

Supplementary files

Supplementary Table 1: Effect of chrysin on intake and absolute organ weights of Sprague-Dawley female rats during acute oral toxicity study

Parameter	C (0)	C (55)	C (175)	C (550)	C (1750)	C (5000)
Terminal Body weight (g)	208.80 ± 1.53	211.2 ± 0.86	206.40 ± 1.33	206.60 ± 1.69	206.20 ± 1.69	205.80 ± 1.53
Food intake (g)	19.60 ± 0.40	20.20 ± 0.37	20.2 ± 0.58	20.40 ± 0.40	20.60 ± 0.51	21.40 ± 0.75
Water intake (ml)	38.00 ± 0.71	38.4 ± 0.68	38.8 ± 0.58	37.8 ± 0.86	38.40 ± 0.68	37.00 ± 0.32
Brain (g)	1.74 ± 0.05	1.64 ± 0.04	1.66 ± 0.06	1.72 ± 0.06	1.64 ± 0.07	1.72 ± 0.04
Liver (g)	9.82 ± 0.09	9.92 ± 0.11	9.78 ± 0.07	9.92 ± 0.10	9.88 ± 0.07	9.80 ± 0.05
Kidneys (g)	1.82 ± 0.03	1.90 ± 0.03	1.94 ± 0.03	1.84 ± 0.03	1.84 ± 0.02	1.82 ± 0.04
Adrenals (g)	0.36 ± 0.007	0.38 ± 0.003	0.37 ± 0.007	0.37 ± 0.005	0.38 ± 0.006	0.37 ± 0.007
Ovaries (g)	0.07 ± 0.002	0.07 ± 0.003	0.07 ± 0.003	0.07 ± 0.004	0.07 ± 0.002	0.08 ± 0.002
Heart (g)	1.13 ± 0.01	1.21 ± 0.04	1.13 ± 0.06	1.26 ± 0.04	1.14 ± 0.06	1.21 ± 0.05

Spleen (g)	0.66 ± 0.006	0.68 ± 0.004	0.66 ± 0.005	0.66 ± 0.008	0.66 ± 0.005	0.67 ± 0.006
Lung (g)	1.65 ± 0.04	1.66 ± 0.04	1.61 ± 0.01	1.63 ± 0.02	1.63 ± 0.03	1.66 ± 0.04
Thymus (g)	0.50 ± 0.03	0.54 ± 0.02	0.51 ± 0.02	0.51 ± 0.03	0.50 ± 0.04	0.51 ± 0.01
Uterus (g)	0.61 ± 0.02	0.58 ± 0.03	0.61 ± 0.03	0.56 ± 0.02	0.62 ± 0.02	0.61 ± 0.02

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. Figures in parenthesis indicate dose in mg/kg. C: Chrysin.

Supplementary Table 2: Effect of chrysin on relative organ weights of Sprague-Dawley female rats during acute oral toxicity study

Parameter	C (0)	C (55)	C (175)	C (550)	C (1750)	C (5000)
Brain (g)	0.83 ± 0.03	0.78 ± 0.02	0.80 ± 0.03	0.83 ± 0.03	0.80 ± 0.04	0.84 ± 0.02
Liver (g)	4.70 ± 0.04	4.70 ± 0.05	4.74 ± 0.03	4.80 ± 0.03	4.79 ± 0.05	4.76 ± 0.05
Kidneys (g)	0.87 ± 0.02	0.90 ± 0.01	0.94 ± 0.01	0.89 ± 0.01	0.89 ± 0.01	0.88 ± 0.02
Adrenals (g)	0.17 ± 0.003	0.18 ± 0.002	0.18 ± 0.002	0.18 ± 0.002	0.18 ± 0.004	0.18 ± 0.004
Ovaries (g)	0.04 ± 0.001	0.03 ± 0.002	0.03 ± 0.002	0.03 ± 0.002	0.03 ± 0.001	0.04 ± 0.001
Heart (g)	0.54 ± 0.01	0.57 ± 0.02	0.55 ± 0.03	0.61 ± 0.02	0.56 ± 0.03	0.59 ± 0.03
Spleen (g)	0.32 ± 0.003	0.32 ± 0.002	0.32 ± 0.003	0.32 ± 0.005	0.32 ± 0.003	0.32 ± 0.003
Lung (g)	0.79 ± 0.02	0.79 ± 0.02	0.78 ± 0.00	0.79 ± 0.01	0.79 ± 0.01	0.80 ± 0.02
Thymus (g)	0.24 ± 0.01	0.26 ± 0.01	0.25 ± 0.01	0.25 ± 0.01	0.24 ± 0.02	0.25 ± 0.01
Uterus (g)	0.29 ± 0.01	0.27 ± 0.01	0.3 ± 0.01	0.27 ± 0.01	0.30 ± 0.01	0.30 ± 0.01

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. Figures in parenthesis indicate dose in mg/kg. C: Chrysin.

