

Supplementary Table S1. Primer sequences for the genes involved in lipid metabolism and lipophagy in *C. elegans*

Genes	Forward sequences (5'–3')	Reverse sequence (5'–3')
<i>daf-16</i>	CCAGACGGAAGGCTTAAACT	ATTCGCATGAAACGAGAATG
<i>hlh-30</i>	ATTCGCATGAAACGAGAATG	AGAACGCGATGCGTGGTGGG
<i>aak-2</i>	TCTTCGCCATCCGCATATC	CCTCTTCATCGGGTCTACGC
<i>lgg-1</i>	AACAACTTTGAGAAGCGTCGTGCC	ATCTTCTGGACGAAGTTGGATGCG
<i>lgg-2</i>	CTGCAAATTCCTAGTACCCGAG	CATAGAATTTGACACCATTGAGC
<i>lipI-2</i>	AATACGAGTCAAATCATTGAA	GTAACACTCGTTTTTCCATAA
<i>lipI-3</i>	ATGGGCAGGCAAATCCACCA	AGTTGTTCTGCGCAATTATA
<i>atg-18</i>	AAATGGACATCGGCTCTTTG	TGATAGCATCGAACCATCCA
<i>act-1</i>	TCGGTATGGGACAGAAGGAC	CATCCCAGTTGGTGACGATA

Supplementary Table S2. Identification of chemical constituents of BMSE by LC/Q-TOF-MS/MS

	RT (min)	Molecular formula	Key ion masses	Adduct and fragmental ion exact masses [M – X] ⁺	Tentatively identified compounds	Relative content
1	5.52	C ₄₂ H ₇₀ O ₁₄	798.4766 [M+H] ⁺	821.4766 [M+Na] ⁺ 641.4116, 411.2465, 184.0775	Kuguaglycoside E	0.25%
2	6.35	C ₄₂ H ₆₈ O ₁₄	796.4609 [M+H] ⁺	797.4732 [M+Na] ⁺ 639.3987, 455.3525, 439.3632, 391.3394	Momordicoside M	2.93%
3	6.48	C ₄₂ H ₇₀ O ₁₅	814.4715 [M+H] ⁺	815.4846 [M+Na] ⁺ 455.3525, 425.2549, 353.2878, 335.2784	Goyaglycoside h	1.44%
4	7.79	C ₃₆ H ₆₀ O ₁₀	652.4187 [M+H] ⁺	653.4296 [M+Na] ⁺ 349.1982, 335.2784, 187.1511	Momordicoside Q	4.59%
5	8.48	C ₄₃ H ₇₀ O ₁₅	826.4715 [M+H] ⁺	849.4661 [M+Na] ⁺ 639.3898, 437.3442, 391.3394	Momordicoside O	0.25%
6	8.6	C ₄₂ H ₆₈ O ₁₃	780.4660 [M+H] ⁺	781.4775 [M+Na] ⁺ 657.4031, 623.3918, 439.3558, 391.3394	Goyaglycoside e	1.51%
7	9.04	C ₄₂ H ₆₆ O ₁₄	794.4453 [M+H] ⁺	795.4578 [M+Na] ⁺ 674.4048, 639.3898, 455.3525, 419.3315	Neokuguaglycoside	1.40%
8	9.38	C ₄₃ H ₇₀ O ₁₄	810.4766 [M+H] ⁺	811.4872 [M+Na] ⁺ 657.4031, 439.3558, 421.3519, 391.3394	Goyaglycoside g	5.18%
9	9.52	C ₃₇ H ₆₀ O ₁₂	696.4085 [M-H] ⁻	695.3966 [M-H] ⁻ 513.3551, 314.9821, 146.9631	Momordicoside E	7.54%
10	9.95	C ₃₇ H ₅₈ O ₈	630.4132 [M-H] ⁻	675.4071 [M+HCOO] ⁻ 633.4081, 405.2952, 352.9889	Charantoside I	1.15%
11	10.35	C ₃₆ H ₅₆ O ₁₀	648.3874 [M-H] ⁻	647.3787 [M-H] ⁻ 326.9796, 264.9877, 240.9861	Momordicine III	0.12%
12	10.38	C ₃₆ H ₅₄ O ₈	614.3819 [M+H] ⁺	615.3940 [M+H] ⁺ 477.3391, 419.3315, 376.2607	Charantosides VII	0.18%
13	10.4	C ₃₆ H ₅₈ O ₉	634.4081 [M+H] ⁺	657.4008 [M+Na] ⁺ 639.3898, 437.3442, 419.3315, 409.3449	Momordicine II	22.02%
14	10.8	C ₃₉ H ₆₀ O ₁₂	720.4085 [M+H] ⁺	743.4030 [M+Na] ⁺ 657.4031, 477.3391, 391.3394	Momordicine V	0.67%
15	10.83	C ₃₆ H ₆₀ O ₈	620.4288 [M+H] ⁺	621.4400 [M+Na] ⁺ 477.3391, 419.3315, 391.3394	3β,7β23-Trihydroxycucurbita-5,24-diene-7-O-β-D-glucoside	0.46%
16	11.47	C ₃₆ H ₅₈ O ₈	618.4132 [M+H] ⁺	619.4238 [M+Na] ⁺ 439.3558, 421.3519, 391.3394, 357.2881	Momordicoside F2	6.67%
17	11.69	C ₃₀ H ₄₈ O ₃	456.3604 [M+H] ⁺	457.3700 [M+H] ⁺ 439.3558, 391.3394, 309.2590, 213.1694	3β-Hydroxy-7β,25-dimethoxy-cucurbita-5,23-dien-19-al	0.64%
18	11.69	C ₃₀ H ₄₆ O ₂	438.3498 [M+H] ⁺	439.3595 [M+H] ⁺ 421.3519, 409.3520, 391.3394, 357.2748	5β,19-Epoxy-cucurbita-6,22E,24-trien-3β-ol	1.59%
19	12.2	C ₃₀ H ₄₄ O ₂	436.3341 [M+H] ⁺	437.3436 [M+H] ⁺ 419.3387, 391.3394, 409.3520, 401.3238	3β-Hydroxycucurbita-5(10),6,22(E),24-tetraen-19-al	6.88%
20	12.2	C ₃₀ H ₄₈ O ₄	472.3553 [M+H] ⁺	495.3475 [M+Na] ⁺ 477.3391, 437.3442, 419.3315, 391.3394	Momordicine I	2.76%
21	12.35	C ₃₇ H ₆₀ O ₉	648.4237 [M-H] ⁻	693.4205 [M+HCOO] ⁻ 376.9863, 264.9877, 183.0082, 146.9631	Goyaglycoside a	0.29%
22	12.44	C ₃₆ H ₅₆ O ₈	616.3975 [M+H] ⁺	617.4081 [M+Na] ⁺ 599.4000, 477.3391, 391.3394, 321.2765	Momordicoside C	6.80%
23	13.14	C ₃₈ H ₆₂ O ₉	662.4394 [M+H] ⁺	685.4324 [M+Na] ⁺ 639.3987, 419.3387, 391.3464, 309.2652	Momordicosides U	1.51%
24	13.34	C ₃₇ H ₅₈ O ₉	646.4081 [M+H] ⁺	669.3997 [M+Na] ⁺ 637.3712, 581.3309, 495.3455	Karavilosides VI	0.66%
25	13.69	C ₃₈ H ₆₄ O ₈	648.4601 [M+H] ⁺	671.4531 [M+Na] ⁺ 405.3599, 391.3464, 349.2969	Karavilosides I	2.11%
26	15.75	C ₃₈ H ₆₂ O ₈	646.4445 [M+H] ⁺	647.4562 [M+Na] ⁺ 605.4295, 561.4016, 495.3455, 391.3394	Charantosides V	0.22%
27	17.27	C ₃₀ H ₄₂ O ₄	466.3083 [M-H] ⁻	511.3030 [M+HCOO] ⁻ 326.986, 255.2324, 183.0129, 146.9631, 100.9326	Kuguacins O	0.25%
28	19.11	C ₃₂ H ₅₂ O ₄	500.3866 [M+H] ⁺	523.3769 [M+Na] ⁺ 487.3723, 443.3338, 391.3394, 368.4304	5β,19-Epoxy-19-methoxy-cucurbita-6,23,25-trien-3-ol	1.41%
29	20.86	C ₃₃ H ₅₄ O ₄	514.4022 [M+H] ⁺	537.3960 [M+Na] ⁺ 522.6019, 495.2672, 439.2010	3β-Acetoxy-7β-methoxy-cucurbita-5,23(E)-dien-25-ol	18.49%

