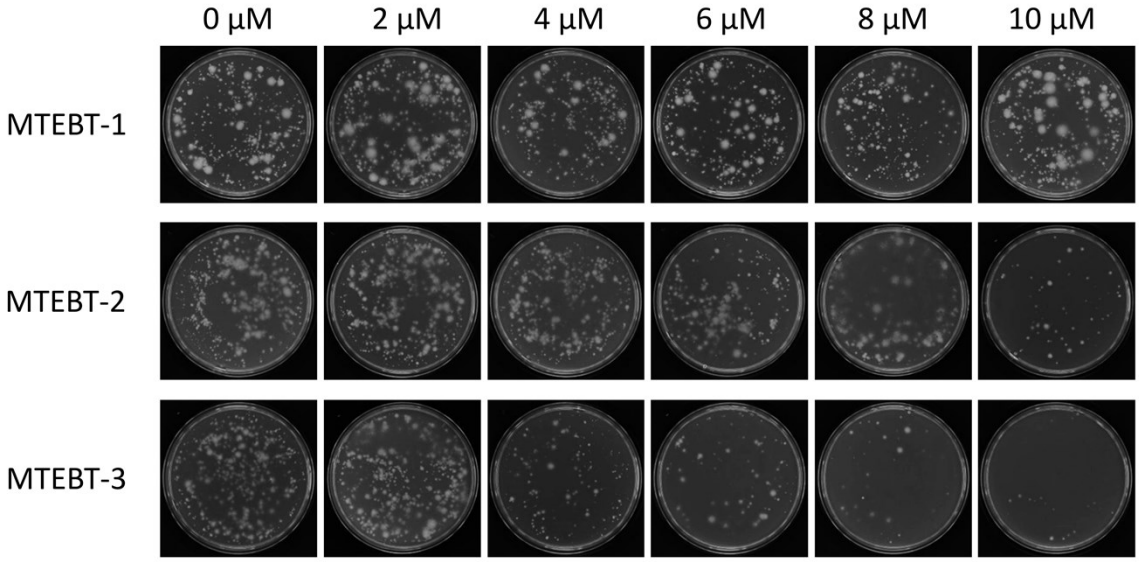


Figure S1. Photographs of *P. aeruginosa* colonies on the plates after treatment of MTEBT-*n* (*n*=1, 2, 3) at different concentrations.

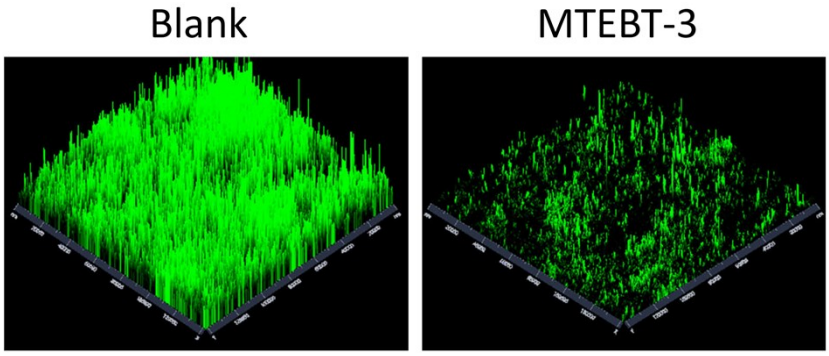


Figure S2. Confocal micrographs of biofilm formation by *P. aeruginosa* in the absence and presence of MTEBT-3 ([MTEBT-3]=80 μM).