Supplementary Table 3: Effect of chrysin on electrocardiographic, hemodynamic and left ventricular function in Sprague-Dawley male rats during 90-days repeated dose toxicity study.

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Heart Rate (BPM)	383.20 ± 2.69	375.60 ± 2.82	377.70 ± 2.74	377.10 ± 4.05	396.20 ± 1.55*	395.10 ± 3.39*
QRS interval (ms)	13.16 ± 0.58	14.79 ± 0.87	13.44 ± 0.46	14.29 ± 0.74	12.90 ± 0.60	13.55 ± 0.60
QT Interval (ms)	51.02 ± 2.25	51.21 ± 2.51	49.75 ± 3.36	55.78 ± 2.38	50.52 ± 2.86	48.25 ± 2.62
QTc Interval (ms)	132.90 ± 1.47	129.90 ± 3.31	129.60 ± 3.00	130.20 ± 3.81	131.30 ± 2.74	130.40 ± 1.64
SBP (mmHg)	112.20 ± 2.48	114.40 ± 2.31	115.10 ± 2.43	111.00 ± 1.34	113.20 ± 1.48	110.90 ± 2.13
DBP (mmHg)	90.66 ± 1.27	89.89 ± 2.48	92.79 ± 1.94	92.75 ± 0.98	93.27 ± 1.53	93.20 ± 2.08
LVEDP (mmHg)	7.02 ± 0.81	7.59 ± 0.60	7.78 ± 0.71	8.09 ± 0.38	7.07 ± 0.80	7.46 ± 0.72
Max_{dp/dt}	3944.00 ± 40.44	4064.00 ± 44.97	4028.00 ± 17.18	3991.00 ± 18.72	4006.00 ± 30.9	4011.00 ± 41.01
Min_{dp/dt}	-2766.00 ± 28.29	-2729.00 ± 41.71	-2748.00 ± 23.13	-2681.00 ± 27.95	-2701.00 ± 30.28	-2775.00 ± 26.47
Pressure time index	19.29 ± 0.56	21.35 ± 0.63	19.54 ± 0.53	20.13 ± 0.75	21.76 ± 0.37	21.87 ± 0.40
Contractility index	56.42 ± 3.10	51.92 ± 1.43	57.12 ± 1.08	55.95 ± 2.80	55.55 ± 2.97	56.08 ± 1.16
Tau (ms)	4.96 ± 0.20	5.50 ± 0.26	5.43 ± 0.30	5.47 ± 0.29	5.50 ± 0.27	5.31 ± 0.32

Data are expressed as Mean $\pm$ Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately, $*p < 0.05$, as compared with a respective parameter value of 0 mg/kg group. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 4: Effect of chrysin on electrocardiographic, hemodynamic and left ventricular function in Sprague-Dawley female rats during 90-days repeated dose toxicity study.

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Heart Rate (BPM)	373.30 ± 1.74	380.30 ± 2.68	377.10 ± 1.66	381.40 ± 3.02	394.40 ± 3.55*	396.50 ± 2.02*
QRS interval (ms)	14.26 ± 0.52	13.12 ± 0.48	13.68 ± 0.77	15.01 ± 0.57	14.65 ± 1.01	13.87 ± 0.64
QT Interval (ms)	51.26 ± 3.84	51.73 ± 3.47	52.80 ± 3.09	49.51 ± 2.81	51.35 ± 3.39	50.16 ± 2.10
QTc Interval (ms)	131.80 ± 2.15	130.70 ± 2.08	127.10 ± 1.48	135.00 ± 2.84	131.20 ± 3.13	136.90 ± 3.21
SBP (mmHg)	111.20 ± 1.82	109.20 ± 1.63	115.20 ± 2.40	112.70 ± 1.72	111.70 ± 2.26	109.30 ± 1.45
DBP (mmHg)	93.09 ± 2.64	96.61 ± 1.01	95.17 ± 1.69	96.61 ± 0.84	92.84 ± 1.94	94.27 ± 1.86
LVEDP (mmHg)	6.85 ± 0.62	7.83 ± 0.37	6.83 ± 0.35	8.20 ± 0.46	7.74 ± 0.54	7.54 ± 0.77
Max_{dp/dt}	3973.00 ± 26.70	4023.00 ± 42.27	3982.00 ± 42.32	3933.00 ± 19.49	4061.00 ± 29.93	4041.00 ± 27.30

