

1 **Supplementary data**

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3 **Cholestatic liver injury model of bile duct ligation and the protection of Huang-**
4 **Lian-Jie-Du decoction by NMR metabolomic profiling**

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27 **Table S1** ¹H NMR assignment of metabolites in serum of NC, BDL and BHD rats

No.	Metabolite	Assignments	Chemical shift (ppm)
1	VLDL/LDL	CH ₃ (CH ₂) _n , CH ₃ CH ₂ CH ₂ C=	0.87-0.92(m)
2	Valine	γCH ₃ , γCH ₃ , βCH, αCH	0.99(d), 1.04(d), 2.28(m), 3.62(d)
3	3- Hydroxybutyrate	γCH ₃ , βCH, αCH ₂	1.20(d), 2.31(m), 2.41(m), 4.16(m)
4	Alanine	βCH ₃ , αCH	1.51(d), 3.78(q)
5	Lysine	γCH ₂ , δCH ₂ , βCH ₂ , N-CH ₂ , CH	1.48(m), 1.73(m), 1.91(m), 3.03(t), 3.76(t)
6	Acetate	CH ₃	1.91(s)
7	Adipate	CH ₂	1.56(m), 2.22(m)
8	NAGP	CH ₃	2.03(s)
9	Glutamate	βCH ₂ , γCH ₂	2.05-2.21(m), 2.40(t)
10	Citrate	1/2CH ₂ , 1/2CH ₂	2.54(dd), 2.67(dd)
11	Cysteine	CH ₂ , CH	3.06(m), 3.97(dd)
12	Creatine	CH ₂ , N-CH ₃	3.04(s), 3.93(s)
13	Tyrosine	=CH, CH	6.89(d), 7.20(t)
14	TMAO	CH ₃	3.27(s)
15	GPC	N-CH ₃	3.27(s)
16	Taurine	SO ₃ -CH ₂ , CH ₂ -NH ₂	3.25(t), 3.43(t)
17	β-glucose	CH	3.24(dd), 3.40(t), 3.49(t), 3.72(dd), 4.63(d)
18	α-glucose	CH	3.41(t), 3.53(dd), 3.71(t), 3.74(m), 5.22(d)
19	Glycine	CH ₂	3.57(s)
20	Glutamine	βCH ₂ , γCH ₂	2.13(m), 2.50(m)
21	Lactate	CH ₃ , CH	1.35(d), 4.15(q)
22	Phenylalanine	CH	7.33(m), 7.43(m)
23	Histidine	CH ₂ , CH, =CH	3.16(dd), 3.23(dd), 3.99(dd), 7.08(d), 7.83(d)
24	Formate	CH	8.46(s)

28 s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets.

