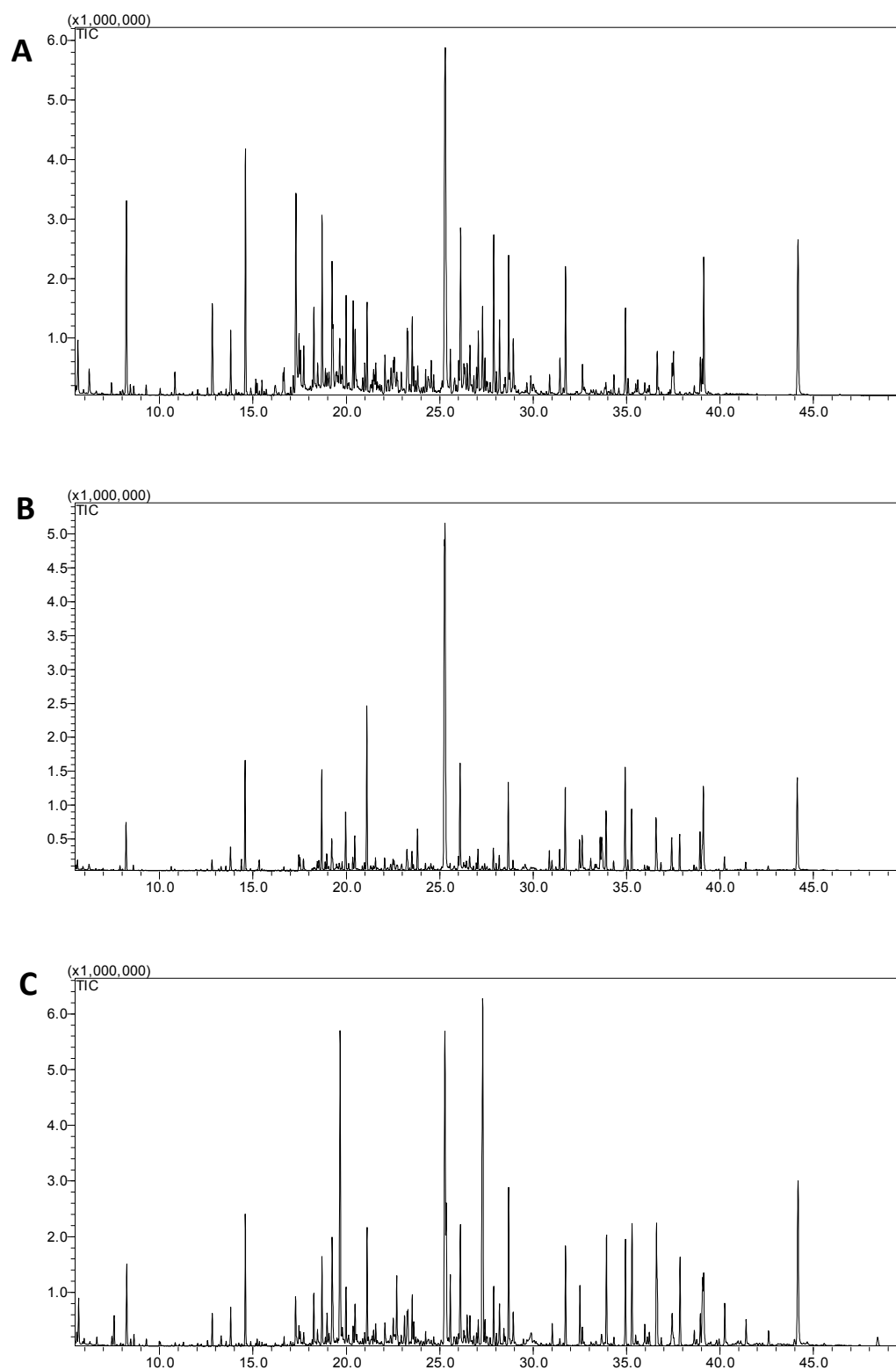
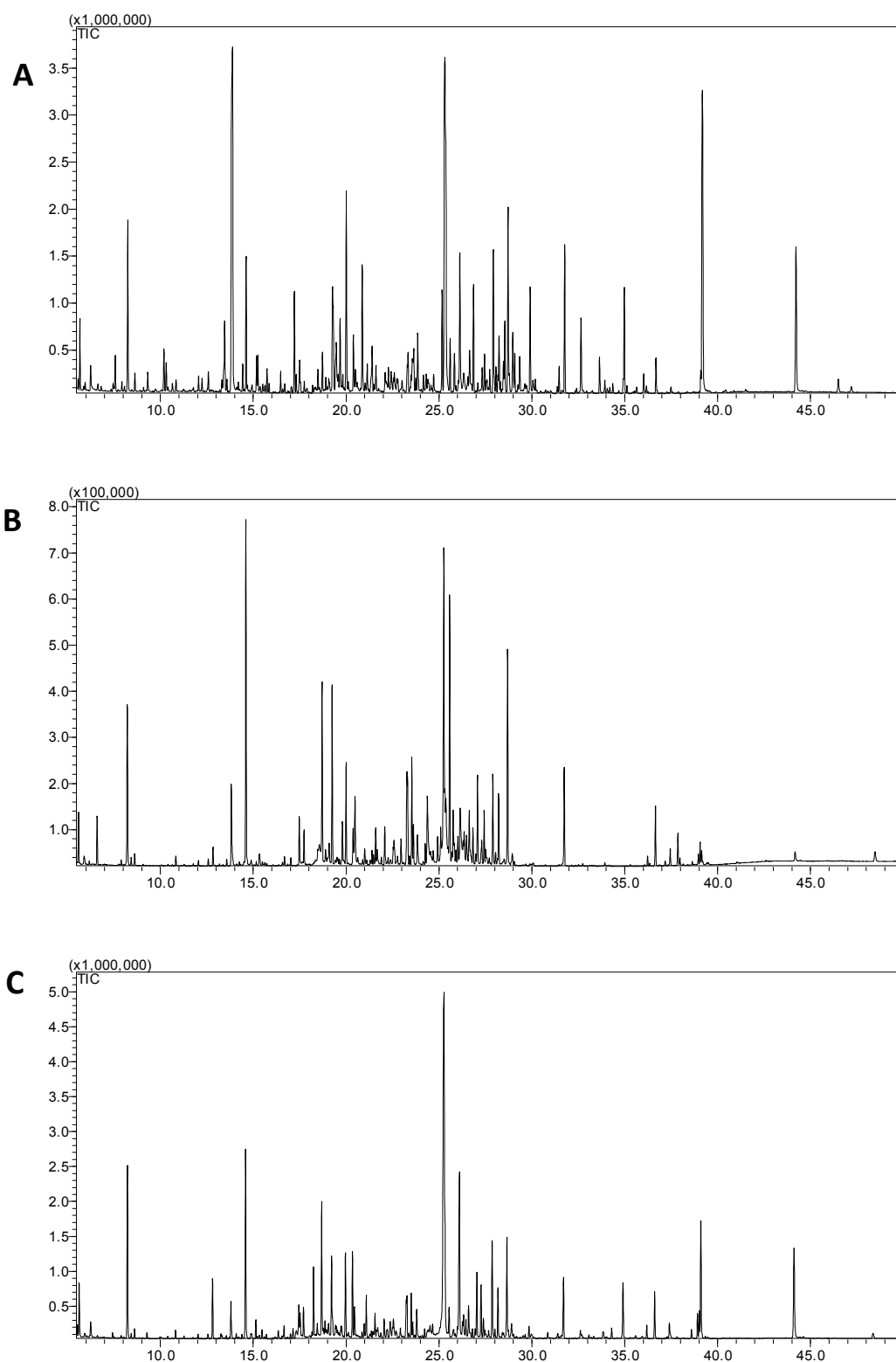


### **Metabolomic analysis**

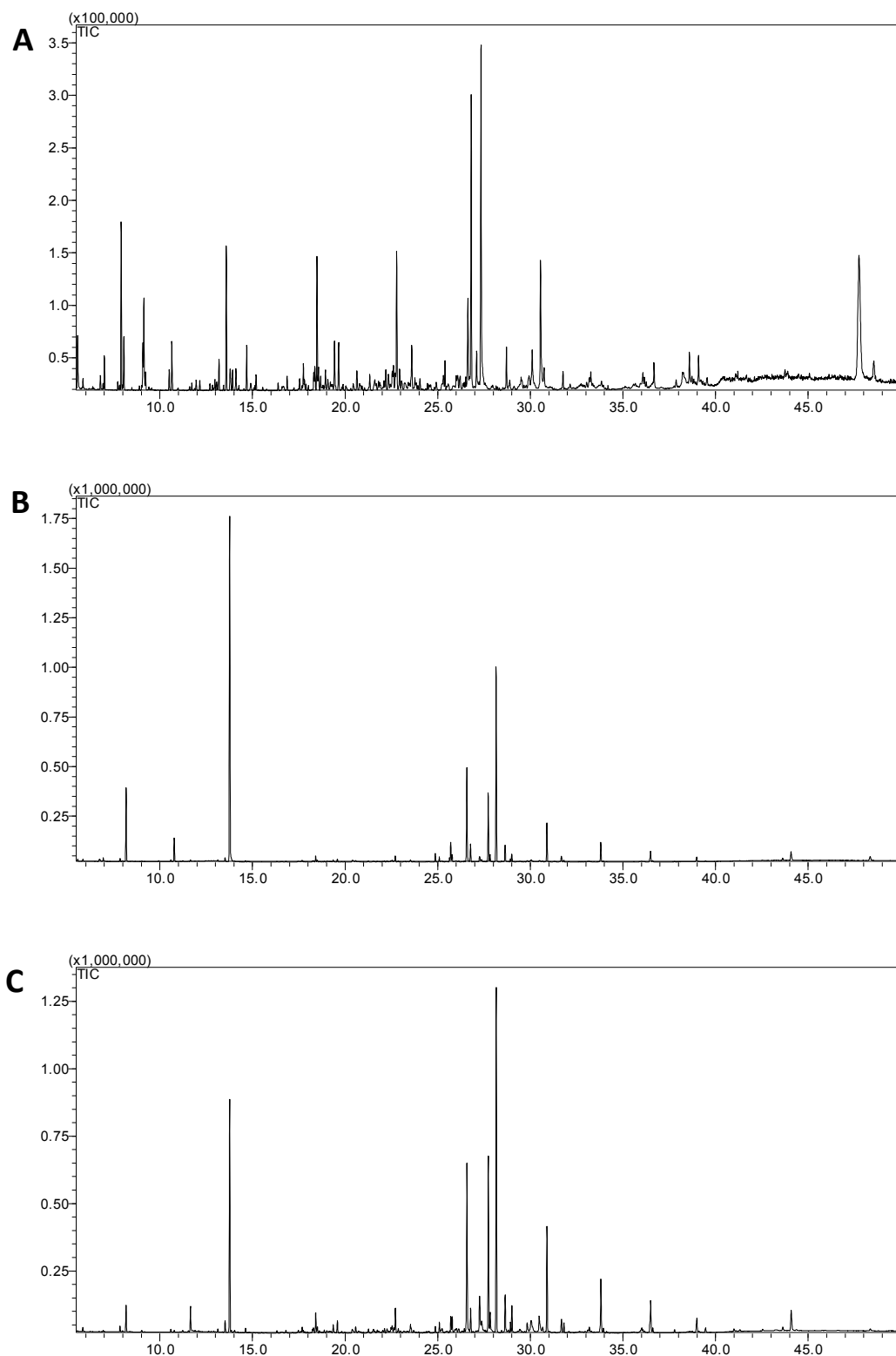
GC-MS raw data and total ion chromatography (TIC) of brain (Fig. S1), liver (Fig. S2), blood (Fig. S3) and urine (Fig. S4) are acquired as metabolic profiling via GC-MS Postrum Analysis (Shimadzu, Tokyo, Japan). XCMS Online was used to deconvolute the raw data via centwave method of mutigroup analysis. Simca-P 13.0 was used to carry out PCA, O-PLS-DA and S-plot analysis. PCA, O-PLS-DA and S-plot analysis of brain, liver, blood and urine were shown in Fig. S5-S8. Separating tendency was observed in the PCA score plots of brain, liver, blood and urine of three groups, indicating that group difference was more remarkable than individual difference. O-PLS-DA results showed that either control and D-gal groups or D-gal+GLP-1 and D-gal groups of brain, liver, blood and urine were definitely divided into two classes. S-plot analysis showed coefficients vs. VIP of brain, liver, blood and urine. The VIP value more than 1.00 was considered as potential biomarkers.