Min_{dp/dt}	-2675.00 ± 17.96	-2707.00 ± 40.10	-2654.00 ± 6.64	-2748.00 ± 34.44	-2720.00 ± 30.06	-2710.00 ± 35.90
Pressure time index	20.57 ± 1.04	20.55 ± 0.87	20.73 ± 0.87	21.44 ± 0.66	20.82 ± 1.06	20.27 ± 0.66
Contractility index	54.58 ± 3.04	54.17 ± 2.64	57.52 ± 0.77	55.58 ± 2.74	55.31 ± 2.21	55.45 ± 2.35
Tau (ms)	5.88 ± 0.28	5.51 ± 0.23	5.21 ± 0.37	5.77 ± 0.19	5.54 ± 0.27	5.71 ± 0.34

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately, * $p < 0.05$, as compared with a respective parameter value of 0 mg/kg group. Figures in parenthesis indicate dose in mg/kg.

C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 5: Effect of chrysin on lung function test in Sprague-Dawley male rats during 90-days repeated dose toxicity study.

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Peak inspiratory flow (PIF) (m/s)	11.09 ± 0.71	10.66 ± 0.64	10.83 ± 0.50	11.34 ± 0.79	10.50 ± 0.66	11.00 ± 0.60
Peak expiratory flow (PEF) (m/s)	21.63 ± 0.96	21.10 ± 0.55	19.67 ± 0.70	20.71 ± 0.63	19.42 ± 0.75	19.72 ± 0.99
Tidal volume (TV) (m)	1.22 ± 0.05	1.26 ± 0.04	1.27 ± 0.01	1.19 ± 0.04	1.25 ± 0.03	1.25 ± 0.03
Expired volume (EV) (m)	1.10 ± 0.04	1.09 ± 0.03	1.10 ± 0.02	1.16 ± 0.03	1.11 ± 0.04	1.13 ± 0.04
Frequency of Breathing (f) (bpm)	221.80 ± 1.56	222.60 ± 1.44	219.40 ± 1.57	224.30 ± 1.50	222.60 ± 1.19	217.9 ± 1.34
Enhanced pause (Penh)	0.89 ± 0.03	0.91 ± 0.02	0.90 ± 0.02	0.94 ± 0.02	0.91 ± 0.02	0.89 ± 0.03

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 6: Effect of chrysin on lung function test in Sprague-Dawley female rats during 90-days repeated dose toxicity study.

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Peak inspiratory flow (PIF) (m/s)	12.10 ± 0.44	11.42 ± 0.96	10.39 ± 0.29	10.94 ± 0.48	11.03 ± 0.56	11.36 ± 0.68
Peak expiratory flow (PEF) (m/s)	20.93 ± 0.54	19.71 ± 0.77	17.82 ± 0.20	18.95 ± 0.32	21.14 ± 0.90	20.62 ± 0.59
Tidal volume (TV) (m)	1.26 ± 0.03	1.23 ± 0.05	1.23 ± 0.03	1.24 ± 0.04	1.27 ± 0.03	1.26 ± 0.03
Expired volume (EV) (m)	1.17 ± 0.04	1.07 ± 0.02	1.17 ± 0.04	1.11 ± 0.04	1.13 ± 0.05	1.13 ± 0.03
Frequency of Breathing (f) (bpm)	221.80 ± 2.24	221.20 ± 2.08	221.40 ± 1.86	221.20 ± 1.96	220.20 ± 2.91	224.70 ± 0.70
Enhanced pause (Penh)	0.91 ± 0.03	0.93 ± 0.01	0.86 ± 0.02	0.87 ± 0.03	0.87 ± 0.03	0.90 ± 0.03

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 7: Effect of chrysin on urine analysis of Sprague-Dawley male rats during 90-days repeated dose toxicity study

