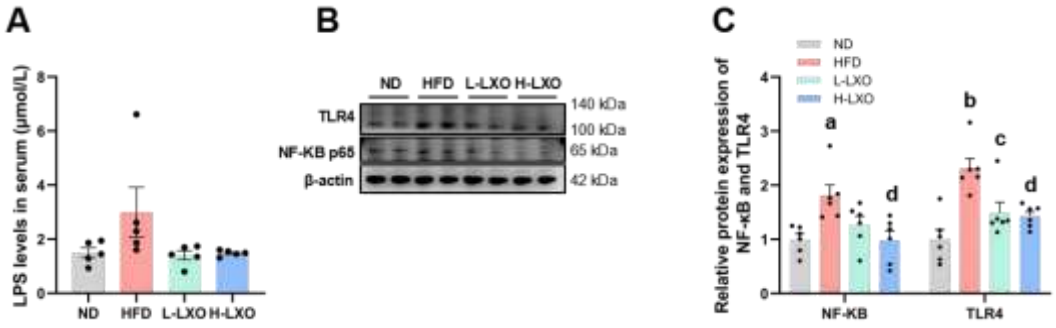
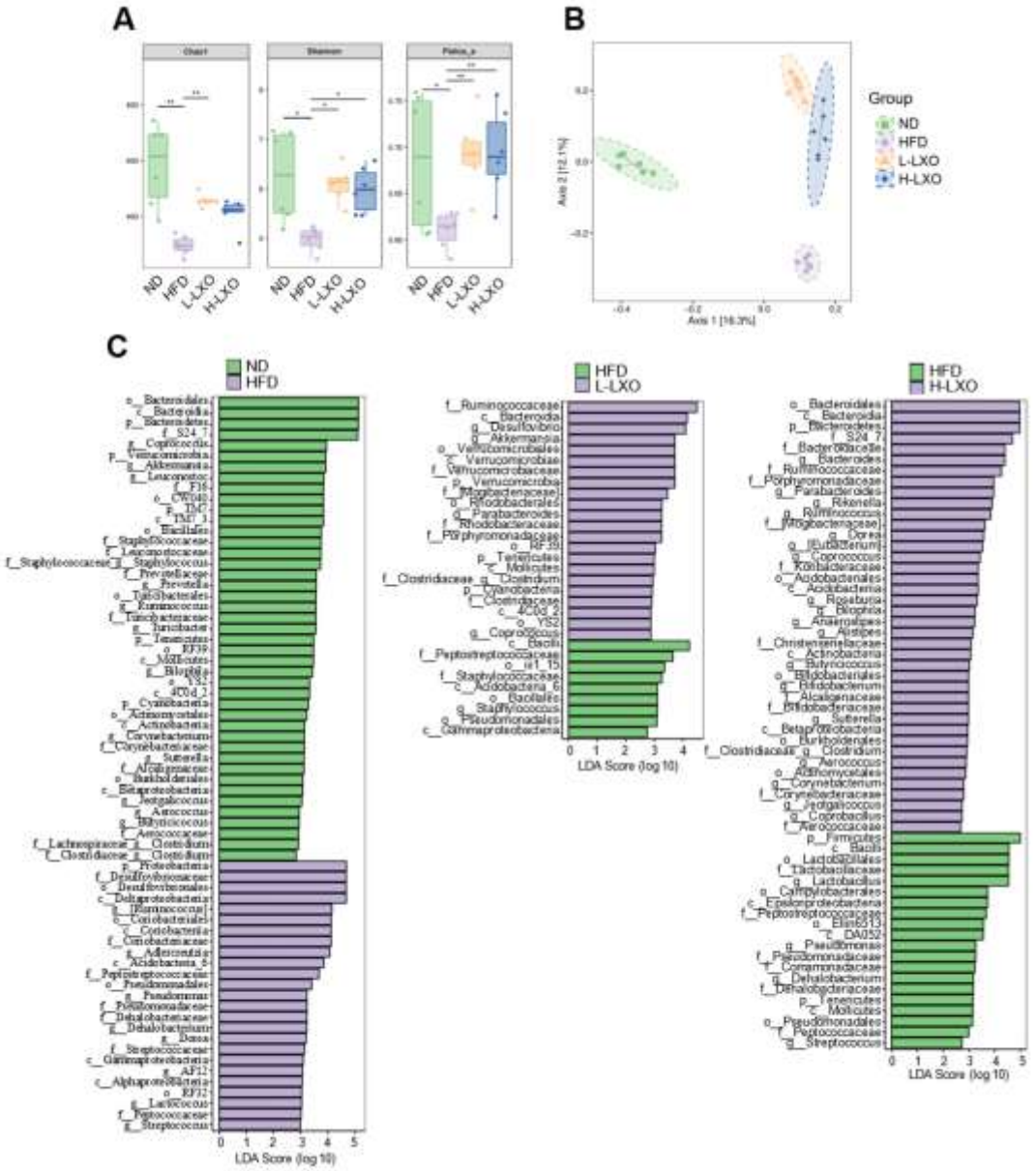


