

Supplementary material for

A novel drug(1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one for varieties of cancer treatment: synthesis, pharmacokinetics, pharmacodynamics study

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SUPPLEMENT DATA AVAILABLE

Fig. S1 $^1\text{H-NMR}$ spectra of 4-(methoxymethoxy)-benzene propanoic acid methyl ester.

Fig. S2 $^1\text{H-NMR}$ spectra of 4-(methoxymethoxy)-benzene propanol.

Fig. S3 $^1\text{H-NMR}$ spectra of (1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one.

Fig. S4 $^{13}\text{C-NMR}$ spectra of (1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one.

Fig. S5 MS spectra of (1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one.

Fig. S6 Tissue slice of liver histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low-dose group, C: Medium-dose group, D: High-dose group, E: Positive control group).

Fig. S7 Tissue slice of spleen histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low-dose group, C: Medium-dose group, D: High-dose group, E: Positive control group).

Fig. S8 Tissue slice of lung histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low-dose group, C: Medium-dose group, D: High-dose group, E: Positive control group).

Fig. S9 Tissue slice of kidney histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low-dose group, C: Medium-dose group, D: High-dose group, E: Positive control group).

Fig. S10 Tissue slice of brain histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low-dose group, C: Medium-dose group, D: High-dose group, E: Positive control group).

Table S1. Mean Tumor volume of various group at indicated time points after tail vein injection of DHDK solution

Table S2. Mean mouse weight of various group at indicated time points after tail vein injection of DHDK solution

Table S3. Plasma concentration of DHDK ($\text{ng}\cdot\text{mL}^{-1}$) after tail vein injection of $14\text{ mg}\cdot\text{kg}^{-1}$ DHDK solution ($n=6$)

Table S4. Concentrations of DHDK ($\text{ng}\cdot\text{mL}^{-1}$) in rat tissues after tail vein injection of $14\text{ mg}\cdot\text{kg}^{-1}$ DHDK solution ($n=6$)