Supplementary Table S3. Corresponding targets of active ingredients in BMSE

Compounds		Targets
1	Kuguaglycoside E	PTAFR, PTPN1, IL2, STAT3, PPP2CA, ATP1A1, PPP1CC, PPM1B, PPP2R5A, KCNH2, CXCR1, BACE1, SLC5A2, SLC5A1
2	Momordicoside M	PTAFR, PPM1B, PPP1CC, PPP2CA, PPP2R5A, PTPN1, STAT3, RORC, ATP1A1, IL2
3	Goyaglycoside h	STAT3
4	Momordicoside Q	STAT3, PTAFR, PTPN1, ATP1A1, PPM1B, PPP2R5A, FAAH, CNR2, PPP1CC, PPP2CA, IL2, SLC5A2, SLC5A1, TACR2, IGF1R, ADORA1, S1PR1, NTRK1, MMP3, MMP2, CTSD, PSEN2, PSENEN, NCSTN, APH1A, PSEN1, APH1B
5	Goyaglycoside e	STAT3, PTPN1, PPM1B, PPP2R5A, MAPK8, SLC28A2, SLC5A2, SLC5A1, ADORA3, MAP2K1, SIRT2, PPP2CA, TACR2, ADORA2A, TYMS, EIF4A1, ADORA1
6	Neokuguaglycoside	PPM1B, PPP1CC, PPP2R5A, PTPN1, PTAFR, PPP2CA, STAT3, IL2, RORC, ATP1A1, OPRD1
7	Momordicoside E	STAT3, PTPN1, IL2, HSD11B2, F2, BCL2L1, SLC5A2, SLC5A1, GLI1, F10, ADORA1, EGFR, TYMS, S1PR3, S1PR1, ADORA2A
8	Charantoside I	PTPN1, PPM1B, PPP2R5A, MAPK8, STAT3, SIRT2, BCL2A1, PDE10A, CDK2, MAPK1, MAPK14, GRB2, TACR2, MTOR, MET, SLC5A2, ATP1A1, PFKFB3, FLT3, CDK4, RORC, PPP1CC, PPP2CA, PIM1, MAP2K1, PIM2, JAK2, S1PR3, S1PR1, SCD, PGK1, NR4A2, MAPK11, SLC6A4, SLC6A3, ADORA2A, ADORA1, AGTR2, PRF1, EGFR, GPR52, MCHR1, CHEK1, LRRK2, AOA, CSF1R, PI4KB, SLC33A1, MAPK9, SLC5A1, LIMK2, EIF2AK1, MAPKAPK2, P2RX3, SLC8A1, CTSL, CTSB, CCNE1 CDK2, CDK5, MMP13, PDE3B, MMP2, ALK, MMP8, PPARG, IKBKE, IGF1R, RPS6KB1, AURKA, TBK1, MAP3K14, KCNH2, CD274, GABRA2, GABRB3, GABRG2, PIK3CA, PIK3R1, GBA, HDAC1, CNR1, APP, UPP1, SIGMAR1, PIK3CA
9	Momordicine III	HSD11B2, IL2, TPN1, PM1B, PPP1CC, PPP2CA, PP2R5A, HSD11B1, SLC28A2, SLC5A2, SLC5A1, STAT3, ADK, GLI1, BCL2L1, S1PR1, PPARG
10	Momordicine II	PTPN1, PPM1B, PPP1CC, PPP2CA, PPP2R5A, BCL2L1, HSD11B2, S1PR1, SLC28A2, STAT3, JUN, SLC5A2, SLC5A1, TTL
11	Momordicine V	PPM1B, PPP1CC, PPP2R5A, JUN, PTPN1, PPP2CA, TTL, TERT, GLI1
12	Momordicoside F2	STAT3, ATP1A1, PTPN1, IL2, PTAFR, PPM1B, PPP1CC, PPP2R5A, CNR2, FAAH, GRB2, RORC, CTSD, SLC5A2, SLC5A1, CA2, S1PR1
13	Momordicine I	PTGFR, PTGIR, SLC22A6, CYP19A1, PTGER1, PTGER2, NR3C1, PTGER4, PTGER3, ESR2, R1H3, PTPN1, NPC1L1, PPARG, PTGES, AR, RORC, RORA, SHBG, FNTA, PPARA, G6PD, PPARG, SLC6A4, ITGAL, HSD11B1, NOS2, SERPINA6, HMGCR, TNF, CES2, CYP51A1, CCR1, PRKCH, BACE1, BCHE, PRKCA, OPRK1, PIK3CB, PTGDR, MAPK8, OXTR, MMP3, MMP1, MMP2, MMP7, MAPK14, PTPRF, ACP1, PGR, GPR55, GPR18, CNR2, PIK3CD, PIK3CG, PIK3CA, CYP24A1, MAPK3, SIGMAR1, PDE10A, PSEN2, CYP27B1, PTPN6, PTGS2, IL6ST, CYP2D6, CYP2C9, CYP3A4, HSD11B2, PYGL, MAPK10, MAPK9, PTPN2, P2RX3, CDC25B, MTNR1A, MTNR1B, F10, MET, MMP8, MDM2, CASR, EGFR, HCRTR2, HCRTR1, SORD, GSK3A, FDF1, CFD, MDM4, PDE4D, CRHR1, CD81, LTB4R, SLC6A3, CDC25A, ADCY1, SMO, HSP90AA1
14	Goyaglycoside a	STAT3, PPM1B, PPP2R5A, PTPN1, ATP1A1, CNR2, PPP2CA, SIRT2, EGFR, BCL2A1, SYK, MAP2K1, IMPDH1, IMPDH2, RORC, LIMK2, TYMS, PTAFR, GBA, TACR2, SLC28A2, CSF1R, PTGFR, IL2
15	Momordicoside C	STAT3, IL2, PTAFR, PPM1B, PPP1CC, PPP2CA, PPP2R5A, HSD11B2, HSD11B1, VEGFA, FGF1FGF2, HPSE, ATP1A1, MDM2
16	Charantagenin E	IL2, PTPN1, PTAFR, PPP1CC, PPP2CA, STAT3, PPM1B, PPP2R5A, S1PR3, S1PR1, ATP1A1, RORC, JAK2, ICAM1, SELE, SLC8A1, UPP1, FAAH, CNR2, PIM1, PIM2, MAPK14, IKBKE, TBK1, PRKDC, JAK1, TYK2, TTK, MAPK8, SLC5A2, SLC5A1, ADORA1, AGTR2, SIRT2, MAP3K14, MTOR, NR4A2, GABRA5, CSF1R, ABL1, CDK2, PIK3CA, MAPK1, EGFR, PI4KB, MAP2K1, BCL2A1, SCD, MAPK10, NAMPT, KCNH2, ADORA2A, ADORA2B, PTK2, SYK, HDAC1, BTK, PFKFB3, MET, GBA, FGFR1, GYS1, SMO, CCNT1, NTRK1, FER, ALK, TNK2, NTRK2, FES, PTK2B, ROS1, NTRK3, LTK
17	Momordicoside I	STAT3, ATP1A1, PTPN1, IL2, PTAFR, PPM1B, PPP1CC, PPP2R5A, CNR2, FAAH, GRB2, RORC, CTSD, SLC5A2, SLC5A1, CA2, S1PR1