Supplementary Figure 1 LXO ameliorated hepatic inflammation in MASLD mice. A: Effect of LXO on LPS concentrations in mouse serum (n = 5). B-C: Representative western blot images (B) and quantitative analysis (C) of NF-κB and TLR4 in liver tissue (n = 6). One-way ANOVA was employed, and the data are presented as mean ± SEM. $^{a}P < 0.05$ vs ND group, $^{b}P < 0.01$ vs ND group, $^{c}P < 0.05$ vs HFD group, $^{d}P < 0.01$ vs HFD group. HFD: High-fat diet; H-LXO: High-dose Lianhe Xiaozhi Ointment; L-LXO: Low-dose Lianhe Xiaozhi Ointment; LPS: Lipopolysaccharide; ND: Normal diet; TLR4: Toll-like receptor 4.



Supplementary Figure 2 Differential microbiota in mouse cecal contents. A: α-Diversity indices of cecal microbiota (n = 6). B: β-Diversity analysis of cecal microbiota (n = 6). C: Differential microbiota at different levels in mouse cecal contents among groups (n = 6). HFD: High-fat diet; H-LXO: High-dose Lianhe Xiaozhi Ointment; L-LXO: Low-dose Lianhe Xiaozhi Ointment; LPS: Lipopolysaccharide; ND: Normal diet.

Supplementary Table 1 List of antibodies

Antibody	Species	Source	Catalog	Application/ dilution
TLR4	Rabbit	CST	14358S	WB (1:1000)
PPARα	Rabbit	Abcam	ab314112	WB (1:1000)
HMGCS2	Rabbit	CST	20940S	WB (1:1000)
NF-κB	Rabbit	CST	8242S	WB (1:1000)
iNOS	Rabbit	CST	13120	WB (1:1000)
COX-2	Rabbit	CST	12282	WB (1:1000)
IL-18	Rabbit	CST	57058S	WB (1:1000)
IL-1β	Rabbit	CST	31202S	WB (1:1000)
GAPDH	Rabbit	Servicebio	GB11002-100	WB (1:5000)
β-actin	Rabbit	Proteintech	81115-1-RR	WB (1:2000)
CPT1A	Mouse	Abcam	ab128568	WB (1:1000)
Acox1	Rabbit	Proteintech	10957-1-AP	WB (1:3000)
anti-Rabbit IgG (H+L)-HRP	Goat	Beyotime	A0208	WB (1:2000)
anti-Mouse IgG (H+L)-HRP	Goat	Beyotime	A0216	WB (1:2000)

Supplementary Table 2 Mobile phase gradient of UPLC-Q/TOF-MS analysis

Time (min)	0.1% formic acid-water (%)	Acetonitrile (%)
0～3	97	3
3～8	97～88	3～12
8～20	88～80	12～20
20～30	80～70	20～30
30～37	70～50	30～50
37～42	50～10	50～90

42～45	10	90
45～45.1	10～97	90～3
45.1～48	97	3

Supplementary Table 3 Mass spectrometry parameters of UPLC-Q/TOF-MS analysis

MS parameters	**Parameter value**	**MS/MS parameters**	**Parameter value**
TOF mass range	50～1700	MS/MS mass range	50～1250
Ion Source Gas 1（psi）	50	Declustering Potential（V）	100
Ion Source Gas 2（psi）	50	Collision Energy（eV）	± 40
Curtain Gas（psi）	35	Collision Energy Spread（eV）	20
Ion Spray Voltage Floating (V)	-4500/5000	Ion Release Delay（ms）	30
Ion Source Temperature (°C)	500	Ion Release Width（ms）	15
Declustering Potential（V）	100		
Collision Energy（eV）	10		

Supplementary Table 4 Real-time PCR primer sequences

Gene	**Species**	**Forward Primer**	**Reverse Primer**
Fxr	Mouse	CGGCGGAGATTTTCAATAAG	GAAACTGAACATCGGGGTTAT