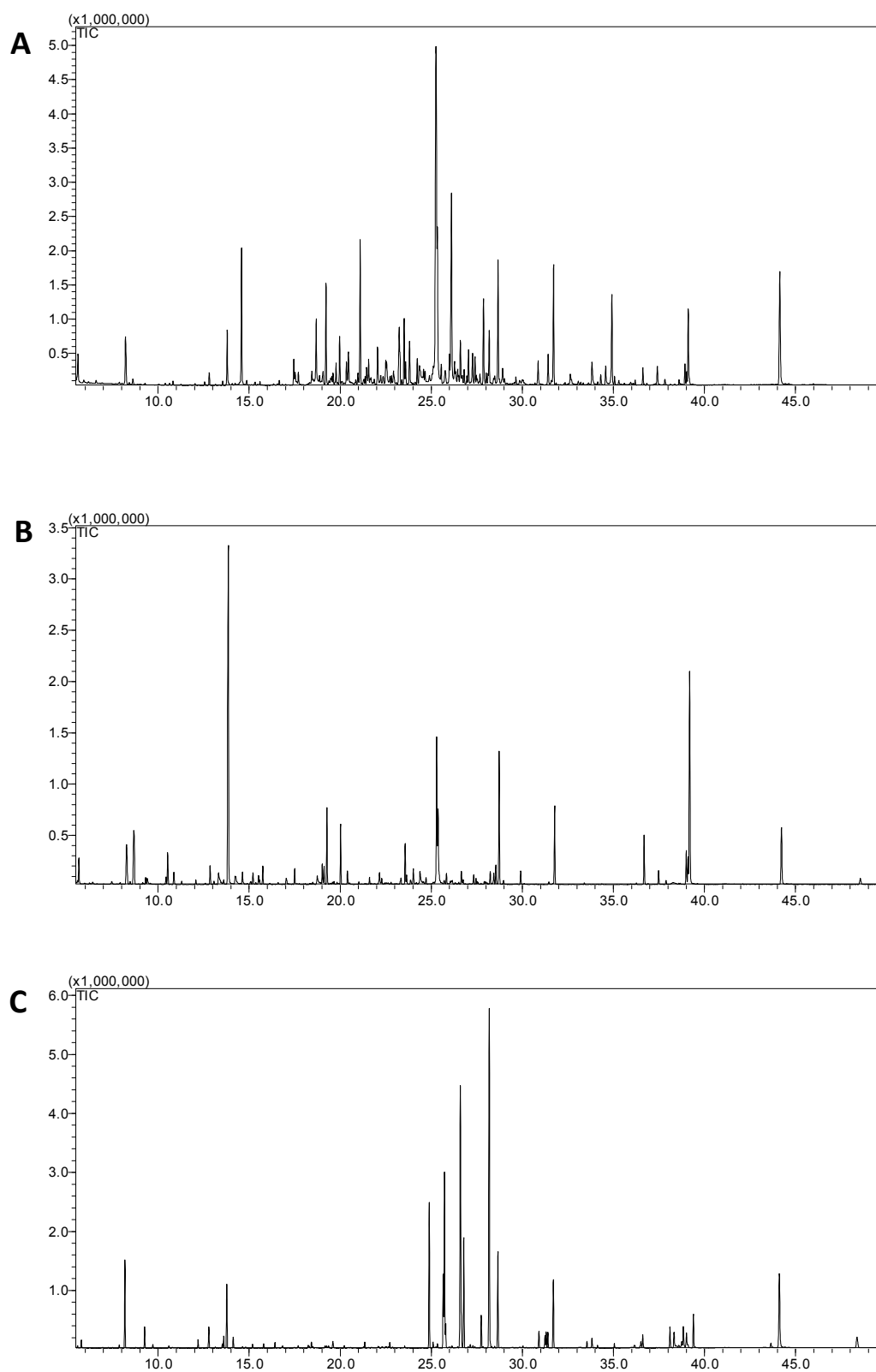
**Fig. S1. TIC of three groups of brain.**  
**Control group (A), D-gal group (B), D-gal+ GLP-1 group (C).