Supplementary Table S4. Representative information of active compounds and targets

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
MC	0.0775	17	2	28.06	17	0.7682	81058
Momordicoside I	0.0125	18	3	9.50	18	0.5558	28154
Charantagenin E	0.2841	75	3	3.89	75	0.6781	321464
Momordicoside C	0.0404	16	3	8.00	16	0.5515	34620
Goyaglycoside a	0.0405	25	3	6.88	25	0.5708	60992
Momordicine I	0.5609	101	3	1.79	101	0.7339	435226
Momordicoside F2	0.0125	18	3	9.50	18	0.5558	28154
Momordicine V	0.0171	10	3	9.20	10	0.5386	14494
Momordicine II	0.0167	15	3	9.53	15	0.5494	26186
Momordicine III	0.0233	18	3	8.89	18	0.5558	38228
Charantoside I	0.3458	83	3	3.46	83	0.6953	406470
Goyaglycoside e	0.0255	18	3	7.83	18	0.5558	31000
Momordicoside E	0.0243	17	3	7.06	17	0.5536	35178
Kuguaglycoside E	0.0144	15	3	10.33	15	0.5494	19582
Neokuguaglucoiside	0.0103	12	3	11.50	12	0.5429	11902
Momordicoside Q	0.0295	23	3	8.22	23	0.5665	50976
Goyaglycoside h	0.0000	2	3	16.00	2	0.5215	154
Momordicoside M	0.0018	11	3	12.45	11	0.5408	6626
LTK	0.0000	1	4	75.00	1	0.4292	0
NTRK3	0.0000	1	4	75.00	1	0.4292	0
ROS1	0.0000	1	4	75.00	1	0.4292	0
PTK2B	0.0000	1	4	75.00	1	0.4292	0
FES	0.0000	1	4	75.00	1	0.4292	0
NTRK2	0.0000	1	4	75.00	1	0.4292	0
TNK2	0.0000	1	4	75.00	1	0.4292	0
FER	0.0000	1	4	75.00	1	0.4292	0
CCNT1	0.0000	1	4	75.00	1	0.4292	0
GYS1	0.0000	1	4	75.00	1	0.4292	0
FGFR1	0.0000	1	4	75.00	1	0.4292	0
BTK	0.0000	1	4	75.00	1	0.4292	0
PTK2	0.0000	1	4	75.00	1	0.4292	0
ADORA2B	0.0000	1	4	75.00	1	0.4292	0
NAMPT	0.0000	1	4	75.00	1	0.4292	0
ABL1	0.0000	1	4	75.00	1	0.4292	0
GABRA5	0.0000	1	4	75.00	1	0.4292	0
TTK	0.0000	1	4	75.00	1	0.4292	0
TYK2	0.0000	1	4	75.00	1	0.4292	0
JAK1	0.0000	1	4	75.00	1	0.4292	0
PRKDC	0.0000	1	4	75.00	1	0.4292	0
SELE	0.0000	1	4	75.00	1	0.4292	0

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Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
ICAM1	0.0000	1	4	75.00	1	0.4292	0
HPSE	0.0000	1	4	16.00	1	0.3026	0
FGF2	0.0000	1	4	16.00	1	0.3026	0
FGF1	0.0000	1	4	16.00	1	0.3026	0
VEGFA	0.0000	1	4	16.00	1	0.3026	0
IMPDH2	0.0000	1	4	25.00	1	0.3219	0
IMPDH1	0.0000	1	4	25.00	1	0.3219	0
SYK	0.0004	2	4	50.00	2	0.4464	764
HSP90AA1	0.0000	1	4	101.00	1	0.4850	0
SMO	0.0099	2	4	88.00	2	0.6245	10986
ADCY1	0.0000	1	4	101.00	1	0.4850	0
CDC25A	0.0000	1	4	101.00	1	0.4850	0
LTB4R	0.0000	1	4	101.00	1	0.4850	0
CD81	0.0000	1	4	101.00	1	0.4850	0
CRHR1	0.0000	1	4	101.00	1	0.4850	0
PDE4D	0.0000	1	4	101.00	1	0.4850	0
MDM4	0.0000	1	4	101.00	1	0.4850	0
CFD	0.0000	1	4	101.00	1	0.4850	0
FDFT1	0.0000	1	4	101.00	1	0.4850	0
GSK3A	0.0000	1	4	101.00	1	0.4850	0
SORD	0.0000	1	4	101.00	1	0.4850	0
HCRTR1	0.0000	1	4	101.00	1	0.4850	0
HCRTR2	0.0000	1	4	101.00	1	0.4850	0
CASR	0.0000	1	4	101.00	1	0.4850	0
MDM2	0.0041	2	4	58.50	2	0.5129	2208
MTNR1B	0.0000	1	4	101.00	1	0.4850	0
MTNR1A	0.0000	1	4	101.00	1	0.4850	0
CDC25B	0.0000	1	4	101.00	1	0.4850	0
PTPN2	0.0000	1	4	101.00	1	0.4850	0
MAPK10	0.0099	2	4	88.00	2	0.6245	10986
PYGL	0.0000	1	4	101.00	1	0.4850	0
CYP3A4	0.0000	1	4	101.00	1	0.4850	0
CYP2C9	0.0000	1	4	101.00	1	0.4850	0
CYP2D6	0.0000	1	4	101.00	1	0.4850	0
IL6ST	0.0000	1	4	101.00	1	0.4850	0
PTGS2	0.0000	1	4	101.00	1	0.4850	0
PTPN6	0.0000	1	4	101.00	1	0.4850	0
CYP27B1	0.0000	1	4	101.00	1	0.4850	0
MAPK3	0.0000	1	4	101.00	1	0.4850	0
CYP24A1	0.0000	1	4	101.00	1	0.4850	0