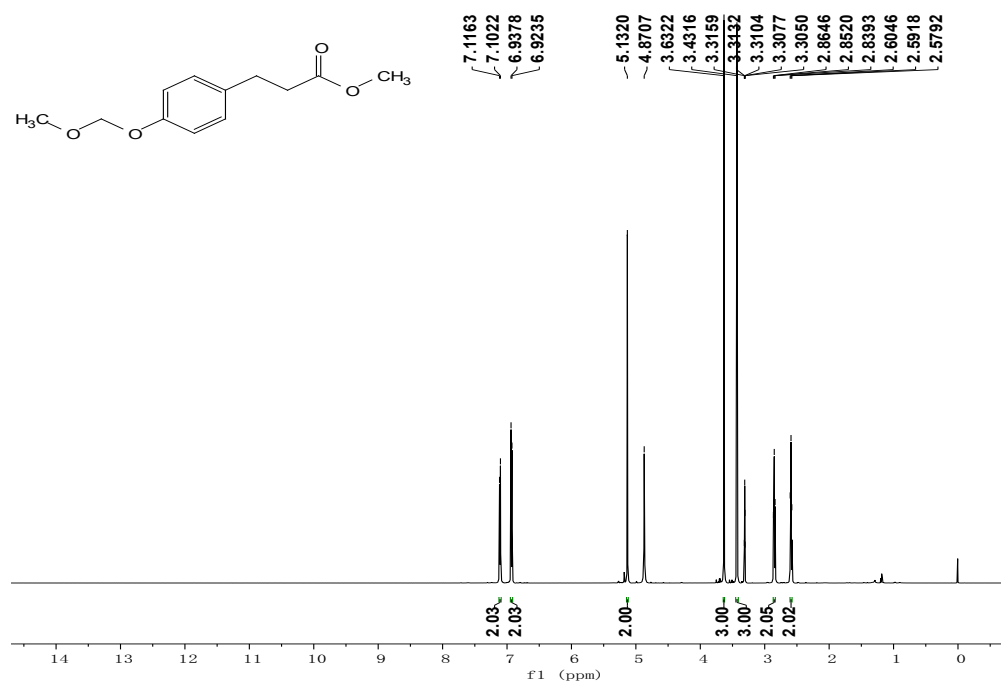


Figure S1 4-(methoxymethoxy)-benzene propanoic acid methyl ester

¹H NMR (600 MHz, CD₃OD) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.6 Hz, 2H), 5.13 (s, 2H), 3.63 (s, 3H), 3.43 (s, 3H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H).

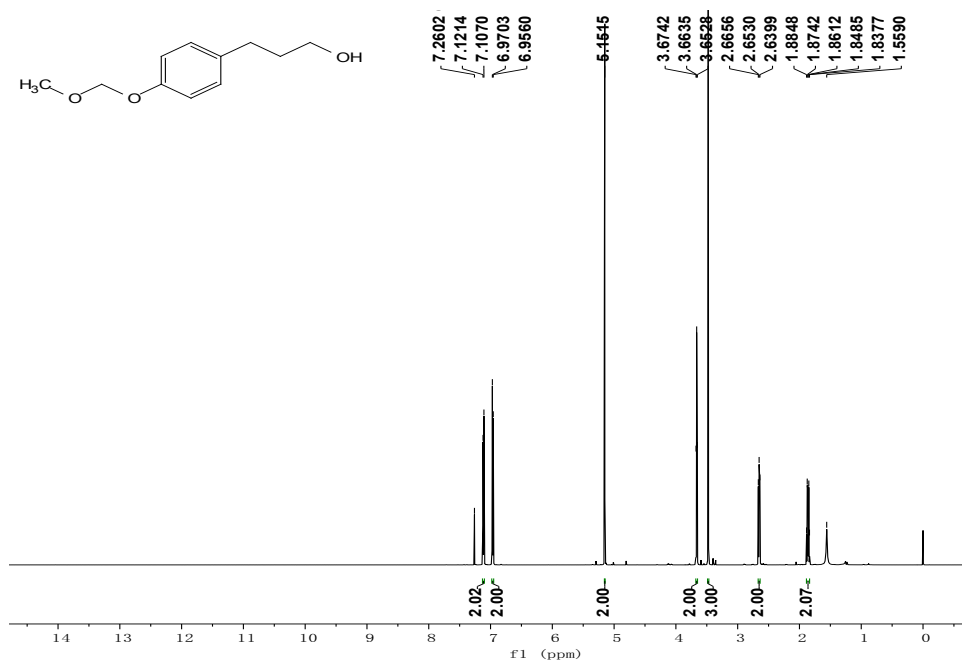


Figure S2 4-(methoxymethoxy)-benzene propanol

¹H NMR (600 MHz, CDCl₃) δ 7.11 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 5.15 (s, 2H), 3.66 (t, *J* = 6.4 Hz, 2H), 3.48 (s, 3H), 2.67 – 2.63 (m, 2H), 1.89 - 1.83 (m, 2H).