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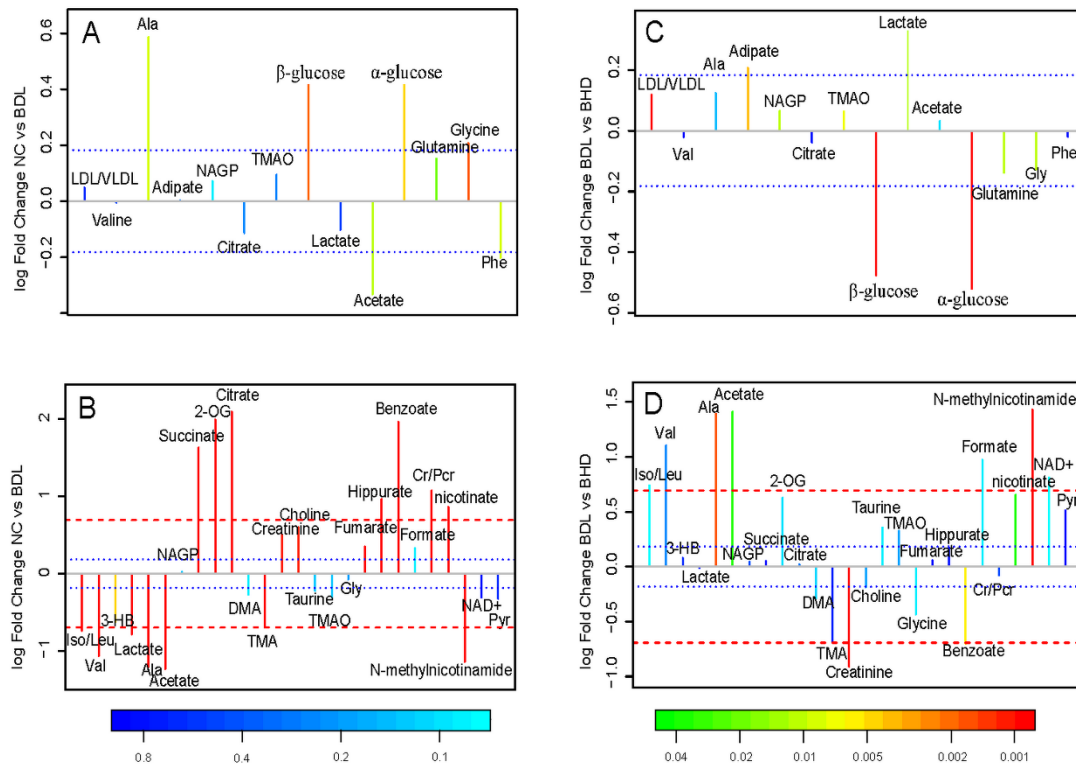
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49 **Table S2** ¹H NMR assignment of metabolites in urine of NC, BDL and BHD rats

No.	Metabolite	Assignments	Chemical shift (ppm)
1	VLDL/LDL	CH ₃ (CH ₂) _n , CH ₃ CH ₂ CH ₂ C=	1.28-1.33(m)
2	Isoleucine	δCH ₃ , βCH ₃ , γCH ₂	0.93(t), 1.02(d), 1.46(m)
3	Valine	γCH ₃ , γCH ₃ , βCH, αCH	0.97(d), 1.07(d), 2.26(m), 3.60(d)
4	3- Hydroxybutyrate	γCH ₃ , βCH, αCH ₂	1.19(d), 4.23(m), 2.31(dd), 2.38(dd)
5	2- Hydroxybutyrate	CH ₃ , CH ₂ , CH	0.90(t), 1.64(m), 1.74(m), 3.99(dd)
6	Lactate	CH ₃ , CH	1.35(d), 4.15(q)
7	Alanine	βCH ₃ , αCH	1.51(d), 3.78(q)
8	Ornithine	γCH ₃ , δCH ₃ , βCH ₂ , CH	1.73(m), 1.81(m), 1.95(m), 3.06(t), 3.79(t)
9	Acetate	CH ₃	1.91(s)
10	Proline	βCH ₃ , γCH ₂ , αCH ₂ , CH	2.01(m), 2.07(m), 2.35(m), 3.33(dt), 3.42(dt), 4.14(dd)
11	NAGP	CH ₃	2.03(s)
12	OAGP	OHCHCH ₃	2.12(s)
13	Methionine	CH ₃ , CH ₂ , S-CH ₂ , CH	2.16(m), 2.65(t), 3.86(dd)
14	Adipate	CH ₂	1.56(m), 2.22(m)
15	Acetoacetate	CH ₃ , CH ₂	2.27(s), 3.45(s)
16	Glutamate	βCH ₂ , γCH ₂	3.28(t), 3.42(t)
17	Oxalacetate	CH ₂	2.38(s)
18	Succinate	CH ₂	2.43(s)
19	Citrate	1/2CH ₂ , 1/2CH ₂	2.54(dd), 2.67(dd)
20	Dimethylamine	CH ₃	2.72(s)
21	Methylguanidine	CH ₃	2.83(s), 3.37(s)
22	Trimethylamine	CH ₃	2.88(s)
23	Dimethylglycine	CH ₃ , CH ₂	2.92(s), 3.71(s)
24	Pyruvate	βCH ₃	2.46(s)
25	2-Oxoglutarate	γCH ₂ , γCH ₂	2.45(t), 3.01(t)
26	Creatinine	CH ₃ , CH ₂	3.10(s), 4.05(s)
27	Choline	N(CH ₃) ₃ , N-CH ₂	3.20(s), 3.51(m)
28	Trimethylamine N-oxide	CH ₃	3.27(s)
29	Taurine	SO ₃ -CH ₂ , CH ₂ -NH ₂	3.25(t), 3.43(t)
30	Glycine	CH ₂	3.57(s)
31	Creatine/Phosphocreatine	CH ₂ , N-CH ₃	3.04(s), 3.93(s)
32	Fumarate	CH=CH	6.53(s)
33	3-Hydroxymandelate	CH, =CH	4.93(s), 6.87(ddd), 6.92(t), 6.98(d), 7.29(t)
34	4-Aminohippurate	CH ₂ , =CH	3.92(d), 8.85(d), 7.67(d)
35	Gallate	=CH	7.03(s)
36	Phenylalanine	CH	7.32(m), 7.40(m)
37	Tryptophan	CH	7.36(s)
38	Benzoate	=CH	7.47(dd), 7.54(t), 7.86(d)
39	Hippurate	CH	7.55(t), 7.63(t), 7.83(d)
40	Formate	CH	8.46(s)
41	Nicotinate	=CH	7.53(dd), 8.26(m), 8.62(dd), 8.95(d)
42	N-methylnicotinamide	CH ₃ , =CH	4.48(s), 8.16(d), 8.87(d), 8.93(d), 9.25(s)
43	NAD+	N ⁺ -CH=C, N ⁺ -CH=C, CH=CH	8.13(s), 8.43(s), 9.19(d), 9.33(s)