**



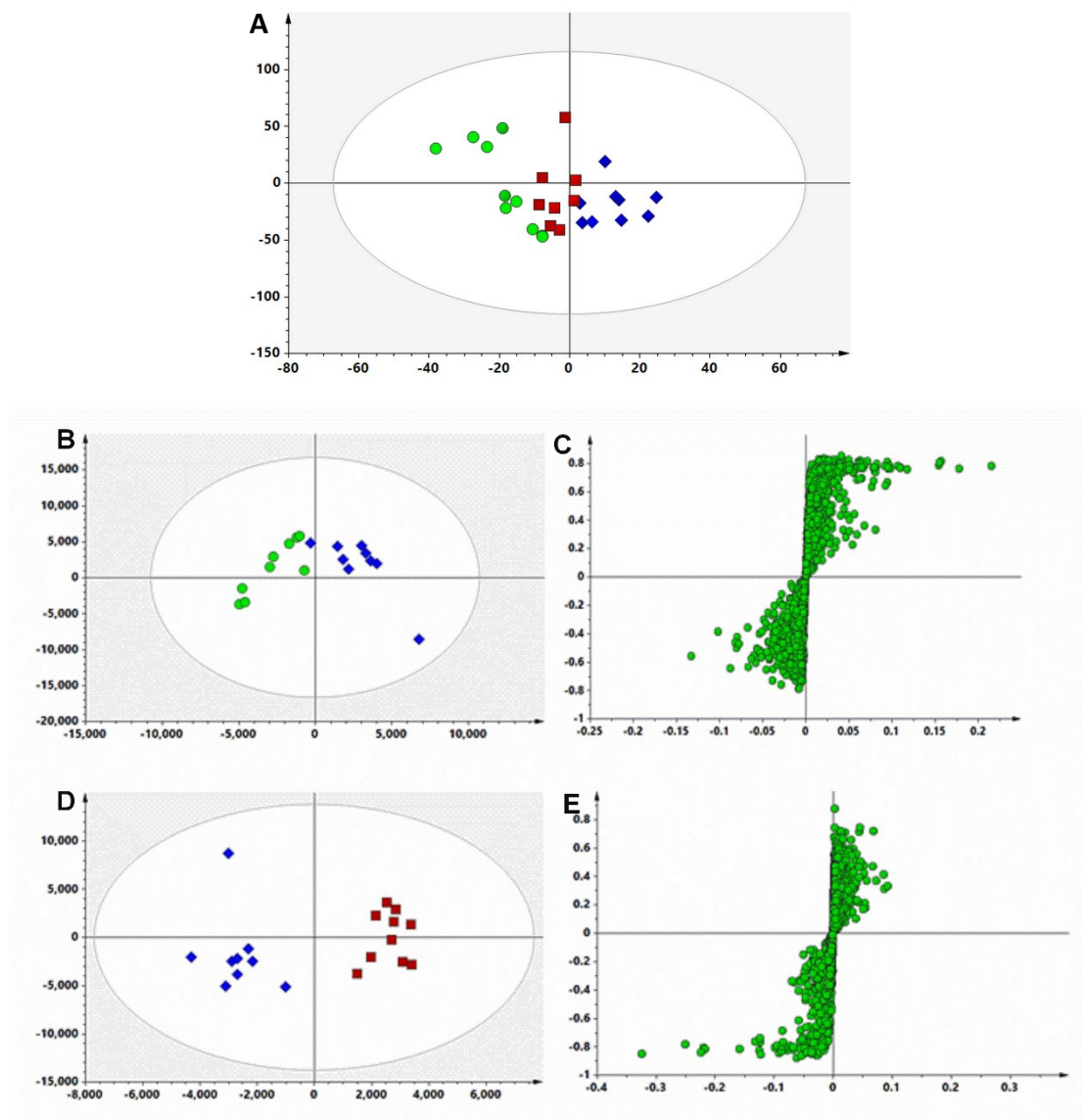
**Fig. S2. TIC of three groups of liver.**  
**Control group (A), D-gal group (B), D-gal+ GLP-1 group (C).