Continued

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
PIK3CG	0.0000	1	4	101.00	1	0.4850	0
PIK3CD	0.0000	1	4	101.00	1	0.4850	0
CHRM1	0.0000	1	4	101.00	1	0.4850	0
GPR18	0.0000	1	4	101.00	1	0.4850	0
GPR55	0.0000	1	4	101.00	1	0.4850	0
PGR	0.0000	1	4	101.00	1	0.4850	0
ACP1	0.0000	1	4	101.00	1	0.4850	0
PTPRF	0.0000	1	4	101.00	1	0.4850	0
MMP7	0.0000	1	4	101.00	1	0.4850	0
MMP1	0.0000	1	4	101.00	1	0.4850	0
OXTR	0.0000	1	4	101.00	1	0.4850	0
PTGDR	0.0000	1	4	101.00	1	0.4850	0
PIK3CB	0.0000	1	4	101.00	1	0.4850	0
OPRK1	0.0000	1	4	101.00	1	0.4850	0
PRKCA	0.0000	1	4	101.00	1	0.4850	0
BCHE	0.0000	1	4	101.00	1	0.4850	0
PRKCH	0.0000	1	4	101.00	1	0.4850	0
CCR1	0.0000	1	4	101.00	1	0.4850	0
CYP51A1	0.0000	1	4	101.00	1	0.4850	0
CES2	0.0000	1	4	101.00	1	0.4850	0
TNF	0.0000	1	4	101.00	1	0.4850	0
HMGCR	0.0000	1	4	101.00	1	0.4850	0
SERPINA6	0.0000	1	4	101.00	1	0.4850	0
NOS2	0.0000	1	4	101.00	1	0.4850	0
ITGAL	0.0000	1	4	101.00	1	0.4850	0
PPARD	0.0000	1	4	101.00	1	0.4850	0
G6PD	0.0000	1	4	101.00	1	0.4850	0
PPARA	0.0000	1	4	101.00	1	0.4850	0
FNTA	0.0000	1	4	101.00	1	0.4850	0
SHBG	0.0000	1	4	101.00	1	0.4850	0
RORA	0.0000	1	4	101.00	1	0.4850	0
AR	0.0000	1	4	101.00	1	0.4850	0
PTGES	0.0000	1	4	101.00	1	0.4850	0
NPC1L1	0.0000	1	4	101.00	1	0.4850	0
NR1H3	0.0000	1	4	101.00	1	0.4850	0
ESR2	0.0000	1	4	101.00	1	0.4850	0
PTGER3	0.0000	1	4	101.00	1	0.4850	0
PTGER4	0.0000	1	4	101.00	1	0.4850	0
NR3C1	0.0000	1	4	101.00	1	0.4850	0
PTGER2	0.0000	1	4	101.00	1	0.4850	0

Continued

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
PTGER1	0.0000	1	4	101.00	1	0.4850	0
CYP19A1	0.0000	1	4	101.00	1	0.4850	0
SLC22A6	0.0000	1	4	101.00	1	0.4850	0
PTGIR	0.0000	1	4	101.00	1	0.4850	0
PTGFR	0.0030	2	4	63.00	2	0.5279	3340
CA2	0.0000	2	4	18.00	2	0.3090	2
TERT	0.0000	1	4	10.00	1	0.2897	0
TTL	0.0000	2	4	12.50	2	0.3069	34
JUN	0.0000	2	4	12.50	2	0.3069	34
ADK	0.0000	1	4	18.00	1	0.3069	0
HSD11B1	0.0064	3	4	45.00	3	0.5300	4664
PIK3CA	0.0189	3	4	86.33	3	0.6910	24468
SIGMAR1	0.0081	2	4	92.00	2	0.6288	11014
UPP1	0.0009	2	4	79.00	2	0.5150	2468
APP	0.0000	1	4	83.00	1	0.4464	0
CNR1	0.0000	1	4	83.00	1	0.4464	0
HDAC1	0.0009	2	4	79.00	2	0.5150	2468
GBA	0.0017	3	4	61.00	3	0.5279	4266
PIK3CA	0.0000	1	4	83.00	1	0.4464	0
GABRA2	0.0000	1	4	83.00	1	0.4464	0
CD274	0.0000	1	4	83.00	1	0.4464	0
MAP3K14	0.0009	2	4	79.00	2	0.5150	2468
TBK1	0.0009	2	4	79.00	2	0.5150	2468
AURKA	0.0000	1	4	83.00	1	0.4464	0
RPS6KB1	0.0000	1	4	83.00	1	0.4464	0
IGFBP3	0.0000	1	4	83.00	1	0.4464	0
IKBKE	0.0009	2	4	79.00	2	0.5150	2468
PPARG	0.0109	3	4	67.33	3	0.6416	14320
MMP8	0.0081	2	4	92.00	2	0.6288	11014
ALK	0.0009	2	4	79.00	2	0.5150	2468
PDE3B	0.0000	1	4	83.00	1	0.4464	0
MMP13	0.0000	1	4	83.00	1	0.4464	0
CDK5	0.0000	1	4	83.00	1	0.4464	0
CCNE1	0.0000	1	4	83.00	1	0.4464	0
CTSB	0.0000	1	4	83.00	1	0.4464	0
CTSL	0.0000	1	4	83.00	1	0.4464	0
SLC8A1	0.0009	2	4	79.00	2	0.5150	2468
P2RX3	0.0081	2	4	92.00	2	0.6288	11014
MAPKAPK2	0.0000	1	4	83.00	1	0.4464	0
EIF2AK1	0.0000	1	4	83.00	1	0.4464	0