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Volume (ml)	3.81 ± 0.04	3.83 ± 0.04	3.95 ± 0.01	3.86 ± 0.05	3.82 ± 0.03	3.84 ± 0.04
Glucose (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Bilirubin (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Ketones (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Sp.Gr	0.64 ± 0.03	0.66 ± 0.02	0.64 ± 0.04	0.69 ± 0.03	0.65 ± 0.02	0.61 ± 0.01
Occult blood	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
pH	6.79 ± 0.01	6.76 ± 0.01	6.80 ± 0.02	6.80 ± 0.02	6.80 ± 0.02	6.79 ± 0.01
Urobilinogen (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Nitrite	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Microscopy						
P	0.73 ± 0.05	0.68 ± 0.05	0.79 ± 0.02	0.67 ± 0.04	0.7 ± 0.04	0.71 ± 0.04
R	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
E	0.37 ± 0.04	0.43 ± 0.05	0.47 ± 0.04	0.45 ± 0.02	0.40 ± 0.06	0.56 ± 0.03

Cr (T)	1.69 ± 0.03	1.71 ± 0.07	1.74 ± 0.04	1.82 ± 0.04	1.7 ± 0.05	1.65 ± 0.05
C	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. P: Pus cells, E: Epithelial cells, C: Casts, R: RBC, Cr (T): Crystals Triple Phosphate and Sp. Gr.: Specific gravity. Qualitative grade: Absent (0), Trace (+), Small amount of analyte (++), Moderate amount of analyte (+++) and Large amount of analyte (+++). Microscopic grade: None found in any field (0), Few found in some fields (1), Few found in many fields (2), and Many found in many fields (3). Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 8: Effect of chrysin on urine analysis of Sprague-Dawley female rats during 90-days repeated dose toxicity study

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Volume (ml)	3.82 ± 0.03	3.82 ± 0.05	3.79 ± 0.03	3.84 ± 0.04	3.84 ± 0.03	3.89 ± 0.03
Glucose (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Bilirubin (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Ketones (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Sp.Gr	0.68 ± 0.02	0.59 ± 0.03	0.65 ± 0.04	0.69 ± 0.04	0.65 ± 0.04	0.70 ± 0.02
Occult blood	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
pH	6.78 ± 0.02	6.78 ± 0.02	6.77 ± 0.01	6.83 ± 0.03	6.81 ± 0.02	6.83 ± 0.01
Urobilinogen (mg%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Nitrite	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Microscopy						
P	0.65 ± 0.04	0.75 ± 0.06	0.76 ± 0.04	0.76 ± 0.05	0.75 ± 0.05	0.72 ± 0.04
R	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
E	0.47 ± 0.07	0.45 ± 0.05	0.44 ± 0.08	0.43 ± 0.06	0.46 ± 0.08	0.48 ± 0.03

Cr (T)	1.66 ± 0.05	1.69 ± 0.06	1.76 ± 0.06	1.76 ± 0.06	1.76 ± 0.04	1.68 ± 0.06
C	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. P: Pus cells, E: Epithelial cells, C: Casts, R: RBC, Cr (T): Crystals Triple Phosphate and Sp. Gr.: Specific gravity. Qualitative grade: Absent (0), Trace (+), Small amount of analyte (++) , Moderate amount of analyte (+++) and Large amount of analyte (++++). Microscopic grade: None found in any field (0), Few found in some fields (1), Few found in many fields (2), and Many found in many fields (3). Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 9: Effect of chrysin on intake and absolute organ weights of Sprague-Dawley male rats during 90-days repeated dose toxicity study