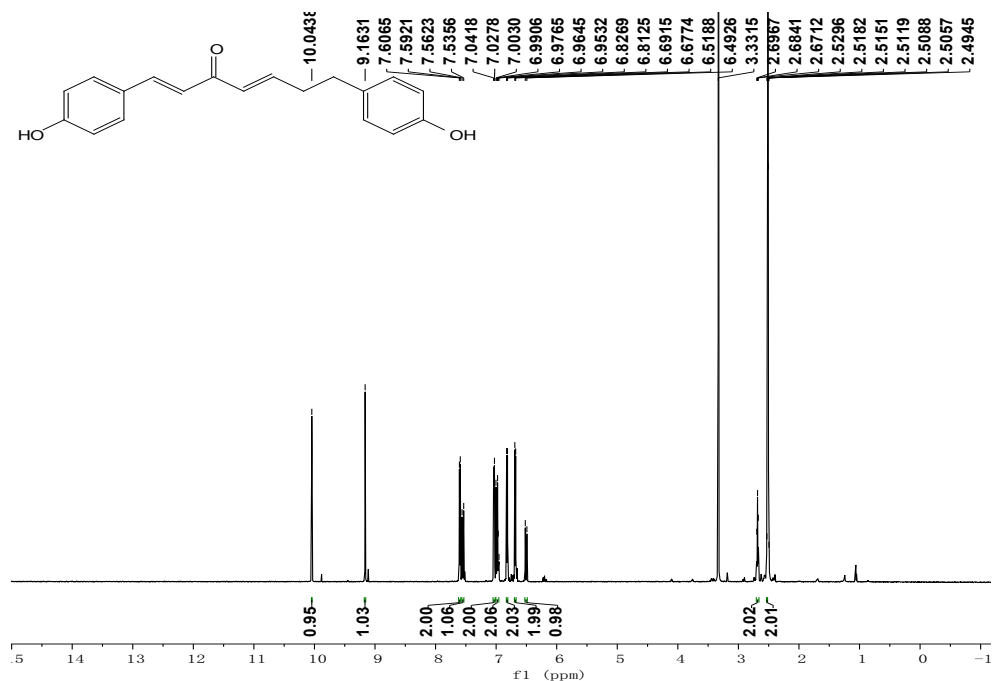


Figure S3 ^1H -NMR spectra of (1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one

^1H NMR (600 MHz, d_6 -DMSO) δ 10.04 (s, 1H), 9.16 (s, 1H), 7.60 (d, $J = 8.6$ Hz, 2H), 7.55 (d, $J = 16.0$ Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 2H), 7.00-6.95 (m, 2H), 6.82 (d, $J = 8.6$ Hz, 2H), 6.68 (d, $J = 8.4$ Hz, 2H), 6.51 (d, $J = 15.7$ Hz, 1H), 2.68 (t, $J = 7.7$ Hz, 2H), 2.53-2.49 (m, 2H).

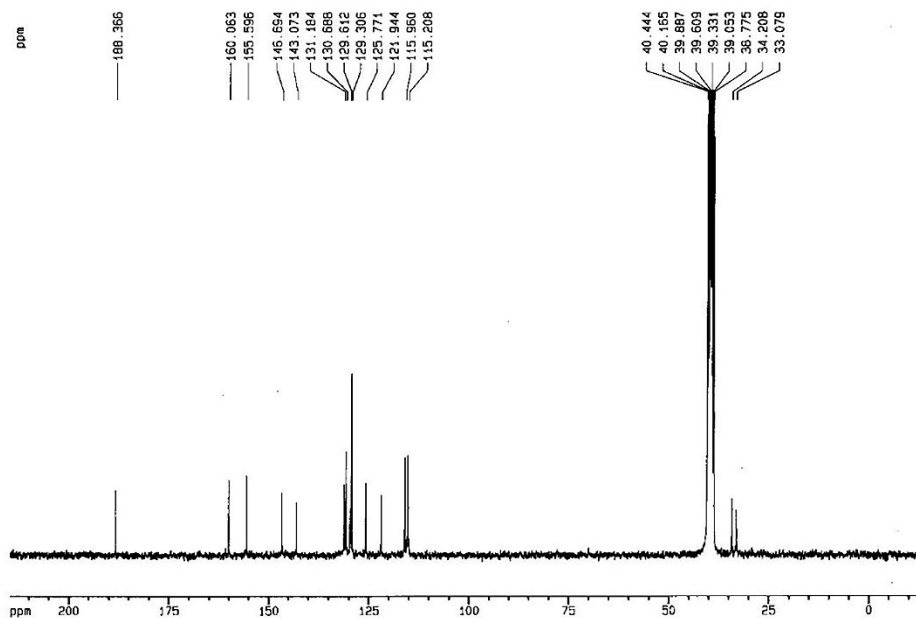


Figure S4 ^{13}C -NMR spectra of (1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one

^{13}C NMR (150 MHz, d_6 -DMSO) δ 188.4, 160.1, 155.6, 146.7, 143.1, 131.2, 130.7, 130.7, 129.6, 129.3, 129.3, 125.8, 121.9, 116.0, 116.0, 115.2, 115.2, 34.2, 33.1.