Acox1	Mouse	CGCCACCTT CAATCC AGAGT	TCTGCGATGCCAAATTCC CT
Cpt1	Mouse	ATGACGGCTATGGTGTTT CC	TGTCCATCATGGCTTGTCT C
Srebp1	Mouse	ATCCAAGGGCATCTGAG AACTC	ATCCAAGGGCAGTTCTTG TG
Actb	Mouse	TGTCCACCTTCCAGCAG ATGT	AGCTCAGTAACAGTCCGC CTAGA
Ppara	Mouse	AACATCGAGTGTCGAAT ATGTGG	CCGAATAGTTCGCCGAAA GAA
Pparγ	Mouse	GGAAGACCACTCGCATT CCTT	GTAATCAGCAACCATTGG GTCA
Pparδ	Mouse	TCCATCGTCAACAAAGA CGGG	ACTTGGGCTCAATGATGT CAC
Hmgcs 2	Mouse	AGAGAGCGATGCAGGA AACTT	AAGGATGCCCACATCTTT TGG
Fgf21	Mouse	GTGTCAAAGCCTCTAGG TTTCTT	GGTACACATTGTAACCGT CCTC

Supplementary Table 5 The components of LXO decoction

No.	**RT/min**	**Ion mode**	***m/z***	**ppm**	**Molecular formula**	**Molecular weight**	**Name**	**MS/MS**	**Belonging herbs**
1	1.87	[M-H$_2$O+H]$^+$	150.092	1.1	$C_9H_{13}NO_2$	167.09	Synephrine	150.0906;135.0667;107.0485;91.0535;77.0377	Tangerine Peel/ Immature Bitter Orang

2	2.54	[M+H]+	127.039	0.2	$C_6H_6O_3$	126.03	5-Hydroxymethyl-2-furaldehyde	127.0383;109.0277;81.0330;68.9968	/
3	3.17	[M+H]+	268.104	-2	$C_{10}H_{13}N_5O_4$	267.10	Adenosine	268.1032;136.0618;119.0353	All
4	3.83	[M+H]+	284.099	-1.2	$C_{10}H_{13}N_5O_5$	283.09	Guanosine	152.0561;135.0292;110.0344	All
5	9.51	[M+H]+	205.097	-0.3	$C_{11}H_{12}N_2O_2$	204.09	L-Tryptophan	188.0708;170.0598;146.0600;118.0647;91.0539	All
6	10.06	[M-H]-	313.057	0.3	$C_{13}H_{14}O_9$	314.06	D-Glucaric acid, monobenzoate	313.0531;191.0194;147.0300;129.0189;121.0289	Tangerine Peel/ Immature Bitter Orang
7	10.25	[M+H]+	272.128	-0.8	$C_{16}H_{17}NO_3$	271.12	Norcoclaurine	272.1272;255.1015;237.0898;161.0593;107.0487	Lotus Leaf
8	10.99	[M-H]-	385.079	2.2	$C_{16}H_{18}O_{11}$	386.08	Feruloylglucaric acid	385.0764;209.0294;191.0187;147.0289;129.0181	Tangerine Peel/ Immature Bitter Orang
9	11	[M	385	1.	$C_{16}H_1$	386.0	Feruloylgl	385.0801;20	Tangerine

	.45	-H]-	.079	2	$_8O_{11}$	8	ucaric acid	9.0306;191.0205;147.0307;129.0195	Peel/ Immature Bitter Orang
10	11.81	[M-H]-	289.072	2.2	$C_{15}H_{14}O_6$	290.08	Epicatechin	289.0714;245.0819;203.0717;151.0406	Lotus Leaf
11	12.53	[M+H]+	300.160	1.9	$C_{18}H_{21}NO_3$	299.15	N-Methylisococlaurine	300.1610;269.1177;237.0907;209.0967;107.0486	Lotus Leaf
12	12.75	[M-H]-	385.080	5.4	$C_{16}H_{18}O_{11}$	386.08	Feruloylglucaric acid	385.0763;209.0307;191.0203;147.0305;129.0200	Tangerine Peel/ Immature Bitter Orang
13	12.79	[M+H]+	286.144	0.8	$C_{17}H_{19}NO_3$	285.14	Coclaurine	286.1444;269.1172;237.0908;175.0754;107.0493	Lotus Leaf
14	13.11	[M+H]+	300.160	3.3	$C_{18}H_{21}NO_3$	299.15	N-Methylcoclaurine	300.1605;269.1180;237.0914;209.0965;107.0491	Lotus Leaf
15	14.11	M+	342.170	1.2	$C_{20}H_{24}NO_4^+$	342.17	Magnoflorine	342.1700;297.1122;282.0875;265.0858;237.0904	Coptidis Rhizoma

