

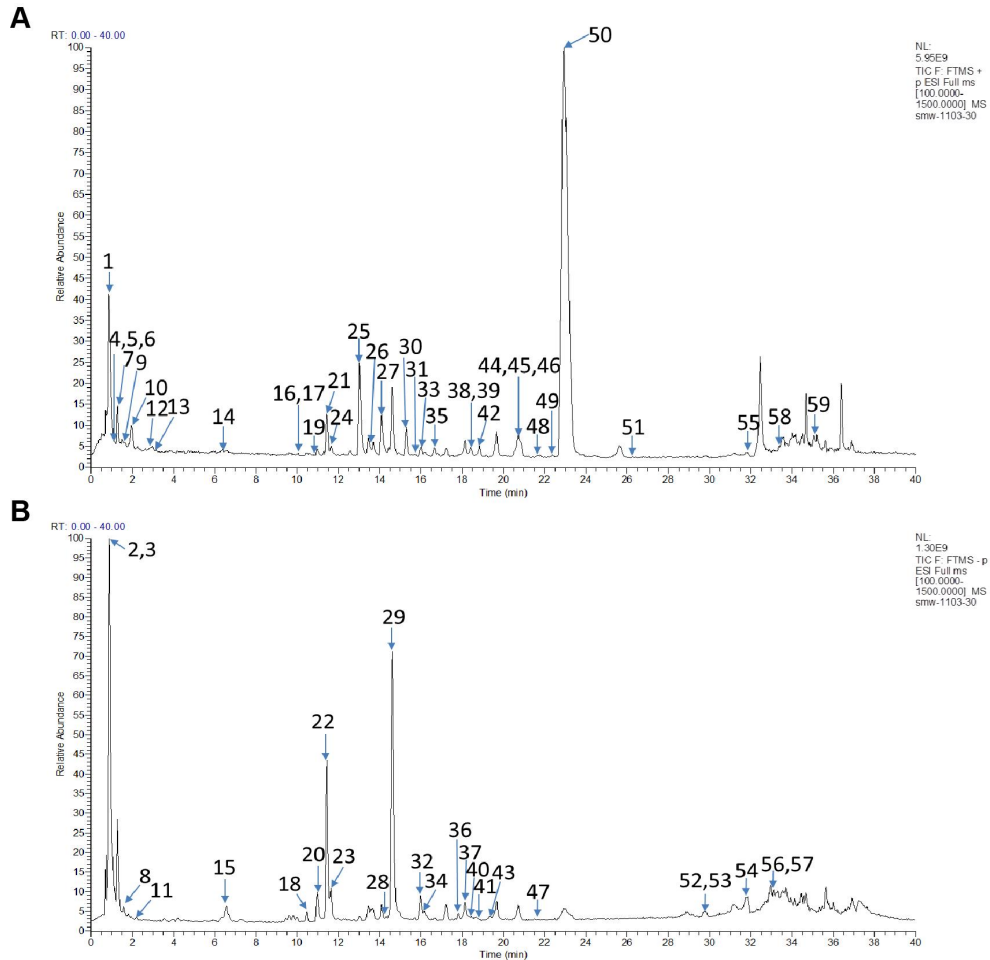


Fig.S1 UPLC-MS Chromatograms of SMD in positive (A) and negative (B) ion mode.