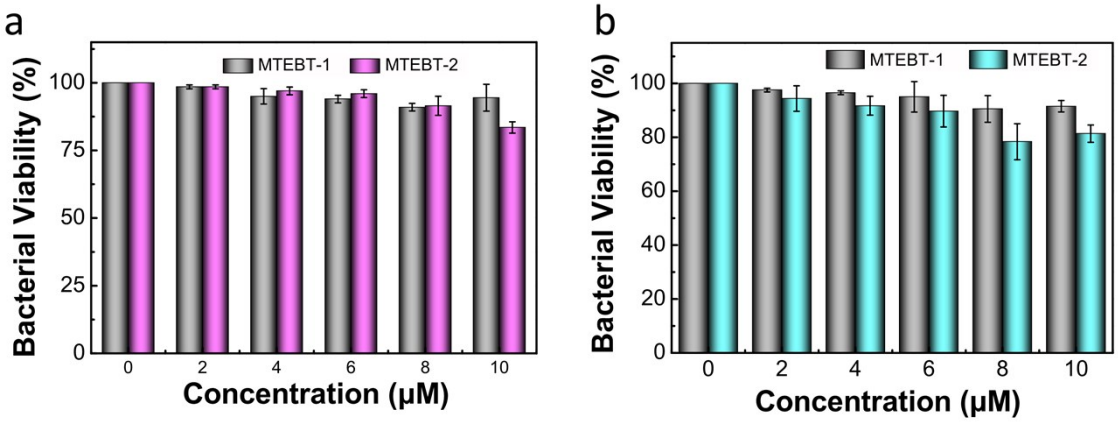


Figure S3. Antibacterial activity of MTEBT-1 and MTEBT-2 at different concentrations toward (a) *C. albicans* and (b) *S. aureus*.

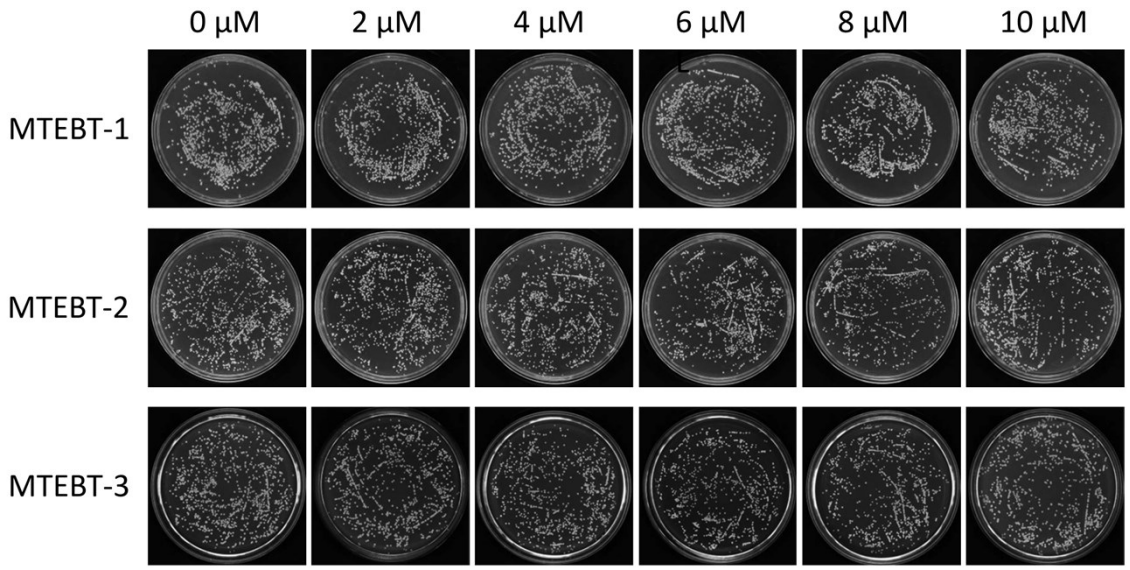


Figure S4. Photographs of *S. aureus* colonies on the plates after treatment of MTEBT-*n* (*n*=1, 2, 3) at different concentrations.