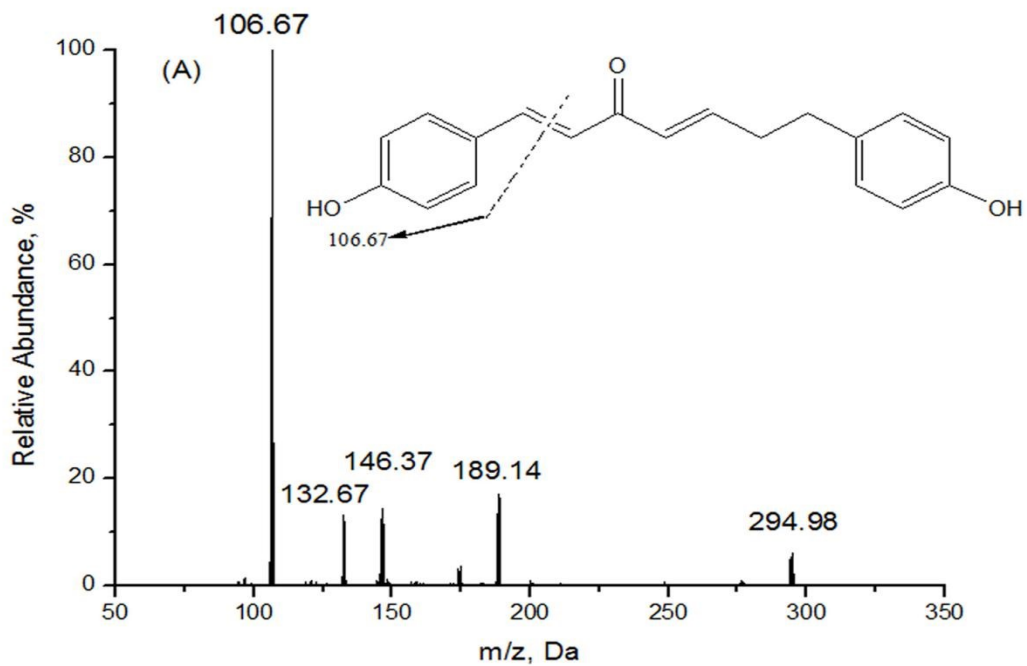


Figure S5 MS spectra of (1E,4E)-1,7-bis(4-hydroxyphenyl) hepta-1,4-dien-3-one

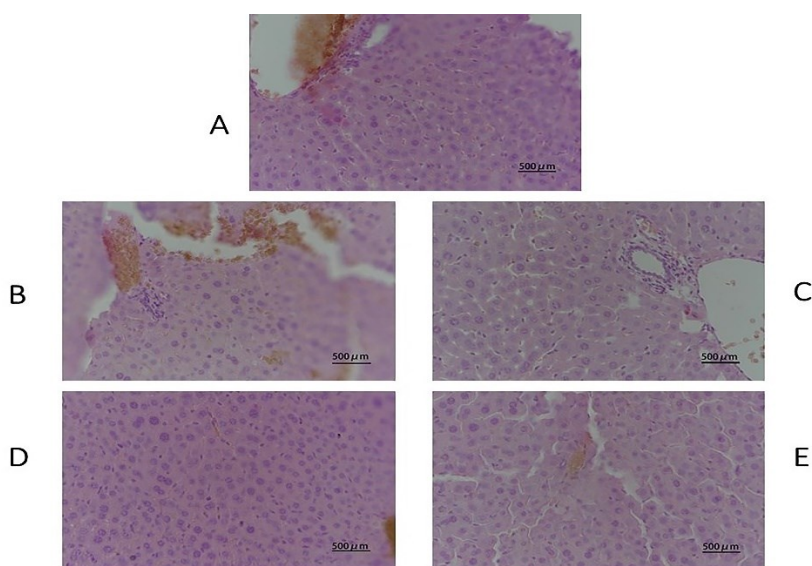


Figure S6 Liver histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low dose group, C: Medium dose group, D: High dose group, E: Positive control group)

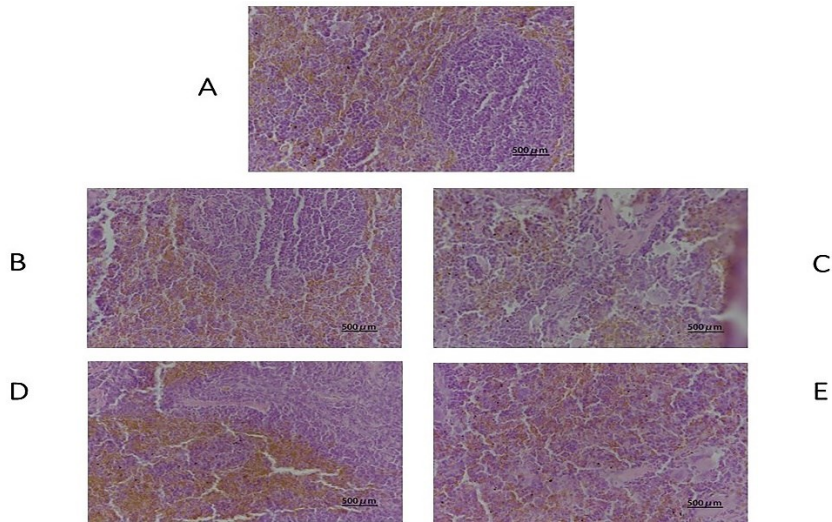