Continued

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
LIMK2	0.0005	2	4	54.00	2	0.4678	1034
MAPK9	0.0081	2	4	92.00	2	0.6288	11014
SLC33A1	0.0000	1	4	83.00	1	0.4464	0
PI4KB	0.0009	2	4	79.00	2	0.5150	2468
CSF1R	0.0017	3	4	61.00	3	0.5279	4266
MAOA	0.0000	1	4	83.00	1	0.4464	0
LRRK2	0.0000	1	4	83.00	1	0.4464	0
CHEK1	0.0000	1	4	83.00	1	0.4464	0
MCHR1	0.0000	1	4	83.00	1	0.4464	0
GPR52	0.0000	1	4	83.00	1	0.4464	0
PRF1	0.0000	1	4	83.00	1	0.4464	0
AGTR2	0.0009	2	4	79.00	2	0.5150	2468
SLC6A3	0.0081	2	4	92.00	2	0.6288	11014
SLC6A4	0.0081	2	4	92.00	2	0.6288	11014
MAPK11	0.0000	1	4	83.00	1	0.4464	0
NR4A2	0.0009	2	4	79.00	2	0.5150	2468
PGK1	0.0000	1	4	83.00	1	0.4464	0
SCD	0.0009	2	4	79.00	2	0.5150	2468
JAK2	0.0009	2	4	79.00	2	0.5150	2468
PIM2	0.0009	2	4	79.00	2	0.5150	2468
PIM1	0.0009	2	4	79.00	2	0.5150	2468
CDK4	0.0000	1	4	83.00	1	0.4464	0
FLT3	0.0000	1	4	83.00	1	0.4464	0
PFKFB3	0.0009	2	4	79.00	2	0.5150	2468
MET	0.0189	3	4	86.33	3	0.6910	24468
MTOR	0.0009	2	4	79.00	2	0.5150	2468
GRB2	0.0006	3	4	39.67	3	0.4635	1394
MAPK14	0.0189	3	4	86.33	3	0.6910	24468
MAPK1	0.0009	2	4	79.00	2	0.5150	2468
CDK2	0.0009	2	4	79.00	2	0.5150	2468
PDE10A	0.0081	2	4	92.00	2	0.6288	11014
BCL2A1	0.0017	3	4	61.00	3	0.5279	4266
S1PR3	0.0020	3	4	58.33	3	0.5300	4284
EGFR	0.0263	5	4	60.20	5	0.7103	33870
F10	0.0023	2	4	59.00	2	0.5129	2198
GLI1	0.0002	3	4	15.00	3	0.3326	274
BCL2L1	0.0001	3	4	16.67	3	0.3305	206
F2	0.0000	1	4	17.00	1	0.3047	0
HSD11B2	0.0120	5	4	33.40	5	0.5494	9598
OPRD1	0.0000	1	4	12.00	1	0.2940	0

Continued

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
EIF4A1	0.0000	1	4	18.00	1	0.3069	0
TYMS	0.0003	3	4	20.00	3	0.3562	508
ADORA2A	0.0029	4	4	48.25	4	0.5386	5710
SIRT2	0.0027	4	4	50.25	4	0.5343	5690
MAP2K1	0.0027	4	4	50.25	4	0.5343	5690
ADORA3	0.0000	1	4	18.00	1	0.3069	0
SLC28A2	0.0004	4	4	19.00	4	0.3648	816
MAPK8	0.0237	4	4	69.25	4	0.7017	28432
PSEN2	0.0021	2	4	62.00	2	0.5236	2930
CTSD	0.0000	3	4	19.67	3	0.3283	102
MMP2	0.0107	3	4	69.00	3	0.6438	14932
MMP3	0.0021	2	4	62.00	2	0.5236	2930
NTRK1	0.0003	2	4	49.00	2	0.4442	658
S1PR1	0.0065	8	4	33.38	8	0.5622	13066
ADORA1	0.0039	5	4	43.20	5	0.5494	7702
IGF1R	0.0000	1	4	23.00	1	0.3176	0
TACR2	0.0017	4	4	37.25	4	0.4893	3184
CNR2	0.0203	6	4	43.33	6	0.6545	25062
FAAH	0.0008	4	4	33.50	4	0.4528	1592
RORC	0.0327	8	4	42.88	8	0.7167	41482
SLC5A1	0.0088	10	4	30.00	10	0.5751	16604
SLC5A2	0.0088	10	4	30.00	10	0.5751	16604
BACE1	0.0025	2	4	58.00	2	0.5129	2090
CXCR1	0.0000	1	4	15.00	1	0.3004	0
KCNH2	0.0016	3	4	57.67	3	0.5215	3378
PPP2R5A	0.0163	14	4	25.50	14	0.6009	24972
PPM1B	0.0163	14	4	25.50	14	0.6009	24972
PPP1CC	0.0127	12	4	26.17	12	0.5837	18862
ATP1A1	0.0091	10	4	29.60	10	0.5751	14684
PPP2CA	0.0144	12	4	26.75	12	0.5944	20874
STAT3	0.0185	15	4	24.40	15	0.6052	26538
IL2	0.0066	11	4	22.55	11	0.5150	10258
PTPN1	0.0636	15	4	30.60	15	0.7554	73762
PTAFR	0.0043	9	4	23.67	9	0.4979	6258

Note. MC, *Momordica Charania*.

Supplementary Table S5. Representative information of protein-protein interaction (PPI) network

name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
TNF	420.7889	17	3	4.59	17	0.9067	690
NTRK2	242.4444	9	3	5.22	9	0.8400	458
PPARG	165.6778	12	3	5.08	12	0.8333	326
MTOR	99.6667	9	3	6.67	9	0.8333	236
LRP1	65.9667	5	3	7.60	5	0.7933	126
ARC	62.6667	3	4	4.67	3	0.7000	124
F2R	58.0000	2	4	9.00	2	0.7267	70
JUND	56.2667	4	3	8.50	4	0.7800	134
TIMP1	38.2111	5	4	8.80	5	0.7867	104
CRHR1	15.6222	4	4	4.75	4	0.7000	34
MAOA	12.8667	4	4	3.50	4	0.6733	26
IFNAR1	12.7667	3	4	8.00	3	0.7467	32
IGF1R	11.8333	6	4	8.83	6	0.7800	42
FGF1	11.7667	4	3	11.00	4	0.7933	44
BCHE	9.0778	2	4	10.50	2	0.7400	28
SLC6A4	5.9556	3	4	5.67	3	0.6867	16
PTGS2	5.4222	6	4	8.67	6	0.7800	22
EPO	2.3333	3	4	9.67	3	0.7467	6
MAPK13	0.6667	2	4	6.50	2	0.6667	2
APLP2	0	1	4	5.00	1	0.6000	0
NTRK3	0	1	5	3.00	1	0.5067	0
CDK5R1	0	1	4	9.00	1	0.6467	0
PIK3R6	0	1	5	2.00	1	0.5333	0
G6PD	0	3	4	12.67	3	0.7533	0
IL26	0	1	4	17.00	1	0.7133	0
JAZF1	0	2	4	10.50	2	0.6933	0
MTUS1	0	1	4	12.00	1	0.6400	0
NOS2	0	3	4	11.67	3	0.7467	0
RANBP9	0	1	4	9.00	1	0.6467	0
SCD5	0	1	4	12.00	1	0.6400	0
TRAF4	0	1	4	17.00	1	0.7133	0