16	14.14	[M-H]-	289.072	1.5	$C_{15}H_{14}O_6$	290.08	Catechin	289.0743;245.0835;203.0712;151.0403;125.0243	Lotus Leaf
17	14.31	[M-H]-	593.152	0.7	$C_{27}H_{30}O_{15}$	594.16	Vicenin-2	593.1510;503.1187;473.1079;383.0766;353.0656	Liquorice Root/ Prepared Pinellia Tuber
18	15.11	[M+FA-H]-	787.233	3.5	$C_{33}H_{42}O_{19}$	742.23	Narirutin-4′-glucoside	741.2311;579.1747;433.1160;271.0609	Tangerine Peel/ Immature Bitter Orang
19	15.45	[M-H]-	367.105	3.9	$C_{17}H_{20}O_9$	368.11	5-O-Feruloylquinic acid	367.1026;191.0557;173.0451;134.0371;93.0344	Tangerine Peel/ Immature Bitter Orang
20	16.00	[M+H]+	314.176	1.7	$C_{19}H_{23}NO_3$	313.17	Armepavine	314.1737;283.1321;252.1129;189.0902;107.0491	Lotus Leaf
21	16.40	[M+H]+	300.159	-0.1	$C_{18}H_{21}NO_3$	299.15	N-Norarmepavine	300.1592;283.1329;268.1079;252.1142;237.0912	Lotus Leaf
22	16.4	[M-H	163.04	3.9	$C_9H_8O_3$	164.05	p-Coumaric acid	163.0400;119.0496;93.0	Bamboo Shavings

	3	]-	1					337;65.0385	
2	16	[M	627	3.	$C_{28}H_{3}$	582.2	(+)-Lyonir	581.2276;41	Bamboo
3	.6	+F	.23	3	$_{8}O_{13}$	3	esinol-9'-	9.1717;404.	Shavings
	7	A-	2				O-glucosi	1477;371.11	
		H]-					de	26;233.0807	
2	17	[M	595	2.	$C_{26}H_{2}$	596.1	Quercetin	595.1314;30	Lotus Leaf
4	.5	-H	.13	9	$_{8}O_{16}$	4	-3-O-samb	0.0271;271.	
	0	]-	2				ubioside	0234;255.02	
								87;178.9991	
2	17	[M	427	0.	$C_{20}H_{2}$	428.1	Citrauran	427.1640;26	Tangerine
5	.6	-H	.16	8	$_{8}O_{10}$	7	oside	5.1081;247.	Peel/
	6	]-	1					0965;221.11	Immature
								77;163.0760	Bitter
									Orang
2	17	[M	286	2.	$C_{17}H_{1}$	285.1	Isococlaur	286.1469;26	Lotus Leaf
6	.9	+H	.14	6	$_{9}NO_{3}$	4	ine	9.1187;237.	
	3	]+	5					0913;209.09	
								73;107.0488	
2	18	[M	282	3.	$C_{18}H_{1}$	281.1	O-Demeth	282.1493;25	Lotus Leaf
7	.8	+H	.15	3	$_{9}NO_{2}$	4	yl	1.1071;236.	
	8	]+	0				nuciferine	0828;219.08	
								05;191.0846	
2	18	[M	435	3.	$C_{20}H_{2}$	390.1	Polydatin	389.1240;22	Polygonu
8	.9	+F	.13	1	$_{2}O_{8}$	3		7.0708;185.	m
	1	A-	1					0598;143.04	Cuspidatu
		H]-						95	m
2	19	[M	549	2.	$C_{26}H_{3}$	550.1	Liquiritin	549.1599;41	Liquorice
9	.1	-H	.16	6	$_{0}O_{13}$	7	apioside	7.1170;255.	Root/
	2	]-	3					0649;135.00	Prepared

								81;119.0495	Pinellia Tuber
30	19.17	[M-H]-	417.120	2.4	$C_{21}H_{20}O_9$	418.13	Liquiritin	417.1216;255.0681;135.0098;119.0510	Liquorice Root/ Prepared Pinellia Tuber
31	19.74	[M-H]-	595.170	5	$C_{27}H_{32}O_{15}$	596.17	Neoeriocitrin	595.1710;459.1168;287.0558;235.0246;151.0035	Tangerine Peel/ Immature Bitter Orang
32	19.86	[M-H]-	463.090	3	$C_{21}H_{20}O_{12}$	464.10	Hyperoside	463.0890;300.0263;271.0234;255.0284;178.9979	Lotus Leaf
33	20.20	[M-H]-	477.069	2.6	$C_{21}H_{18}O_{13}$	478.07	Quercetin-3-O-β-D-glucuronide	477.0699;301.0352;255.0288;178.9980;151.0035	Lotus Leaf
34	20.32	[M-H]-	463.089	0.9	$C_{21}H_{20}O_{12}$	464.10	Isoquercitrin	463.0878;300.0269;271.0238;255.0291;178.9981	Lotus Leaf
35	21.79	[M-H]-	579.173	1.3	$C_{27}H_{32}O_{14}$	580.18	Narirutin	579.1750;313.0719;295.0617;271.0623;151.0045	Tangerine Peel/ Immature Bitter Orang