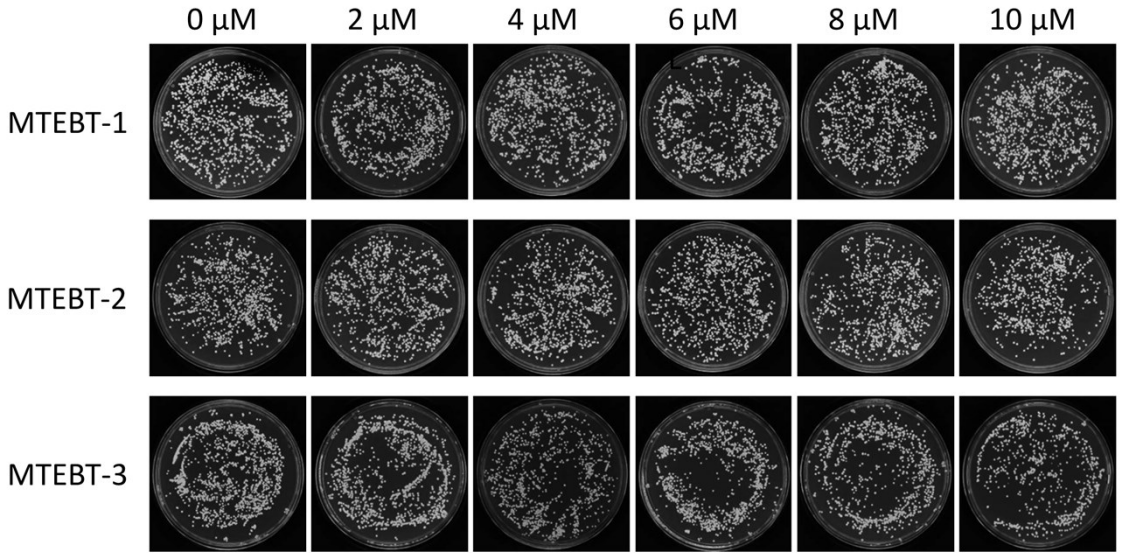


Figure S5. Photographs of *C. albicans* colonies on the plates after treatment of MTEBT-*n*

(n=1, 2, 3) at different concentrations.

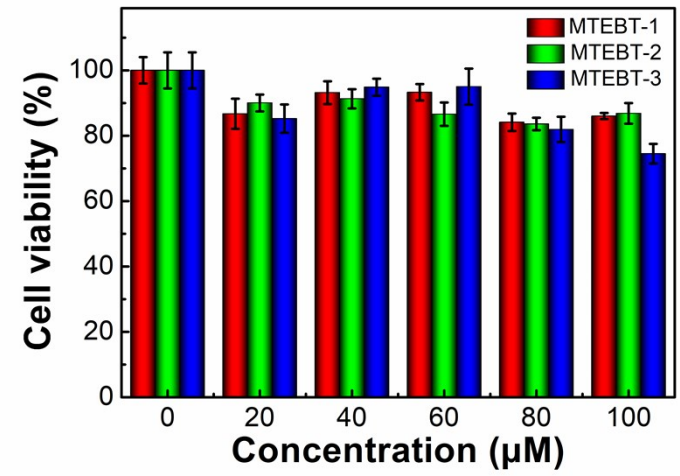


Figure S6. Cytotoxicity of MTEBT-*n* on mouse fibroblast cell line L-929 cells.