Supplementary Table S6. KEGG enrichment pathway and corresponding target classification and number

ID	Pathway	Count	Gene
hsa04933	AGE-RAGE signaling pathway in diabetic complications	12	ICAM1, JAK2, JUN, PIK3CA, PIK3CB, PIK3CD, MAPK1, MAPK8, SELE, STAT3, TNF , VEGFA
hsa04931	Insulin resistance	12	MTOR , PIK3CA, PIK3CB, PIK3CD, PPARA, APK8, PTPN1, PTPRF, RPS6KB1, STAT3, TNF , NR1H3
hsa05417	Lipid and atherosclerosis	13	ICAM1, JAK2, JUN, MMP3, PIK3CA, PIK3CB, PIK3CD, PPARG , MAPK1, MAPK8, SELE, STAT3, TNF
hsa04152	AMPK signaling pathway	10	MTOR , HMGCR, IGF1R, PFKFB3, PIK3CA, PIK3CB, PIK3CD, PPARG , RPS6KB1, SCD
hsa04151	PI3K-Akt signaling pathway	15	CDK2, CHRM1, FGFR1, MTOR , IGF1R, IL2, JAK2, NTRK2 , PIK3CA, PIK3CB, PIK3CD, PIK3CG, MAPK1, RPS6KB1, VEGFA
hsa04930	Type II diabetes mellitus	7	MTOR , PIK3CA, PIK3CB, PIK3CD, MAPK1, MAPK8, TNF

Supplementary Table S7. Representative information of target pathway network

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
MC	0.0000	17	2	10.59	17	0.7441	0
Obesity	0.0000	20	2	5.50	20	0.6721	0
Goyaglycoside a	0.0001	7	1	11.71	7	0.6324	6
Momordicoside I	0.0001	8	1	11.88	8	0.6360	7
Charantagenin E	0.0010	26	1	5.62	26	0.7081	25
Momordicoside C	0.0001	7	1	10.00	7	0.6360	6
Momordicine I	0.0026	39	1	3.85	39	0.7586	38
Momordicoside F2	0.0001	8	1	11.88	8	0.6360	7
Momordicine V	0.0001	4	1	10.75	4	0.6288	3
Momordicine II	0.0001	6	1	12.50	6	0.6360	5
Momordicine III	0.0001	8	1	11.13	8	0.6360	7
Charantoside I	0.0011	25	1	5.00	25	0.7045	24
Momordicoside E	0.0001	7	1	12.14	7	0.6324	6
Neokuguagluco side	0.0001	6	1	12.67	6	0.6288	5
Goyaglycoside e	0.0000	5	1	14.20	5	0.6288	4
Momordicoside Q	0.0002	10	1	10.10	10	0.6468	9
Goyaglycoside h	0.0000	2	1	17.50	2	0.6108	1
Momordicoside M	0.0000	5	1	15.00	5	0.6252	4
Kuguaglycoside E	0.0001	7	1	12.57	7	0.6324	6
hsa05142	0.0002	10	1	8.60	10	0.6973	9
hsa05200	0.0017	37	1	5.35	37	0.7982	36
hsa05205	0.0000	1	0	20.00	1	0.4739	0
hsa05224	0.0000	1	0	20.00	1	0.4739	0
hsa05235	0.0000	1	0	20.00	1	0.4739	0
hsa04152	0.0000	1	0	20.00	1	0.4739	0
hsa05212	0.0000	1	0	20.00	1	0.4739	0
hsa05161	0.0000	1	0	20.00	1	0.4739	0
hsa01522	0.0002	11	1	7.36	11	0.6613	10
hsa05215	0.0000	1	0	20.00	1	0.4739	0

Continued

Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
hsa05171	0.0003	12	1	8.67	12	0.7081	11
hsa04151	0.0000	1	0	20.00	1	0.4739	0
hsa05417	0.0000	1	0	20.00	1	0.4739	0
hsa01521	0.0000	1	0	20.00	1	0.4739	0
hsa04668	0.0000	2	1	11.50	2	0.5243	1
hsa04066	0.0000	1	0	20.00	1	0.4739	0
hsa05207	0.0003	12	1	6.33	12	0.6613	11
hsa04931	0.0003	13	1	8.54	13	0.7117	12
hsa05167	0.0000	1	0	20.00	1	0.4739	0
hsa04933	0.0000	1	0	20.00	1	0.4739	0
NAMPT	0.0000	1	0	26.00	1	0.5099	0
IMPDH1	0.0000	1	0	7.00	1	0.4342	0
MTNR1B	0.0000	1	0	39.00	1	0.5604	0
OPRK1	0.0000	1	0	39.00	1	0.5604	0
BCHE	0.0000	1	0	39.00	1	0.5604	0
SERPINA6	0.0000	1	0	39.00	1	0.5604	0
SHBG	0.0000	1	0	39.00	1	0.5604	0
NR3C1	0.0000	1	0	39.00	1	0.5604	0
CYP19A1	0.0000	1	0	39.00	1	0.5604	0
HSD11B1	0.0000	3	0	18.00	3	0.5856	0
APP	0.0000	1	0	25.00	1	0.5063	0
SLC8A1	0.0000	2	0	25.50	2	0.5495	0
MAOA	0.0000	1	0	25.00	1	0.5063	0
MCHR1	0.0000	1	0	25.00	1	0.5063	0
AGTR2	0.0000	2	0	25.50	2	0.5495	0
SLC6A3	0.0000	2	0	32.00	2	0.6288	0
SLC6A4	0.0000	2	0	32.00	2	0.6288	0
CNR2	0.0000	6	0	16.33	6	0.6613	0
FAAH	0.0000	4	0	13.00	4	0.5279	0
SLC5A2	0.0000	10	0	11.00	10	0.6000	0
KCNH2	0.0000	3	0	19.33	3	0.5532	0
PTAFR	0.0000	9	0	9.33	9	0.5640	0
CDK5	0.0000	1	0	25.00	1	0.5063	0
PRKCH	0.0000	2	0	38.00	2	0.6468	0
CNR1	0.0000	1	0	25.00	1	0.5063	0
HSD11B2	0.0000	6	0	17.33	6	0.6685	0
OPRD1	0.0000	1	0	6.00	1	0.4306	0
ACP1	0.0000	2	0	38.00	2	0.6468	0
PDE4D	0.0000	2	0	38.00	2	0.6468	0
CRHR1	0.0000	2	0	38.00	2	0.6468	0