36	23.04	[M+FA-H]-	625.180	4.6	$C_{27}H_{32}O_{14}$	580.18	Naringin	579.1724;459.1157;313.0714;271.0604;151.0033	Tangerine Peel/ Immature Bitter Orang
37	23.87	[M-H]-	609.185	3.8	$C_{28}H_{34}O_{15}$	610.19	Neohesperidin	609.1845;343.0797;325.0698;301.0707;286.0459	Tangerine Peel/ Immature Bitter Orang
38	24.18	M^+	338.1382	-1.4	$C_{20}H_{20}NO_4^+$	338.14	Jatrorrhizine	338.1402;322.1086;308.0917;294.1135;279.0895	Coptidis Rhizoma
39	24.37	M^+	336.123	2.3	$C_{20}H_{18}NO_4^+$	336.12	Epiberberine	336.1240;320.0917;308.0916;292.0964;279.0886	Coptidis Rhizoma
40	24.49	M^+	320.092	1.5	$C_{19}H_{14}NO_4^+$	320.09	Coptisine	320.0913;292.0963;277.0729;262.0860;249.0781	Coptidis Rhizoma
41	24.71	M^+	338.138	-1.1	$C_{20}H_{20}NO_4^+$	338.14	Columbamine	338.1379;322.1061;308.0900;294.1113;279.0881	Coptidis Rhizoma
42	24.88	[M-H]-	609.184	2.5	$C_{28}H_{34}O_{15}$	610.19	Hesperidin	609.1875;403.1063;343.0847;301.07	Tangerine Peel/ Immature

								32;286.0497	Bitter Orang
43	25.62	[M+H]+	296.165	2.7	$C_{19}H_{21}NO_2$	295.16	Nuciferine	296.1660;265.1233;250.0994;235.0765;219.0804	Lotus Leaf
44	25.83	[M-H]-	431.100	3.8	$C_{21}H_{20}O_{10}$	432.11	Emodin-8-glucoside	431.0985;269.0441;240.0416;225.0535	Polygonum Cuspidatum
45	26.12	[M-H]-	549.164	5	$C_{26}H_{30}O_{13}$	550.17	Isoliquiritin apioside	549.1654;255.0670;151.0406;135.0094;119.0504	Liquorice Root/ Prepared Pinellia Tuber
46	27.00	[M+H]+	353.150	1.5	$C_{20}H_{20}N_2O_4$	352.14	N-Feruloylserotonin	177.0544;145.0279	Bamboo Shavings
47	27.86	M+	352.156	5.6	$C_{21}H_{22}NO_4^+$	352.15	Palmatine	352.1553;336.1229;322.1072;308.1286;294.1119	Coptidis Rhizoma
48	28.09	M+	336.124	1.7	$C_{20}H_{18}NO_4^+$	336.12	Berberine	336.1228;320.0901;304.0959;292.0956;278.0795	Coptidis Rhizoma
49	29.71	[M-H]-	593.189	2.2	$C_{28}H_{34}O_{14}$	594.19	Neoponcirin	593.1897;327.0862;309.0756;285.07	Tangerine Peel/ Immature

								67;270.0528	Bitter Orang
50	30.17	[M-H]-	407.137	4.5	$C_{20}H_{24}O_9$	408.14	Torachrysone 8-O-glucoside	407.1358;245.0818;230.0576;215.0346	Polygonum Cuspidatum
51	30.60	[M-H]-	593.189	2.9	$C_{28}H_{34}O_{14}$	594.19	Poncirin	593.1874;473.1438;327.0847;309.0766;285.0755	Tangerine Peel/ Immature Bitter Orang
52	30.85	[M-H]-	431.100	3.3	$C_{21}H_{20}O_{10}$	432.11	Aloe-emodin-8-O-β-D-glucopyranoside	431.0961;311.0533;293.0419;269.0436;240.0406	Polygonum Cuspidatum
53	31.69	[M+FA-H]-	765.373	3.8	$C_{38}H_{56}O_{13}$	720.37	Arvenin I	765.3750;719.3696;661.3632;575.2899;413.2352	Pericarpium Trichosanthis
54	33.21	[M-H]-	271.062	2.6	$C_{15}H_{12}O_5$	272.07	Narigenin	271.0606;177.0197;151.0038;119.0513;107.0153	Tangerine Peel/ Immature Bitter Orang
55	33.71	[M-H]-	723.216	2.2	$C_{33}H_{40}O_{18}$	724.22	Natsudaidain-3-O-[3-hydroxy-3-methylglutarate(1	723.2165;417.1209;402.0974;387.0744;359.0790	Tangerine Peel/ Immature Bitter Orang