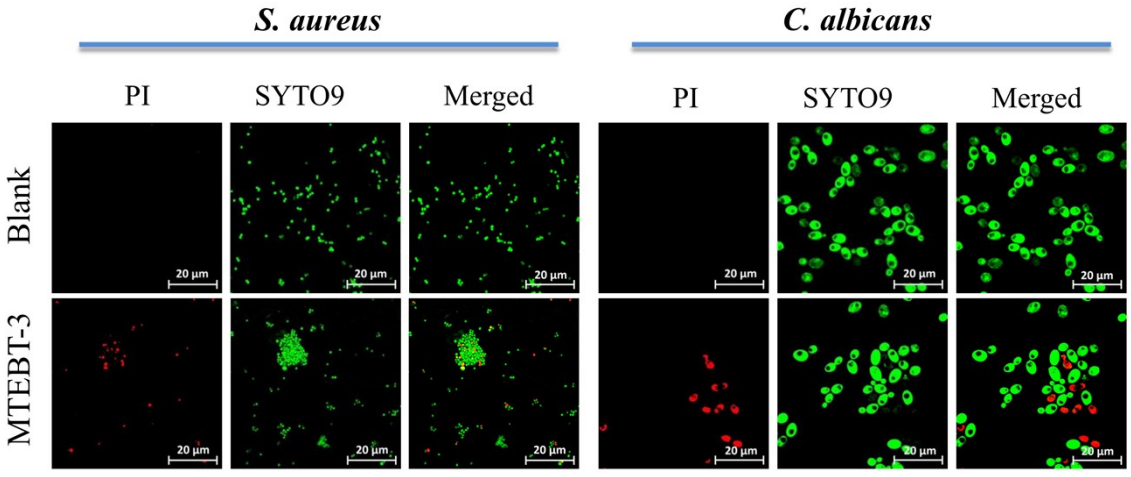


Figure S7. The CLSM images of (a) *S. aureus* and (b) *C. albicans* stained by SYTO9 and PI after treated by MTEBT-3 (10 μM).

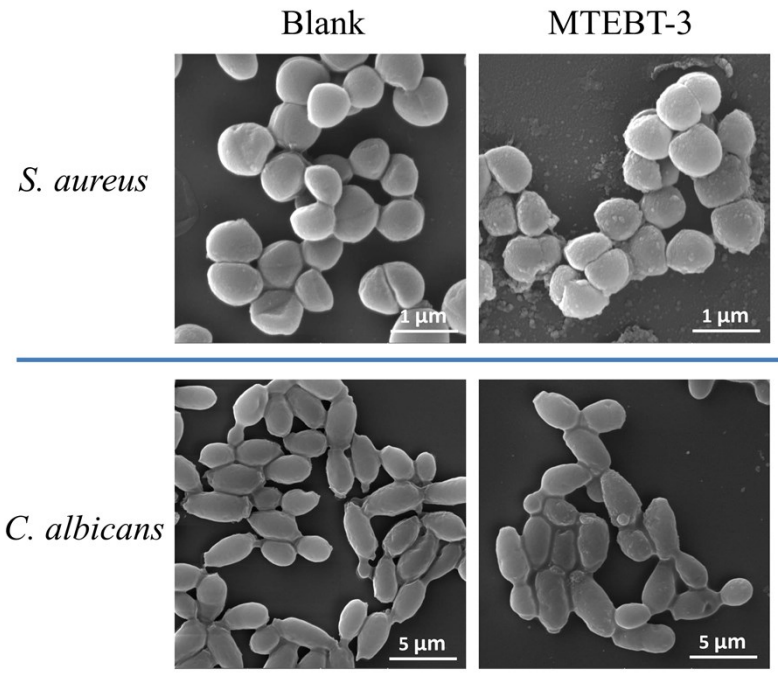


Figure S8. The SEM images of *S. aureus* and *C. albicans* without and with the treatment of MTEBT-3 (10 μM).

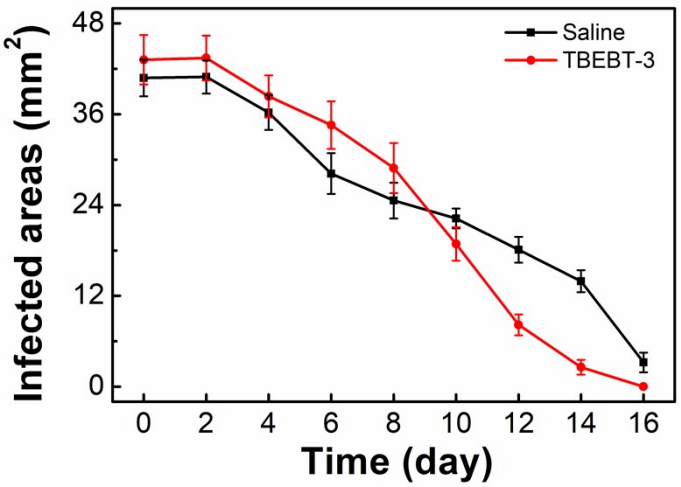


Figure S9. Curve of infected wound area in mice without and with the treatment of MTEBT-3.