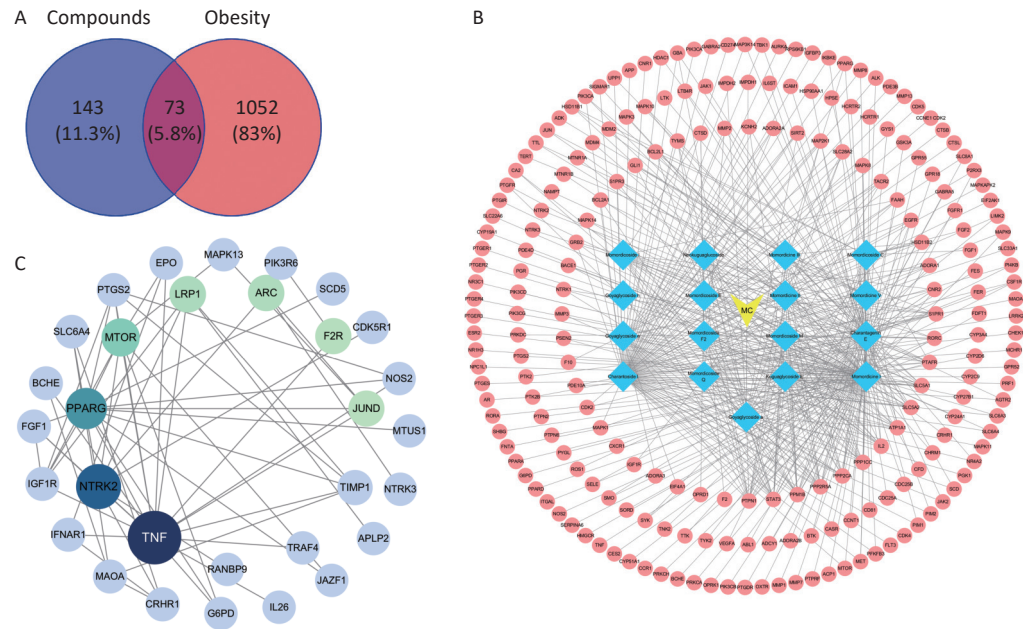
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Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
IGFBP3	0.0000	1	0	25.00	1	0.5063	0
NTRK3	0.0000	1	0	26.00	1	0.5099	0
G6PD	0.0000	2	0	38.00	2	0.6468	0
SCD	0.0000	2	0	25.50	2	0.5495	0
HMGCR	0.0000	2	0	38.00	2	0.6468	0
CFD	0.0000	3	0	29.33	3	0.6505	0
NTRK2	0.0000	1	0	26.00	1	0.5099	0
CHRM1	0.0000	2	0	38.00	2	0.6468	0
MMP3	0.0000	4	0	24.50	4	0.6685	0
PFKFB3	0.0000	2	0	25.50	2	0.5495	0
CYP3A4	0.0000	3	0	29.33	3	0.6505	0
NR1H3	0.0000	3	0	29.67	3	0.6505	0
PTPRF	0.0000	3	0	29.67	3	0.6505	0
PTPN1	0.0000	17	0	13.00	17	0.7946	0
PPARA	0.0000	4	0	25.25	4	0.6541	0
TYK2	0.0000	1	0	26.00	1	0.5099	0
PIK3CG	0.0000	2	0	38.00	2	0.6468	0
TNF	0.0000	5	0	22.20	5	0.6577	0
SELE	0.0000	1	0	26.00	1	0.5099	0
ICAM1	0.0000	1	0	26.00	1	0.5099	0
VEGFA	0.0000	3	0	18.67	3	0.6180	0
TERT	0.0000	2	0	20.50	2	0.6072	0
STAT3	0.0000	18	0	11.06	18	0.7730	0
RPS6KB1	0.0000	5	0	19.60	5	0.6793	0
PTGS2	0.0000	3	0	26.00	3	0.6505	0
MAPK8	0.0000	9	0	19.78	9	0.7586	0
MAPK1	0.0000	7	0	19.00	7	0.7225	0
PPARG	0.0000	4	0	27.25	4	0.7045	0
PPARD	0.0000	2	0	38.00	2	0.6468	0
PIK3CD	0.0000	7	0	19.14	7	0.6685	0
PIK3CB	0.0000	7	0	19.14	7	0.6685	0
PIK3CA	0.0000	7	0	23.00	7	0.7514	0
NOS2	0.0000	3	0	28.67	3	0.6505	0
JUN	0.0000	7	0	13.14	7	0.6324	0
JAK2	0.0000	2	0	25.50	2	0.5495	0
IL2	0.0000	14	0	11.29	14	0.7297	0
IGF1R	0.0000	2	0	10.50	2	0.5423	0
MTOR	0.0000	6	0	20.67	6	0.7189	0
FGFR1	0.0000	1	0	26.00	1	0.5099	0
F2	0.0000	3	0	18.67	3	0.6144	0

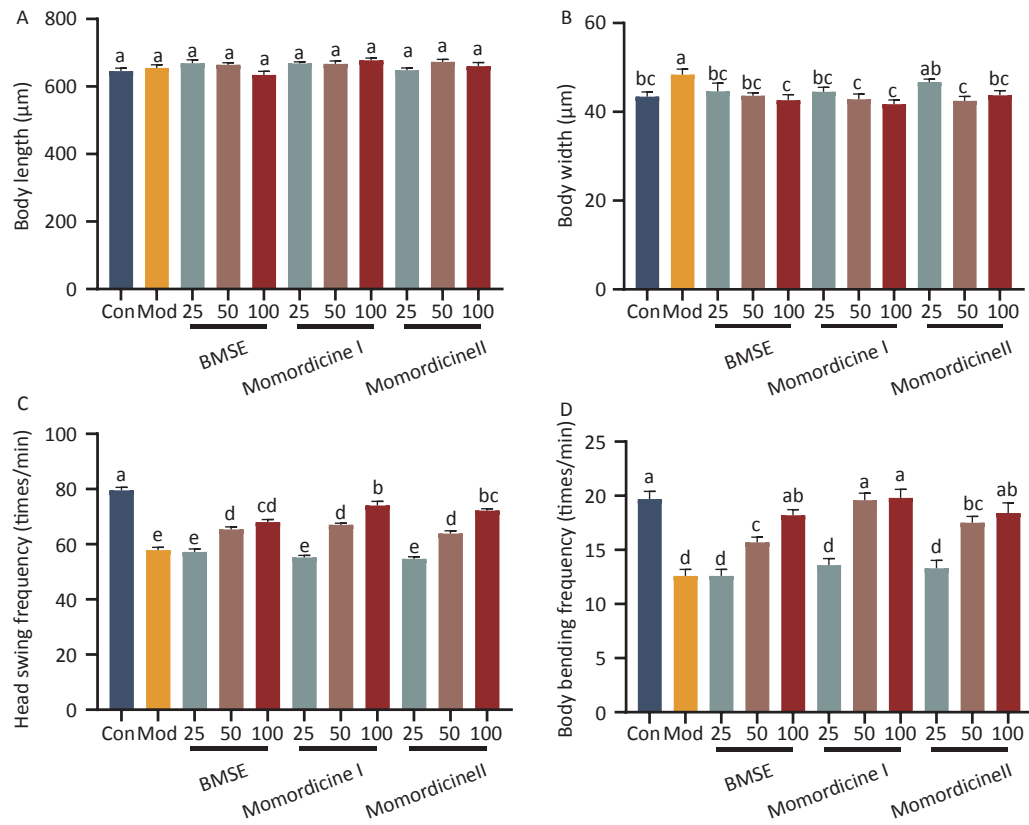
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Name	Betweenness	Degree	Eccentricity	Neighborhood connectivity	Number of directed edges	Radiality	Stress
ESR2	0.0000	4	0	24.75	4	0.6577	0
CDK2	0.0000	2	0	25.50	2	0.5495	0
AR	0.0000	3	0	29.33	3	0.6505	0

