



SUPPLEMENTARY MATERIAL TO

The synthesis, characterization and biological evaluation of a new nitric oxide donor agent

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PHYSICAL, ANALYTIC AND SPECTRAL DATA FOR THE SYNTHESISED COMPOUNDS

7-[3-(4-(Acetylamino)phenoxy)-2-hydroxypropyl]-1,3-dimethyl-8-(morpholin-4-yl)xanthine (**5**). Yield: 68.6 %; m.p. 228–230 °C; Anal. Calcd. for C₂₂H₂₈N₆O₆: C, 55.92, H, 5.92, N, 17.78. Found: C, 56.14; H, 6.21, N, 18.03; IR (KBr, cm⁻¹): 3400, 1200 (linked OH), 3120, 2968 (>N–CH₃), 2900 (CH₃, –CH₂–), 2884 (–CH<), 1720 (>C=N), 1620 (–NH–CO), 1660 (>C=C<N–), 1580 (>C=C<CO), 1480, 780, 710 (–C₆H₄–), 1350 (–O–CH₂), 1370 (–CO–CH₃); ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 2.02 (1H, *d*, OH, *J* = 7.2 Hz), 2.10 (3H, *s*, CH₃–CO), 2.68 (6H, *s*, 2CH₃–N<), 2.90 (4H, *m*, 2CH₂–N<, *J* = 7.4 Hz), 3.77 (4H, *m*, 2CH₂–O, *J* = 7.4 Hz), 3.88 (2H, *d*, CH₂–C, *J* = 7.6 Hz), 4.15 (2H, *d*, CH₂–O, *J* = 7.6 Hz), 4.38 (1H, *m*, CH), 6.78 (2H, *d*, aromatic, *J* = 8.4 Hz), 7.53 (2H, *d*, aromatic, *J* = 8.4 Hz), 8.05 (1H, *s*, NH); ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 17.62, 28.34, 36.71 (CH₃), 38.56, 58.84, 58.92, 71.42, 71.68, 77.60 (CH₂), 74.91 (CH), 136.81, 141.04, 149.80 (xanthine), 114.42, 114.68, 121.08, 121.25, 132.40, 154.70 (aromatic), 156.81, 166.84, 168.23 (CO); Mass (*m/z*): 472 [M⁺].

7-[3-(4-(acetylamino)phenoxy)-2-((2-chloroacetyl)oxy)propyl]-1,3-dimethyl-8-(morpholin-4-yl)xanthine (**6**). Yield: 74.6 %; m.p. 189–192 °C; Anal. Calcd. for C₂₄H₂₉ClN₆O₇: C, 52.50, H, 5.32, N, 15.30. Found: C, 52.12; H, 5.80, N, 14.84; IR (KBr, cm⁻¹): 3141, 2954 (>N–CH₃), 2908 (CH₃, –CH₂–), 2875

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(-CH<), 1704 (>C=N), 1740 (-CO-O), 1658 (-NH-CO), 1606 (>C=C<N-), 1540 (>C=C<CO), 1511, 751, 675 (-C₆H₄-), 1453 (-O-CH₂), 1363 (-CO-CH₃), 690 (C-Cl); ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 2.05 (3H, s, CH₃-CO), 2.75 (6H, s, 2CH₃-N<), 2.95 (4H, *m*, 2CH₂-N<, *J* = 7.4 Hz), 3.70 (4H, *m*, 2CH₂-O, *J* = 7.4 Hz), 3.95 (2H, *d*, CH₂-C, *J* = 7.3 Hz), 4.15 (2H, *d*, CH₂-O, *J* = 7.3 Hz), 4.45 (2H, s, CH₂-CO), 4.55 (1H, *m*, CH), 6.78 (2H, *d*, aromatic, *J* = 8.5 Hz), 7.59 (2H, *d*, aromatic, *J* = 8.5 Hz), 8.05 (1H, s, NH); ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 18.24, 29.26, 37.41 (CH₃), 41.23, 50.57, 59.18, 59.34, 71.48, 71.81, 74.49 (CH₂), 75.34 (CH), 136.47, 140.52, 149.67 (xanthine), 114.38, 114.87, 121.72, 122.15, 132.48, 154.83 (aromatic), 156.95, 166.54, 168.82, 172.47 (CO); Mass (*m/z*): 549 [M⁺].

7-[3-(4-(acetylamino)phenoxy)-2-((2-(nitrooxy)acetyl)oxy)propyl]-1,3-dimethyl-8-(morpholin-4-yl)xanthine (**7**, TSP-81). Yield: 63.5 %, m.p. 161–163 °C; Anal. Calcd. for C₂₄H₂₉N₇O₁₀: C, 50.08, H, 5.07 N, 17.03. Found: C, 50.36, H, 4.78, N, 17.36; IR (KBr, cm⁻¹): 3144, 2957 (>N-CH₃), 2914 (CH₃, -CH₂-), 2872 (-CH<), 1755 (-CO-O), 1712 (>C=N), 1648 (-NH-CO), 1610 (>C=C<N-), 1548 (>C=C<CO), 1524, 743, 684 (-C₆H₄-), 1457 (-O-CH₂), 1371 (-CO-CH₃), 1314 (-O-NO₂); ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 2.08 (3H, s, CH₃-CO), 2.72 (6H, s, 2CH₃-N<), 2.92 (4H, *m*, 2CH₂-N<, *J* = 7.5 Hz), 3.64 (4H, *m*, 2CH₂-O, *J* = 7.5 Hz), 3.91 (2H, *d*, CH₂-C, *J* = 7.4 Hz), 4.12 (2H, *d*, CH₂-O, *J* = 7.4 Hz), 4.41 (2H, s, CH₂-CO), 4.52 (1H, *m*, CH), 6.69 (2H, *d*, aromatic, *J* = 8.4 Hz), 7.52 (2H, *d*, aromatic, *J* = 8.4 Hz), 8.11 (1H, s, NH). ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 17.82, 28.67, 37.23 (CH₃), 40.84, 58.67, 58.84, 68.81, 71.76, 72.08, 74.75 (CH₂), 75.21 (CH), 137.12, 141.24, 149.36 (xanthine), 115.12, 115.54, 122.46, 122.83, 133.08, 155.23 (aromatic), 158.23, 167.48, 169.52, 171.87 (CO); Mass (*m/z*): 575 [M⁺]; UV-Vis (ethanol:water, 9:1, λ_{max} / nm): 277, 248.