							→6)]-β-glucoside		
56	34.46	[M-H]-	301.073	4.8	$C_{16}H_{14}O_6$	302.08	Hesperetin	301.0743;286.0506;242.0593;164.0127;151.0045	Tangerine Peel/ Immature Bitter Orang
57	34.75	[M-H]-	837.394	3.2	$C_{42}H_{62}O_{17}$	838.40	Licorice saponin G2	837.3933;351.0564;193.0357	Liquorice Root/ Prepared Pinellia Tuber
58	35.62	[M+FA-H]-	603.319	1.7	$C_{32}H_{46}O_8$	558.32	Cucurbitacin B	603.3141;557.3117;539.3012;497.2893;165.0924	Pericarpium Trichosanthis
59	36.03	[M-H]-	837.393	1.9	$C_{42}H_{62}O_{17}$	838.40	Uralsaponin U	837.3893;351.0582;193.0349	Liquorice Root/ Prepared Pinellia Tuber
60	36.80	[M+H]+	839.412	6.6	$C_{42}H_{62}O_{17}$	838.40	Uralsaponin N	839.4078;663.3739;645.3636;487.3416;469.3311	Liquorice Root/ Prepared Pinellia Tuber
61	37.03	[M-H]-	821.397	0.2	$C_{42}H_{62}O_{16}$	822.40	Glycyrrhizic acid	821.3948;351.0548;193.0346	Liquorice Root/ Prepared

									Pinellia Tuber
62	37.90	[M+FA-H]-	515.193	1.6	$C_{26}H_{30}O_8$	470.19	Limonin	515.1917;469.1876;321.1130;278.1301;229.1235	Tangerine Peel/ Immature Bitter Orang
63	37.95	[M-H]-	821.398	1.6	$C_{42}H_{62}O_{16}$	822.40	Uralsaponin B	821.3980;351.0558;193.0348	Liquorice Root/ Prepared Pinellia Tuber
64	38.89	[M+H]+	403.141	6.6	$C_{21}H_{22}O_8$	402.13	Nobiletin	403.1408;388.1168;373.0935;358.0691;327.0862	Tangerine Peel/ Immature Bitter Orang
65	39.80	[M+H]+	433.152	5.1	$C_{22}H_{24}O_9$	432.14	3',4',3,5,6,7,8-Heptamethoxyflavone	433.1516;418.1270;403.1045;385.0937;373.0570	Tangerine Peel/ Immature Bitter Orang
66	40.27	[M+H]+	373.130	5.7	$C_{20}H_{20}O_7$	372.12	Tangeretin	373.1300;358.1061;343.0830;328.0597;297.0777	Tangerine Peel/ Immature Bitter Orang
67	41.2	[M+H	389.12	1	$C_{20}H_{20}O_8$	388.12	5-O-Demethylnobile	389.1229;374.0986;359.	Tangerine Peel/

	4	]+	4				tin	0766;341.0661;197.0078	Immature Bitter Orang
68	41.34	[M-H]-	269.047	6.1	$C_{15}H_{10}O_5$	270.05	Emodin	269.0473;241.0514;225.0567;210.0336;197.0616	Polygonum Cuspidatum
69	44.07	[M-H]-	469.333	0.4	$C_{30}H_{46}O_4$	470.34	16α-Hydroxydehydrotrametenolic acid	469.3315;425.3364	Poria Cocos

LXO: Lianhe Xiaozhi Ointment; MS: Mass spectrometry; RT: Retention time.

Supplementary Table 6 Displays of the active components screened from the LXO decoction according to the conditions that the oral bioavailability (OB) is no less than 30% and the drug-likeness (DL) is no less than 0.18

Components	**OB (%)**	**DL**
Coclaurine	79.64	0.24
Hesperetin	70.31	0.27
Armepavine	69.31	0.29
Palmatine	64.6	0.65
Arvenin I	63.76	0.38
Nobiletin	61.67	0.52
Catechin	54.83	0.24
Epicatechin	48.96	0.24
Epiberberine	43.09	0.78
Berberine	36.86	0.78
Poncirin	36.55	0.74
Nuciferine	34.43	0.4

Coptisine	30.67	0.86
Quercetin-3-O-β-D-glucuronide	30.66	0.74

DL: Drug-likeness; LXO: Lianhe Xiaozhi Ointment; OB: Oral bioavailability.