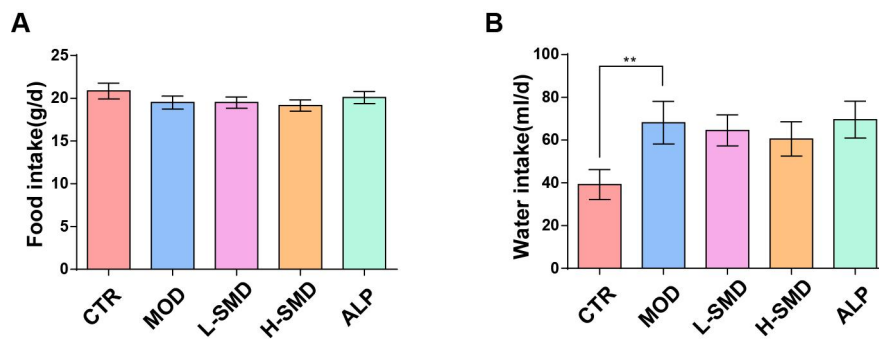
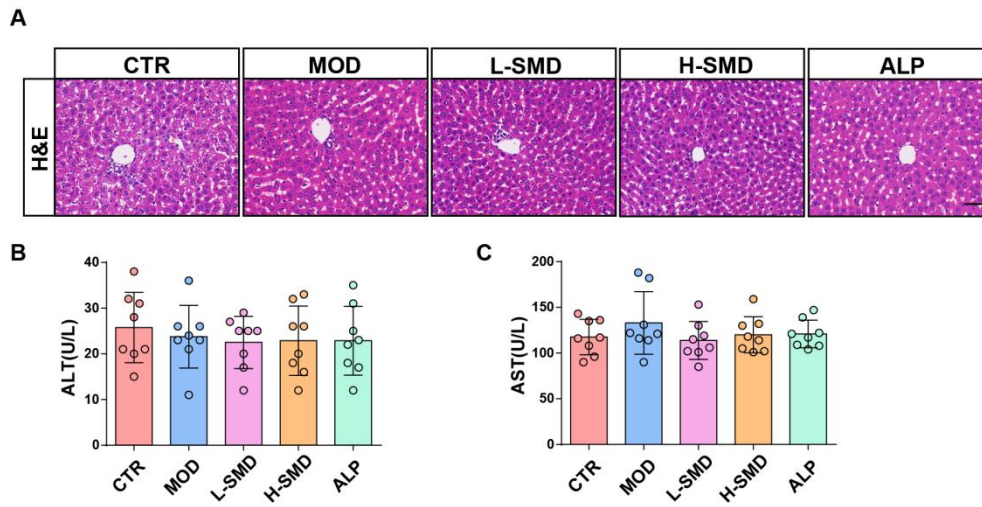


Fig.S2 Effects of SMD on food and water intake. **A** Food intake of different groups (n=5). **B** Food intake of different groups (n=5). Data are represented as mean $\pm$ SD. Statistical comparison was performed using One-way ANOVA followed by the post

9 hoc LSD tests. $**p<0.01$.

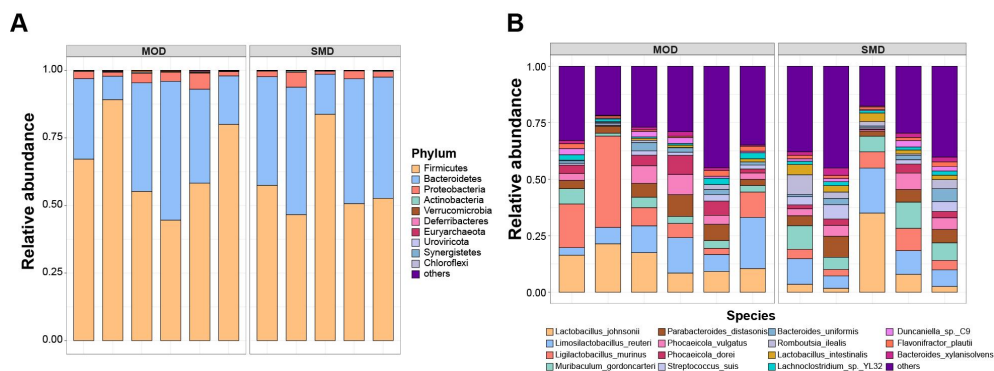
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12 **Fig.S3** Effects of SMD on liver function and histology. **A** Representative liver H&E
 13 staining of different groups. Scale bar, 100 μ m. **B** Serum ALT concentrations of
 14 different groups (n=8). **C** Serum AST concentrations of different groups (n=8). Data
 15 are represented as mean $\pm$ SD. Statistical comparison was performed using One-way
 16 ANOVA followed by the post hoc LSD tests.