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Terminal Body weight (g)	338.60 ± 0.51	338.60 ± 0.75	337.20 ± 1.11	337.00 ± 0.45	324.90 ± 1.45**	338.00 ± 0.89
Food intake (g)	30.98 ± 0.44	31.32 ± 0.41	30.52 ± 0.38	30.32 ± 0.36	31.50 ± 0.17	30.32 ± 0.32
Water intake (ml)	60.40 ± 0.40	60.8 ± 0.58	60.80 ± 0.37	60.00 ± 0.32	61.20 ± 0.49	60.60 ± 0.24
Brain (g)	2.68 ± 0.07	2.74 ± 0.06	2.78 ± 0.02	2.64 ± 0.02	2.73 ± 0.04	2.78 ± 0.04
Liver (g)	12.27 ± 0.12	13.02 ± 0.39	13.20 ± 0.21	13.20 ± 0.27	13.47 ± 0.22*	13.64 ± 0.44*
Kidneys (g)	3.58 ± 0.12	3.59 ± 0.06	3.80 ± 0.11	3.58 ± 0.09	3.74 ± 0.14	3.79 ± 0.07
Adrenals (g)	0.05 ± 0.002	0.05 ± 0.002	0.04 ± 0.002	0.05 ± 0.002	0.05 ± 0.00	0.04 ± 0.002
Testes (g)	3.01 ± 0.03	3.05 ± 0.03	3.05 ± 0.04	3.09 ± 0.02	3.02 ± 0.03	3.08 ± 0.03
Heart (g)	1.29 ± 0.04	1.36 ± 0.06	1.34 ± 0.05	1.33 ± 0.04	1.45 ± 0.04	1.28 ± 0.05
Spleen (g)	1.36 ± 0.03	1.37 ± 0.02	1.39 ± 0.03	1.31 ± 0.02	1.33 ± 0.05	1.32 ± 0.03
Lung (g)	1.87 ± 0.02	1.83 ± 0.04	1.77 ± 0.03	1.83 ± 0.04	1.92 ± 0.01	1.84 ± 0.04
Thymus (g)	0.21 ± 0.01	0.20 ± 0.01	0.20 ± 0.01	0.19 ± 0.01	0.21 ± 0.01	0.20 ± 0.01

Epididymis (g)	1.39 ± 0.04	1.26 ± 0.03	1.32 ± 0.05	1.35 ± 0.05	1.32 ± 0.04	1.37 ± 0.06
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Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately, * $p < 0.05$ and ** $p < 0.01$ as compared with a respective parameter value of 0 mg/kg group. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 10: Effect of chrysin on intake and absolute organ weights of Sprague-Dawley female rats during 90-days repeated dose toxicity study

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Terminal Body weight (g)	338.20 ± 0.92	336.20 ± 0.92	337.40 ± 1.12	336.80 ± 1.07	337.00. ± 0.89	337.40 ± 1.25
Food intake (g)	31.34 ± 0.31	31.32 ± 0.43	30.52 ± 0.18	30.86 ± 0.28	31.00 ± 0.25	31.80 ± 0.16
Water intake (ml)	60.60 ± 0.40	61.00 ± 0.45	60.80 ± 0.58	60.60 ± 0.24	60.8 ± 0.2	61.80 ± 0.2
Brain (g)	2.73 ± 0.05	2.64 ± 0.03	2.64 ± 0.05	2.74 ± 0.05	2.67 ± 0.06	2.72 ± 0.05
Liver (g)	13.03 ± 0.38	13.09 ± 0.28	12.73 ± 0.26	12.17 ± 0.16	12.88 ± 0.34	12.52 ± 0.31
Kidneys (g)	3.63 ± 0.12	3.78 ± 0.12	3.74 ± 0.04	3.65 ± 0.11	3.79 ± 0.1	3.76 ± 0.12
Adrenals (g)	0.05 ± 0.002	0.04 ± 0.002	0.04 ± 0.002	0.04 ± 0.002	0.05 ± 0.002	0.05 ± 0.002
Ovaries (g)	0.08 ± 0.002	0.08 ± 0.002	0.08 ± 0.004	0.08 ± 0.003	0.08 ± 0.004	0.08 ± 0.002
Heart (g)	1.37 ± 0.05	1.41 ± 0.03	1.35 ± 0.03	1.31 ± 0.07	1.36 ± 0.03	1.31 ± 0.03
Spleen (g)	1.300 ± 0.03	1.34 ± 0.01	1.33 ± 0.03	1.33 ± 0.04	1.32 ± 0.04	1.35 ± 0.04
Lung (g)	1.79 ± 0.02	1.81 ± 0.03	1.85 ± 0.03	1.8 ± 0.04	1.84 ± 0.02	1.86 ± 0.04
Thymus (g)	0.20 ± 0.01	0.21 ± 0.01	0.20 ± 0.01	0.19 ± 0.01	0.20 ± 0.01	0.21 ± 0.01
Uterus (g)	0.34 ± 0.02	0.32 ± 0.01	0.32 ± 0.02	0.35 ± 0.02	0.31 ± 0.01	0.31 ± 0.02

Data are expressed as Mean $\pm$ Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 11: Effect of chrysin on relative organ weights of Sprague-Dawley male rats during 90-days repeated dose toxicity study