Supplementary Table 7 Targeting effects of LXO in the treatment of MASLD

Data bank	**Targets**
DisGeNet, GeneCards	TNF, APP, TERT, PPARG, ALB, RET, YARS1, SERPINA1, ACADM, PPARA, CBS, STAT3, EGFR, F2, AKT1, INSR, NR1H4, TTR, MET, AR, PTGS2, NOS3, VDR, FABP4, ERBB2, HRAS, OTC, PTPN11, PTK2, SERPINE1, IGF1, ARSA, REN, KIT, MMP9, SCD, ARG1, RBP4, HMGCR, FGFR1, GCK, CCND1, CTSD, NR1H3, MME, MTOR, NTRK1, NR1H2, ABCB1, RAF1, XIAP, MAP2K1, TYMP, ESR1, SRC, STAT1, JAK2, PKLR, FGFR2, TGFBR2, ALDH2, IGF1R, CYP2D6, CYP1A2, MMP1, IKBKB, BCL2, TH, XBP1, PAH, PIK3R1, AKT2, FABP6, CYP2C9, CSF1R, DNMT1, MMP2, NOS2, PMS2, SOD2, TGFBR1, ELANE, GSTP1, NR3C1, MAPK8, PDGFRB, PLAU, GSTM1, CYP1A1, TGFB2, JUN, BCHE, KDR, PCK1, RXRA, CASP3, ERBB4, MAPK1, PIK3CG, CYP1B1, SLC6A3, PLG, MIF, XDH, F3, ACHE, PRKCD, NR1I2, ADH1C, MMP3, MAOA, GSK3B, CCL5, PRKACA, JAK1, ADH1B, BMP2, CDC42, GALK1, MDM2, LCN2, RHOA, SIGMAR1, FLT4, CTSB, MAPK14, CDK4, EPHX2, ADRB2, GPI, BMP7, AHCY, CHIT1, PLA2G2A, PARP1, SHBG, LGALS3, APOA2, DPP4, GSR, RAC1, HSP90AA1, CASP1, EPHB4, HSD11B1, NAMPT, CTNNA1, SLC6A4, ABCG2, TEK, TYMS, CDK6, HDAC1, NQO1, RPS6KA3, BACE1, S100A9, ABCC1, HSPA1A, BCL2L1, ADK, RARA, MAOB, ADRB3, AURKA, FDFT1, ANXA5, BHMT, HSPA8, PGR,

	MMP7, DRD2, CDK2, HDAC8, KDM1A, PRKCA, RARB, CDK1, ALOX12, THRB, SLC1A3, IDO1, CES2, SULT2A1, CFD, MMP12, CHEK1, HTR2A, PTPN1, ADH5, CCNA2, CCNE1, FHIT, HSP90AB1, HTR1A, TSPO, NOX4, EPHA2, PLK1, CTSS, PDE3B, KAT2B, CCNB1, DRD4, PRKCB, ROCK1, ABO, AURKB, BIRC2, FDPS, NR4A1, MTAP, TREM1, OPRM1, HNMT, CRABP2, ARHGAP1, PIM2, ARG2, REG1A, PRKCE, PDPK1, HTR3A, HRH2, PFKFB3, GRM5, PRF1, B3GAT1, GSTA1

MASLD: Metabolic dysfunction-associated steatotic liver disease; LXO: Lianhe Xiaozhi Ointment.

Supplementary Table 8 Topological parameter analysis of components in "Ingredient-Disease- Pathway-Target" Network

Compound name	Degree	Betweenness Centrality	Closeness Centrality
Hesperetin	110	3299.7842	0.48975793
Palmatine	107	3240.4087	0.4843462
Armepavine	103	2778.245	0.47731397
Arvenin I	96	2516.7334	0.46714032
Catechin	89	1440.4431	0.45423144
Epicatechin	89	1440.4431	0.45423144
Coclaurine	88	1898.6525	0.4526678
Quercetin-3-O-β-D-glucuronide	88	2013.6536	0.4526678
Poncirin	87	1770.545	0.45111492
Nuciferine	87	2143.1816	0.45111492
Berberine	73	887.5814	0.4304419
Coptisine	71	956.9334	0.4276423
Epiberberine	66	666.24347	0.4208
Nobiletin	61	810.4726	0.41417322

Mean value	86.79	1847.380076	0.451974583

Supplementary Table 9 The relative abundance (%) of different microbiota at the phylum level in the cecal contents

Variables	ND	HFD	L-LXO	H-LXO
Firmicutes	54.35±3.24	73.18±5.42[a]	64.40±3.19	51.43±4.67[c]
Bacteroidetes	35.03±2.82	7.50±1.98[b]	13.16±2.56	26.31±3.63[c]
Proteobacteria	2.70±0.40	12.48±4.15	12.77±2.55	15.99±2.59
Actinobacteria	3.76±0.72	6.06±0.64	6.35±1.39	5.24±1.01
Verrucomicrobia	1.74±0.57	0.24±0.11	1.39±0.56	0.55±0.26
TM7	1.55±0.31	0.17±0.05[b]	0.67±0.27	0.06±0.05
Deferribacteres	0.19±0.14	0.34±0.06	1.04±0.39	0.39±0.10
Tenericutes	0.61±0.23	0.016±0.070	0.17±0.05	0.0003±0.0003
Acidobacteria	0.023±0.007	0.013±0.003	0.0053±0.0012	0.0040±0.0018
Cyanobacteria	0.012±0.004	0.0007±0.00066	0.016±0.006	0.0020±0.0014
Gemmatimonadetes	0.0026±0.002	0.000±0.000	0.000±0.000	0.0010±0.0010
Chloroflexi	0.000±0.000	0.0003±0.0003	0.0030±0.0030	0.000±0.000
Fusobacteria	0.0007±0.00066	0.0007±0.00066	0.0013±0.0008	0.000±0.000
Nitrospirae	0.000±0.000	0.000±0.000	0.0013±0.0013	0.0013±0.0013
Planctomycetes	0.0007±0.00066	0.001±0.0007	0.0003±0.0003	0.000±0.000
WPS2	0.0003±0.000	0.0007±0.000	0.000±0.000	0.0007±0.00