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19 **Fig.S4** A Relative abundance profiles at the phylum (A) and species (B) level.

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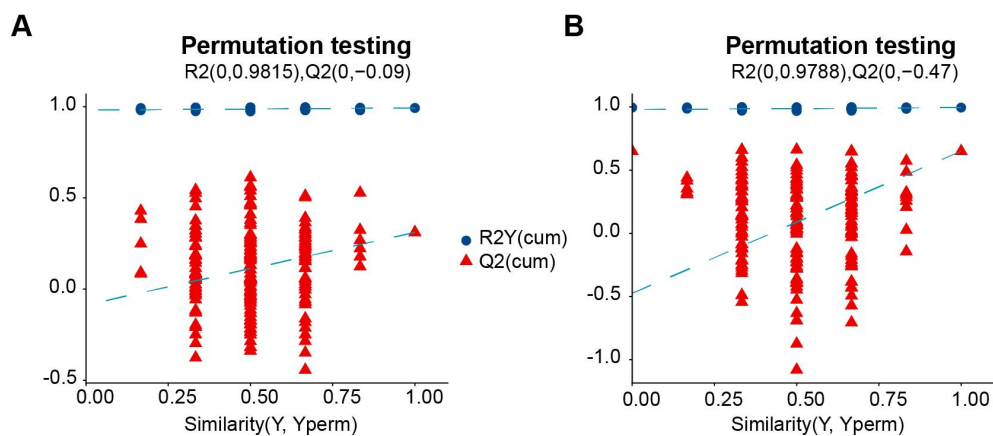


Fig.S5 Random permutation test with 200 permutations to evaluate the robustness of the OPLS-DA model in fecal (A) and kidney (B) metabolomic analysis.