Figure S7 Spleen histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low dose group, C: Medium dose group, D: High dose group, E: Positive control group)

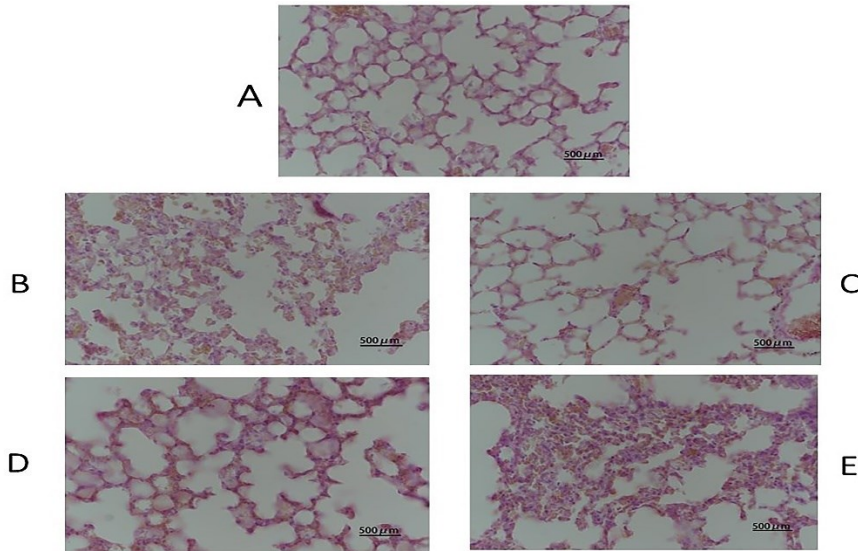


Figure S8 Lung histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low dose group, C: Medium dose group, D: High dose group, E: Positive control group)