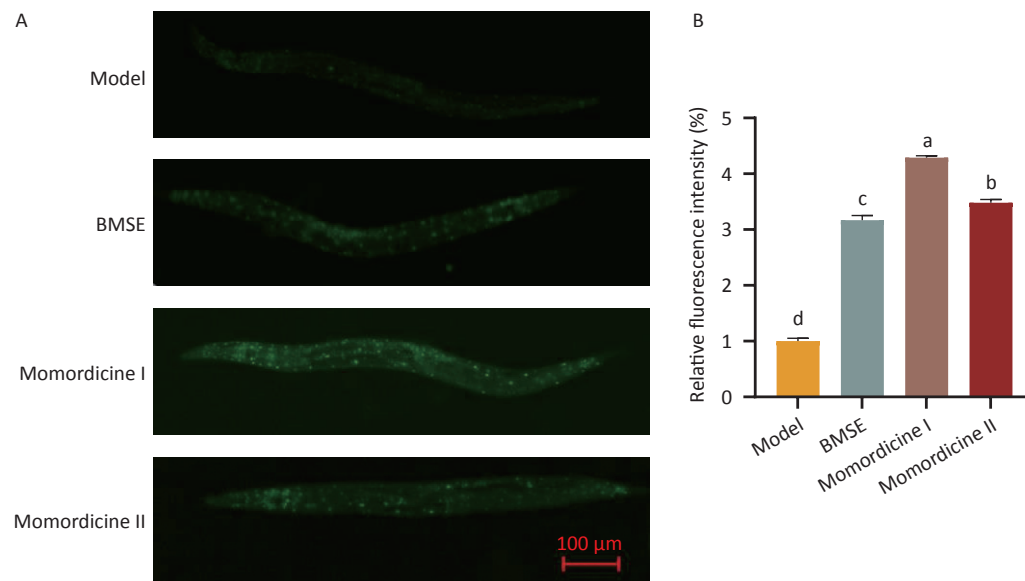
Note. MC, *Momordica Charania*.



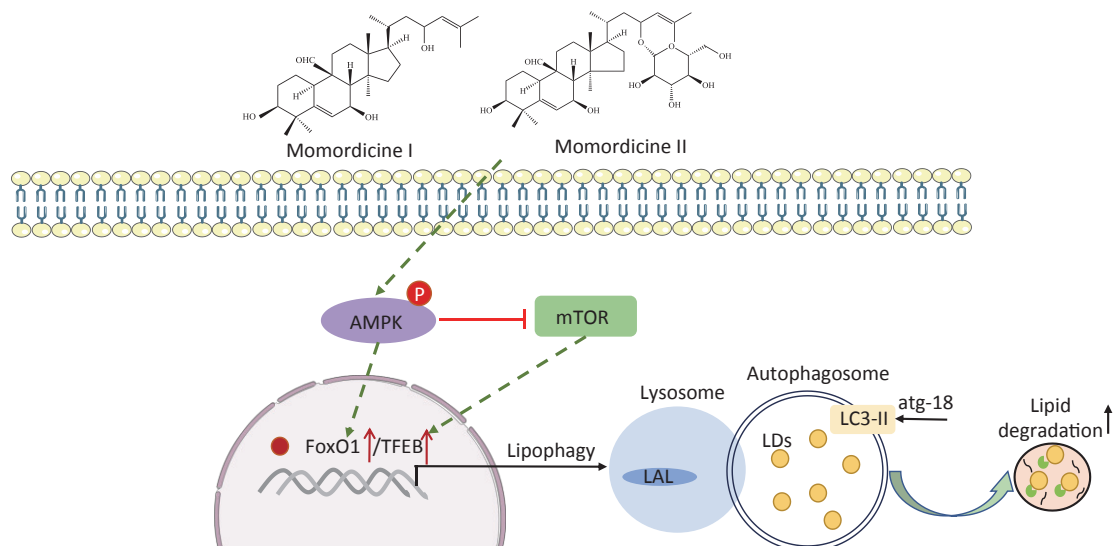
Supplementary Figure S1. Network pharmacology was applied to screen the active saponins of bitter melon saponin extract (BMSE). (A) Venn diagram showing intersection of active saponins with obesity targets. (B) Diagram of bitter melon-active saponin-targets. (C) Diagram of protein-protein interaction (PPI) network of saponins for the treatment of obesity targets. MC, *Momordica Charania*.



Supplementary Figure S2. Effects of bitter melon saponin extract (BMSE) on worm size and locomotive activity. (A) Body length and (B) body width were analyzed using Image J software ($n > 30$ per group). (C) Head swing frequency and (D) body bending frequency were counted under a microscope for 1 min ($n > 30$ worms per group). Results are showed as mean $\pm$ SEM. Values with different superscripts are significantly different ($P < 0.05$).



Supplementary Figure S3. Effect of bitter melon saponin extract (BMSE) on autophagosome formation in obese nematodes. (A) and (B) Worms were treated from L1 to L4 stage for 48 h followed by Monodansylcadaverine (MDC) fluorescent staining. The relative fluorescence intensities were quantitatively analyzed by Image J for over 20 worms. Results are showed as mean $\pm$ SEM. Values with different superscripts being significantly different ($P < 0.05$).



Supplementary Figure S4. The diagram of the lipid-lowering mechanism of bitter melon saponin extract (BMSE) and its potential active compounds.