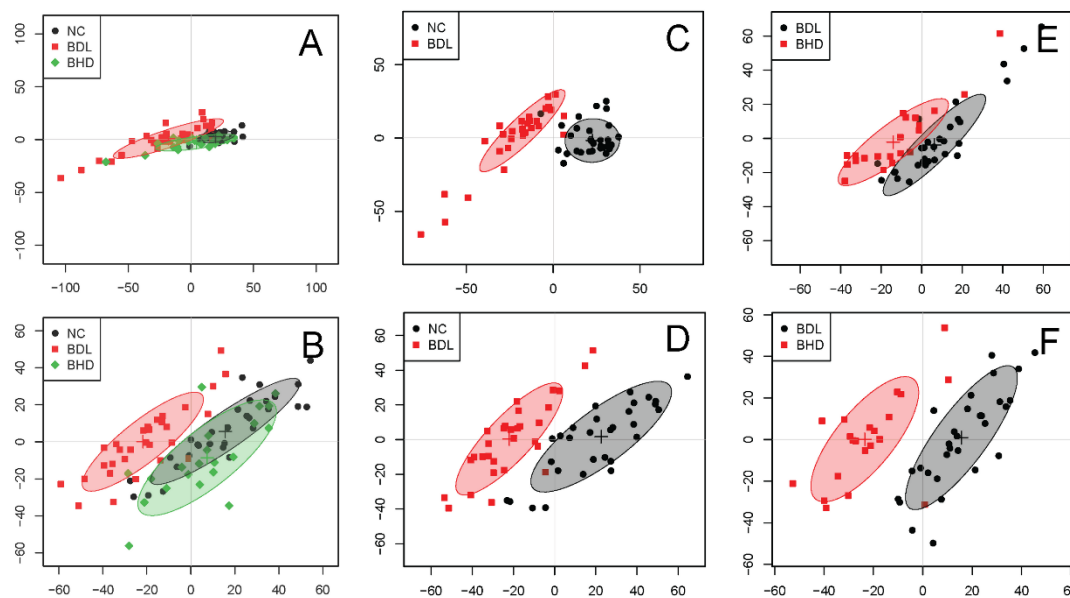
50 s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets.