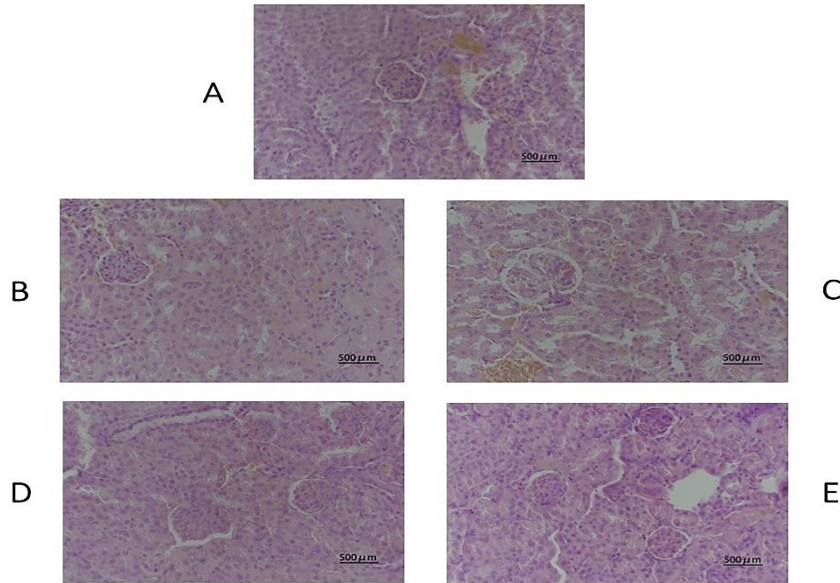


Figure S9 Kidney histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low dose group, C: Medium dose group, D: High dose group, E: Positive control group)

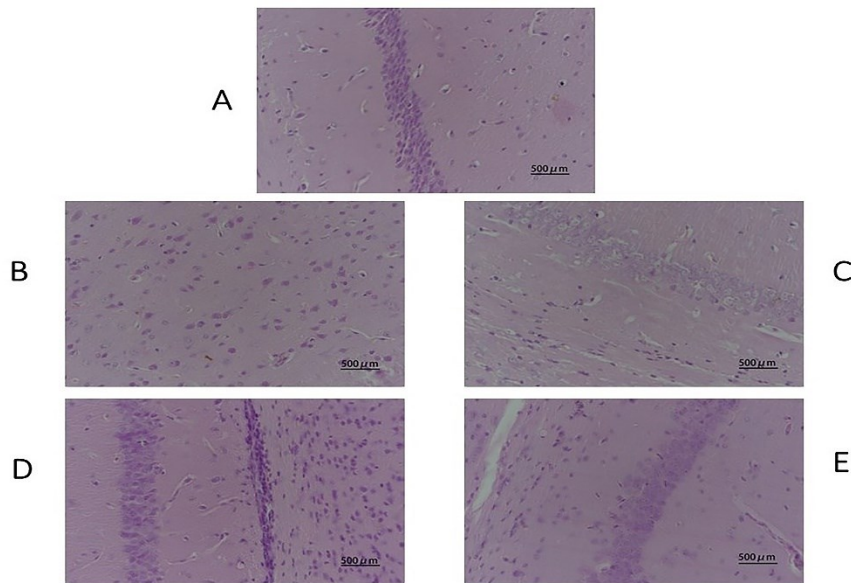


Figure S10 Brain histopathology of various group obtained after the mice were sacrificed(A: Negative control group, B: Low dose group, C: Medium dose group, D: High dose group, E: Positive control group)

Table S1. Mean Tumor volume of various group at indicated time points after tail vein injection of DHDK solution