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Brain (g)	0.79 ± 0.02	0.81 ± 0.02	0.83 ± 0.01	0.78 ± 0.01	0.84 ± 0.01	0.82 ± 0.01
Liver (g)	3.62 ± 0.04	3.85 ± 0.12	3.92 ± 0.06	3.92 ± 0.08	4.15 ± 0.07**	4.04 ± 0.13**
Kidneys (g)	1.06 ± 0.04	1.06 ± 0.02	1.13 ± 0.03	1.06 ± 0.03	1.15 ± 0.04	1.12 ± 0.02
Adrenals (g)	0.014 ± 0.001	0.014 ± 0.001	0.013 ± 0.001	0.014 ± 0.001	0.015 ± 0.00	0.013 ± 0.001
Testes (g)	0.89 ± 0.01	0.90 ± 0.01	0.91 ± 0.01	0.92 ± 0.01	0.93 ± 0.01	0.91 ± 0.01
Heart (g)	0.38 ± 0.01	0.40 ± 0.02	0.40 ± 0.01	0.40 ± 0.01	0.45 ± 0.01	0.38 ± 0.02
Spleen (g)	0.40 ± 0.01	0.41 ± 0.01	0.41 ± 0.01	0.39 ± 0.01	0.41 ± 0.02	0.39 ± 0.01
Lung (g)	0.55 ± 0.01	0.54 ± 0.01	0.53 ± 0.01	0.54 ± 0.01	0.59 ± 0.00	0.54 ± 0.01
Thymus (g)	0.06 ± 0.003	0.06 ± 0.003	0.06 ± 0.003	0.06 ± 0.003	0.06 ± 0.002	0.06 ± 0.002
Epididymis (g)	0.41 ± 0.01	0.37 ± 0.01	0.39 ± 0.02	0.40 ± 0.01	0.41 ± 0.01	0.40 ± 0.02

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately, ** $p < 0.01$ as compared with a respective parameter value of 0 mg/kg group. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.

Supplementary Table 12: Effect of chrysin on relative organ weights of Sprague-Dawley female rats during 90-days repeated dose toxicity study

Parameter	C (0)	C (0)-R	C (250)	C (500)	C (1000)	C (1000)-R
Brain (g)	0.81 ± 0.01	0.79 ± 0.01	0.78 ± 0.01	0.81 ± 0.02	0.79 ± 0.02	0.81 ± 0.02
Liver (g)	3.85 ± 0.11	3.89 ± 0.08	3.77 ± 0.08	3.61 ± 0.05	3.82 ± 0.11	3.71 ± 0.09
Kidneys (g)	1.07 ± 0.04	1.13 ± 0.04	1.11 ± 0.01	1.08 ± 0.03	1.12 ± 0.03	1.11 ± 0.04
Adrenals (g)	0.014 ± 0.001	0.013 ± 0.001	0.014 ± 0.001	0.012 ± 0.001	0.014 ± 0.001	0.014 ± 0.001
Ovaries (g)	0.02 ± 0.001	0.02 ± 0.001	0.02 ± 0.001	0.02 ± 0.001	0.02 ± 0.001	0.02 ± 0.001
Heart (g)	0.41 ± 0.02	0.42 ± 0.01	0.40 ± 0.01	0.39 ± 0.02	0.40 ± 0.01	0.39 ± 0.01
Spleen (g)	0.38 ± 0.01	0.40 ± 0.00	0.39 ± 0.01	0.40 ± 0.01	0.39 ± 0.01	0.40 ± 0.01
Lung (g)	0.53 ± 0.01	0.54 ± 0.01	0.55 ± 0.01	0.53 ± 0.01	0.55 ± 0.01	0.55 ± 0.01
Thymus (g)	0.06 ± 0.003	0.06 ± 0.002	0.06 ± 0.003	0.06 ± 0.003	0.06 ± 0.002	0.06 ± 0.002
Uterus (g)	0.10 ± 0.003	0.10 ± 0.003	0.09 ± 0.005	0.10 ± 0.005	0.09 ± 0.004	0.09 ± 0.006

Data are expressed as Mean ± Standard Error of Mean and analyzed by one-way ANOVA followed by Dunnett's test for each parameter separately. Figures in parenthesis indicate dose in mg/kg. C: Chrysin. C (0)-R: Chrysin (0 mg/kg) reversal treated and C (1000)-R: Chrysin (1000 mg/kg) reversal treated.