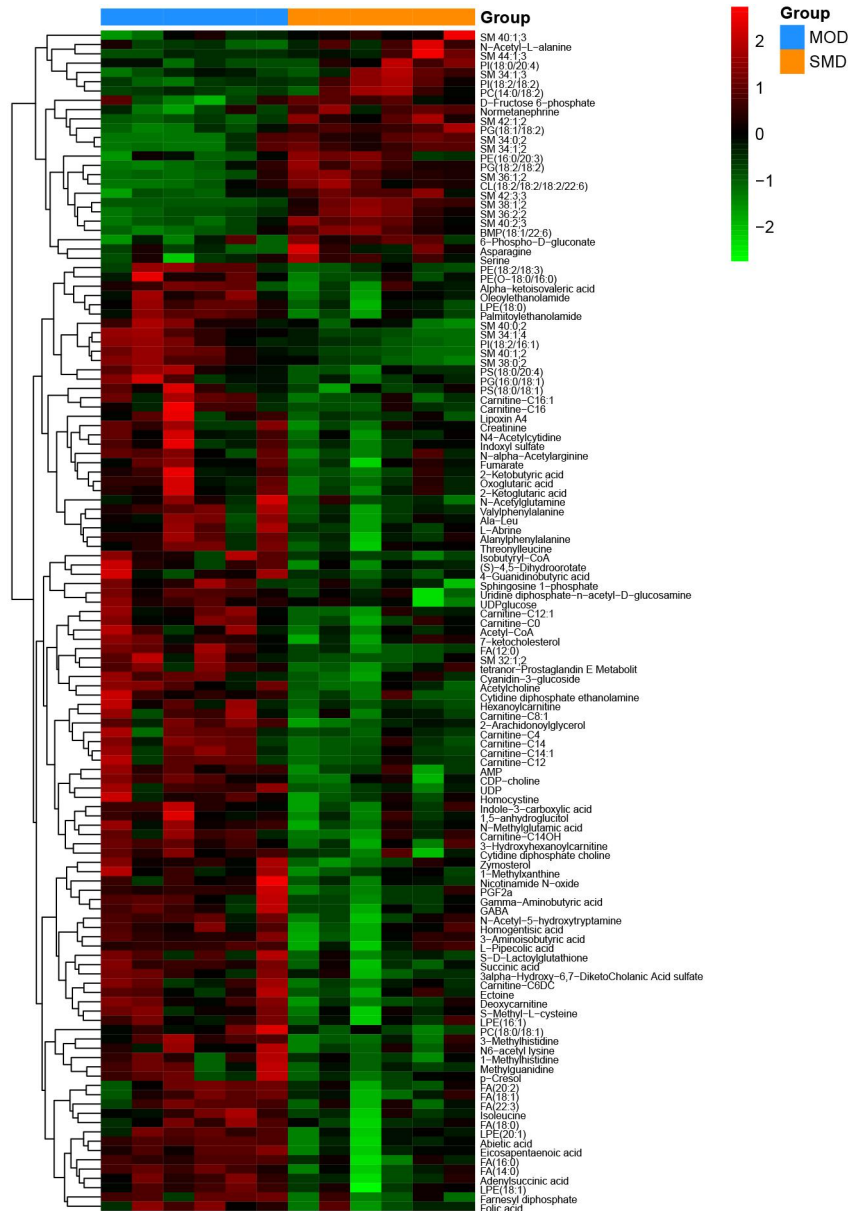


Fig.S6 Heatmap of differential metabolites in the kidneys of MOD and SMD groups

(n=6).

Table S1 Composition of SMD.

Chinese name	Botanical plant name	Part used	Weight(g)
Huangbai	Phellodendron amurense Rupr	barkl	10
Cangzhu	Atractylodes lancea (Thunb.) DC.	rhizome	5
Yiyiren	Coix lacryma-jobi L.	seed	10
Niuxi	Cyathula officinalis K.C.Kuan	root	5

Table S2 The chemical compounds identification of SMD.

Peak No.	Retention Time(min)	Addut	m/z	Formula	CAS No.	Compound
1	0.86	[M+H] +	118.08643	C5H11NO2	6600-40-4	L-Norvaline
2	0.90	[M-H]-	191.05522	C7H12O6	77-95-2	Quinic acid
3	0.90	[M-H]-	341.10861	C12H22O11	57-50-1	Sucrose
4	0.94	[M+H] +	136.0618	C5H5N5	73-24-5	Adenine
5	0.97	[M+H] +	196.13324	C11H17NO2	/	/
6	1.26	[M+H] +	152.05666	C5H5N5O	73-40-5	guanine
7	1.29	[M+H] +	196.13319	C11H17NO2	/	/
8	1.52	[M-H]-	191.01884	C6H8O7	77-92-9	Citric acid
9	1.53	[M+H] +	268.10391	C10H13N5O4	58-61-7	Adenosine
10	1.96	[M]+	180.13808	C11H17NO	552-79-4	(-)-N-Methylephedrine
11	2.18	[M-H]-	169.01347	C7H6O5	149-91-7	Gallic acid
12	2.84	[M+H] +	166.08617	C9H11NO2	63-91-2	L-Phenylalanine
13	3.17	[M+H] +	127.03902	C6H6O3	67-47-0	5-Hydroxymethylfurfural

14	6.36	[M+H] +	205.097	C11H12N2O2	73-22-3	L-Tryptophan
15	6.59	[M-H]-	353.08759	C16H18O9	906-33-2	Neochlorogenic acid
16	9.98	[M+H] +	233.15349	C15H20O2	/	/
17	10.06	[M+H] +	217.09715	C12H12N2O2	6052-68-2	2,3,4,9-Tetrahy dro-1H-beta-car boline-3-carbox ylic acid
18	10.45	[M-H]-	431.15576	C19H28O11	/	/
19	10.91	[M+H] +	330.16983	C19H23NO4	115-53-7	sinomenine
20	10.96	[M-H]-	353.08746	C16H18O9	327-97-9	Chlorogenic acid
21	11.42	[M+H] +	177.05437	C10H8O3	90-33-5	4-methylumbell iferone
22	11.44	[M-H]-	367.10297	C17H20O9	1899-29-2	3/4/5-O-Feruloy lquinic acid
23	11.64	[M-H]-	353.08737	C16H18O9	905-99-7	Cryptochloroge nic acid
24	11.66	[M]+	314.17462	C19H24NO3	6801-40-7	magnocurarine
25	13.01	[M]+	342.16934	C20H24NO4	6873-13-8	phellodendrine
26	13.52	[M+H] +	153.05455	C8H8O3	121-33-5	Vanillin
27	14.10	[M+H] +	342.16937	C20H24NO4	700342-15-0	Magnoflorine
28	14.25	[M-H]-	515.11957	C25H24O12	1182-34-9	Cynarin
29	14.62	[M-H]-	367.103	C17H20O9	1899-29-2	3/4/5-O-Feruloy lquinic acid
30	15.29	[M]+	314.17453	C19H24NO3	6871-67-6	Lotusine
31	15.81	[M+H] +	217.10712	C10H16O5	127393-89-9	Decarestrictine D