	3	66		066
Synergistetes	0.0007±0.000	0.0003±0.000	0.000±0.000	0.000±0.000
	66	3		
Armatimonadetes	0.0003±0.000	0.000±0.000	0.000±0.000	0.000±0.000
	3			

One-way ANOVA was employed, and the data are presented as mean ± SEM (n = 6). [a]$P < 0.05$ vs ND group, [b]$P < 0.001$ vs ND group, [c]$P < 0.01$ vs HFD group. HFD: High-fat diet; H-LXO: High-dose Lianhe Xiaozhi Ointment; L-LXO: Low-dose Lianhe Xiaozhi Ointment; ND: Normal diet.

Supplementary Table 10 The relative abundance (%) of different microbiota at the genus level in the cecal contents

Variables	**ND**	**HFD**	**L-LXO**	**H-LXO**
Allobaculum	9.53 ± 4.11	25.40 ± 6.86	10.06 ± 5.35	14.12 ± 3.26
Lactobacillus	18.17 ± 7.99	7.19 ± 1.80	3.96 ± 1.92	0.62 ± 0.23
Adlercreutzia	2.97 ± 0.75	5.16 ± 0.73	5.55 ± 1.18	4.47 ± 0.83
Oscillospira	3.68 ± 1.38	2.72 ± 0.55	4.71 ± 0.81	2.90 ± 0.55
[Ruminococcus]	0.43 ± 0.10	3.52 ± 0.95[b]	3.67 ± 0.65	3.13 ± 0.58
Bacteroides	0.92 ± 0.21	0.42 ± 0.18	1.19 ± 0.23	5.36 ± 1.71[d]
Desulfovibrio	0.98 ± 0.23	0.82 ± 0.32	3.15 ± 0.51[d]	1.56 ± 0.33
Rikenella	0.83 ± 0.29	0.48 ± 0.12	1.01 ± 0.31	2.19 ± 0.47[d]
Akkermansia	1.73 ± 0.57	0.23 ± 0.11	1.39 ± 0.56	0.55 ± 0.26
Ruminococcus	0.95 ± 0.31	0.22 ± 0.07[a]	0.67 ± 0.18	1.54 ± 0.31[d]
Parabacteroides	0.21 ± 0.07	0.10 ± 0.03	0.46 ± 0.11	1.92 ± 0.77[d]
Coprococcus	1.61 ± 1.13	0.05 ± 0.02	0.18 ± 0.04	0.51 ± 0.16
Coprobacillus	0.00 ± 0.00	0.00 ± 0.00	2.20 ± 1.55	0.016 ± 0.008
Mucispirillum	0.19 ± 0.14	0.34 ± 0.06	1.04 ± 0.39[c]	0.39 ± 0.10
Dorea	0.033 ± 0.008	0.30 ± 0.10	0.56 ± 0.12	1.01 ± 0.19
Odoribacter	0.63 ± 0.21	0.39 ± 0.12	0.33 ± 0.11	0.35 ± 0.11

Dehalobacterium	0.14 ± 0.03	0.43 ± 0.06	0.30 ± 0.07	0.14 ± 0.03
Anaerotruncus	0.21 ± 0.06	0.29 ± 0.10	0.30 ± 0.13	0.17 ± 0.03
Clostridium	0.09 ± 0.04	0.003 ± 0.002	0.14 ± 0.04[c]	0.035 ± 0.006
Staphylococcus	0.0046 ± 0.0028	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00

Notes: One-way ANOVA was employed, and the data are presented as mean ± SEM (n = 6). [a]$P < 0.05$ vs ND group, [b]$P < 0.001$ vs ND group, [c]$P < 0.05$ vs HFD group, [d]$P < 0.01$ vs HFD group. HFD: High-fat diet; H-LXO: High-dose Lianhe Xiaozhi Ointment; L-LXO: Low-dose Lianhe Xiaozhi Ointment; ND: Normal diet.