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53 **Fig. S1** On week 1, color-coded fold change plots adjusted by Benjamini-Hochberg method
 54 indicating significance of altered metabolites in serum (A and C) and urine (B and D) of NC rats
 55 versus BDL rats (A and B) and BDL rats versus BHD rats (C and D). The blue dotted lines and red
 56 dashed lines representing an increase or decrease of 20% and 100%, respectively.

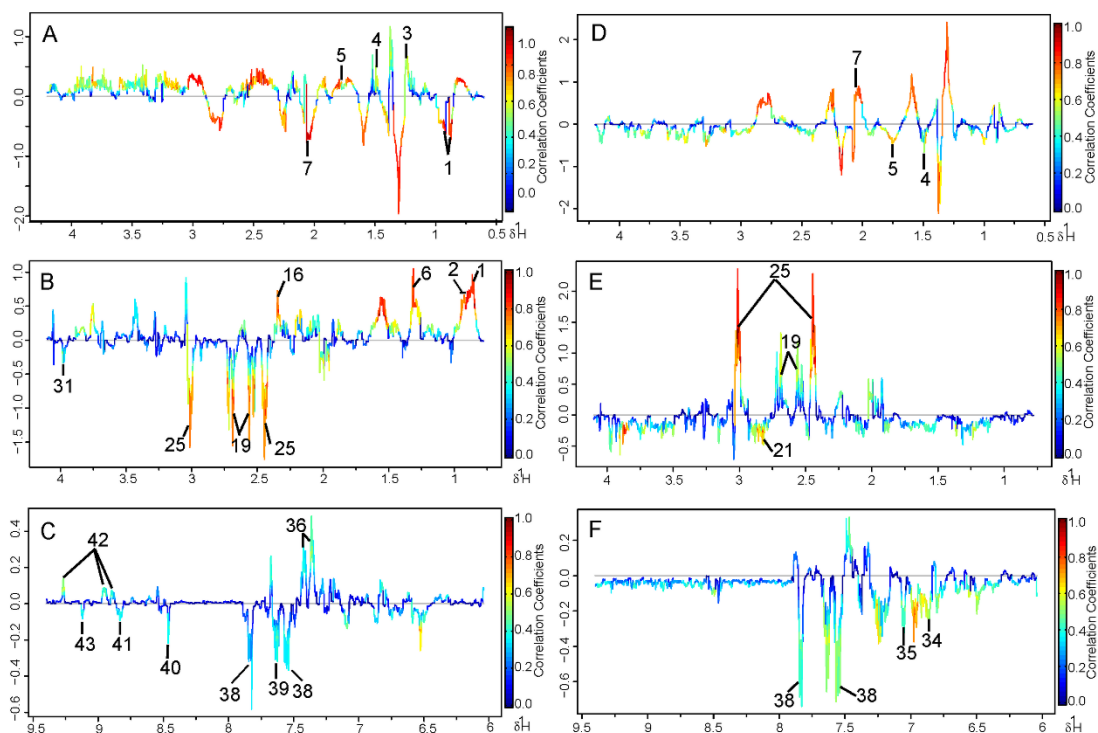
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59 **Fig. S2** On week 3, 5, 7, score plots from OPLS-DA analysis of NMR data from serum and urine
 60 of rats: NC, BDL and BHD group for serum (A) and urine (B); NC and BDL group for serum (C)
 61 and urine (D); BDL and BHD group for serum (E) and urine (F), respectively.

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 64 **Fig. S3** On week 3, 5, 7, loadings plots from OPLS-DA analysis of NMR data from serum and urine
 65 of rats: NC and BDL group for serum (A) and urine (B and C); BDL and BHD group for serum (D)
 66 and urine (E and F), respectively.