32	15.96	[M-H]-	385.11386	C17H22O10	57092-16-7	Densifloside
33	16.02	[M+H] +	356.18533	C21H25NO4	10097-84-4	Rotundine
34	16.20	[M-H]-	193.04988	C10H10O4	1135-24-6	Ferulic acid
35	16.64	[M]+	356.18524	C21H26NO4	25342-82-9	menisperine
36	17.83	[M+H COO]-	525.30707	C27H44O7	5289-74-7	Hydroxyecdysone
37	18.17	[M+H COO]-	525.30701	C27H44O7	19682-38-3	25R-Inokosterone
38	18.39	[M+H] +	356.18517	C21H25NO4	3520-14-7	D-Tetrahydropalmatine
39	18.42	[M]+	324.12262	C19H18NO4	25459-91-0	DeMethyleneberberine
40	18.44	[M+H COO]-	525.30682	C27H44O7	19595-18-7	25S-Inokosterone
41	18.82	[M-H]-	283.06134	C16H12O5	40957-83-3	Glycitein
42	18.84	[M+H] +	352.11765	C20H17NO5	19716-60-0	Oxyepiberberine
43	19.38	[M-H]-	187.09692	C9H16O4	123-99-9	Azelaic acid
44	20.53	[M]+	338.13824	C20H20NO4	3621-36-1	Columbamine
45	20.63	[M+H] +	322.10706	C19H15NO4	15401-69-1	Berberrubine
46	20.86	[M]+	338.13806	C20H20NO4	3621-38-3	Jatrorrhizine
47	21.61	[M-H]-	445.07785	C21H18O11	21967-41-9	Baicalin
48	21.81	[M]+	322.10712	C19H16NO4	18207-71-1	Thalifendine
49	22.37	[M+H] +	352.11768	C20H17NO5	\	\
50	22.92	[M+H] +	336.12228	C20H18NO4	2086-83-1	Berberine

51	26.32	[M+H] +	260.09174	C14H13NO4	83-95-4	skimmianine
52	29.67	[M-H]-	1117.50842	C53H82O25	168009-91-4	Achyranthoside D
53	29.77	[M-H]-	955.49127	C48H76O19	34367-04-9	GinsenosideRO
54	31.76	[M-H]-	793.43811	C42H66O14	51415-02-2	Chikusetsusapo nin IVa
55	31.84	[M+H] +	471.20084	C26H30O8	1180-71-8	Limonin
56	33.11	[M-H]-	955.45538	C47H72O20	168009-90-3	Achyranthoside C
57	33.11	[M-H]-	793.43866	C42H66O14	80930-74-1	Zingibroside R1
58	33.36	[M+H] +	455.20605	C26H30O7	751-03-1	Obacunon
59	35.07	[M+H] +	282.2789	C18H35NO	301-02-0	Oleamide