Time (d)	Tumor volume (Mean \pm SD , mm ³)				
	Negative control group	Low dose group	Medium dose group	High dose group	Positive control group
0	194.39 \pm 55.23	200.03 \pm 83.6	211.35 \pm 83.83	188.15 \pm 49.52	210.98 \pm 49.52
	381.11 \pm 100.86	246.35 \pm 71.87	260.22 \pm 108.20	225.84 \pm 74.56	276.40 \pm 82.75
4	598.82 \pm 218.37	406.06 \pm 91.74	389.01 \pm 132.76	302.74 \pm 85.43	598.82 \pm 141.73
	780.10 \pm 218.98	530.17 \pm 91.74	487.17 \pm 132.76	458.62 \pm 85.43	401.86 \pm 141.73
8	1046.27 \pm 149.64	772.06 \pm 128.85	632.13 \pm 158.48	562.46 \pm 59.20	1046.27 \pm 93.49
	1256.25 \pm 190.75	753.66 \pm 153.92	695.48 \pm 149.87	450.20 \pm 173.21	472.68 \pm 121.94

SD: Standard deviation

Table S2. Mean mice weight of various group at indicated time points after tail vein injection of DHDK solution

Time (d)	Weight (Mean \pm SD , g)				
	Negative control group	Low dose group	Medium dose group	High dose group	Positive control group
0	19.53 \pm 0.38	19.45 \pm 1.67	19.9 \pm 0.76	20.05 \pm 1.17	19.32 \pm 0.70
2	19.28 \pm 0.77	19.43 \pm 1.46	20.55 \pm 0.92	19.98 \pm 1.12	18.8 \pm 0.77
4	19.70 \pm 0.66	19.53 \pm 1.36	20.45 \pm 1.10	19.61 \pm 0.98	17.06 \pm 0.60
6	20.03 \pm 0.76	19.60 \pm 1.55	20.5 \pm 1.04	19.87 \pm 1.19	15.1 \pm 0.74
8	20.48 \pm 0.79	19.62 \pm 1.46	20.38 \pm 0.93	19.75 \pm 0.92	14.52 \pm 1.25
9	20.43 \pm 0.77	20.48 \pm 1.50	20.65 \pm 1.07	20.03 \pm 1.00	14.18 \pm 1.19

SD: Standard deviation

Table S3. Plasma concentration of DHDK (ng·mL⁻¹) after tail vein injection of 14 mg·kg⁻¹ DHDK solution (n=6)

Time(h)	Mean	SD
0.033	1710.4	72.76
0.167	482.08	7.83
0.25	165.3	4.47
0.5	78.7	2.96
0.75	72.19	3.50
1	42.49	8.84
2	22.36	2.89
4	11.12	1.05
8	9.73	0.57
12	5.43	0.83

SD: Standard deviation

Table S4. Concentrations of DHDK ($\text{ng}\cdot\text{mL}^{-1}$) in rat tissues after tail vein injection of $14\text{ mg}\cdot\text{kg}^{-1}$ DHDK solution ($n=6$)

Tissues	Concentration (Mean \pm SD, $\text{ng}\cdot\text{g}^{-1}$)					
	0.083 h	0.5 h	2 h	4 h	8 h	12 h
Heart	171.59 \pm 50.32	7.05 \pm 4.66	4.73 \pm 3.03	5.38 \pm 2.05	4.29 \pm 3.12	3.94 \pm 2.99
Liver	581.40 \pm 75.23	180.19 \pm 30.57	151.84 \pm 20.52	144.21 \pm 30.66	132.39 \pm 27.98	132.83 \pm 22.37
Spleen	18.47 \pm 7.69	45.55 \pm 23.79	31.59 \pm 14.13	31.20 \pm 14.23	31.21 \pm 10.12	30.45 \pm 10.66
Lung	1744.21 \pm 90.611	540.57 \pm 79.06	455.53 \pm 78.77	432.64 \pm 34.98	397.16 \pm 21.90	398.48 \pm 34.84
Kidney	55.41 \pm 10.09	136.65 \pm 31.23	94.78 \pm 10.26	93.61 \pm 20.13	93.62 \pm 14.09	91.34 \pm 24.98

SD: Standard deviation