Fig. 3E

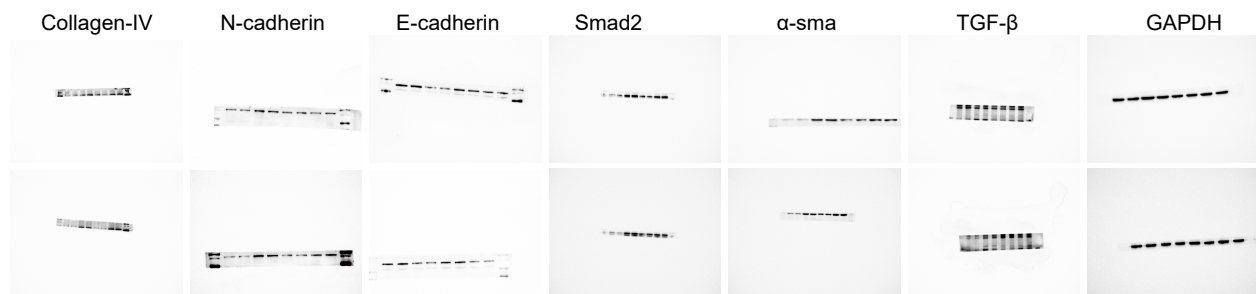


Fig. 4F

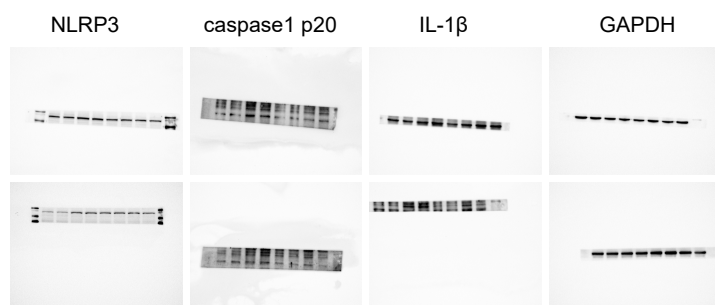


Fig. 4H

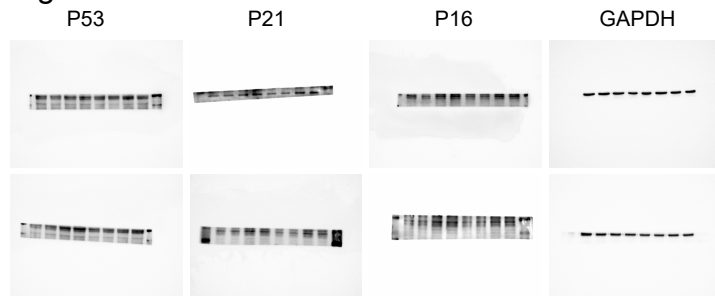


Fig. 5E

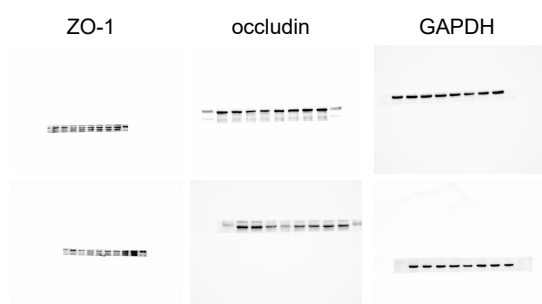


Fig. 10G

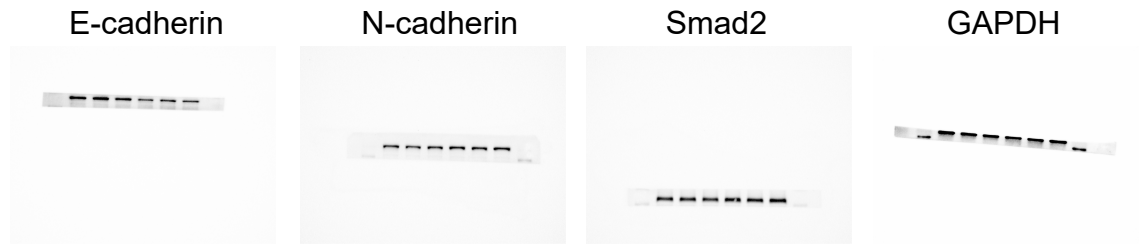


Fig. 11G