**



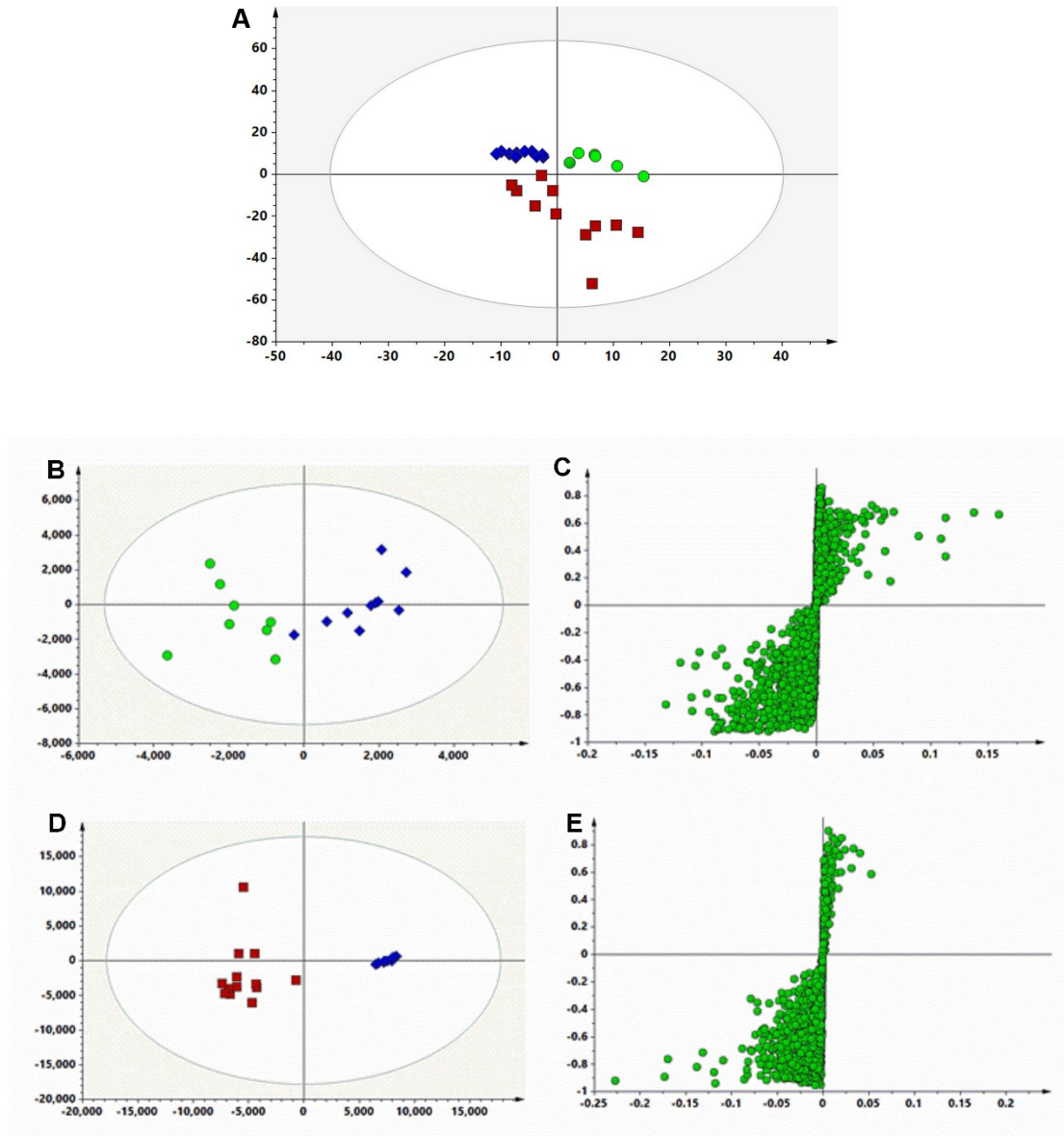
**Fig. S3. TIC of three groups of blood.**  
**Control group (A), D-gal group (B), D-gal+ GLP-1 group (C).**



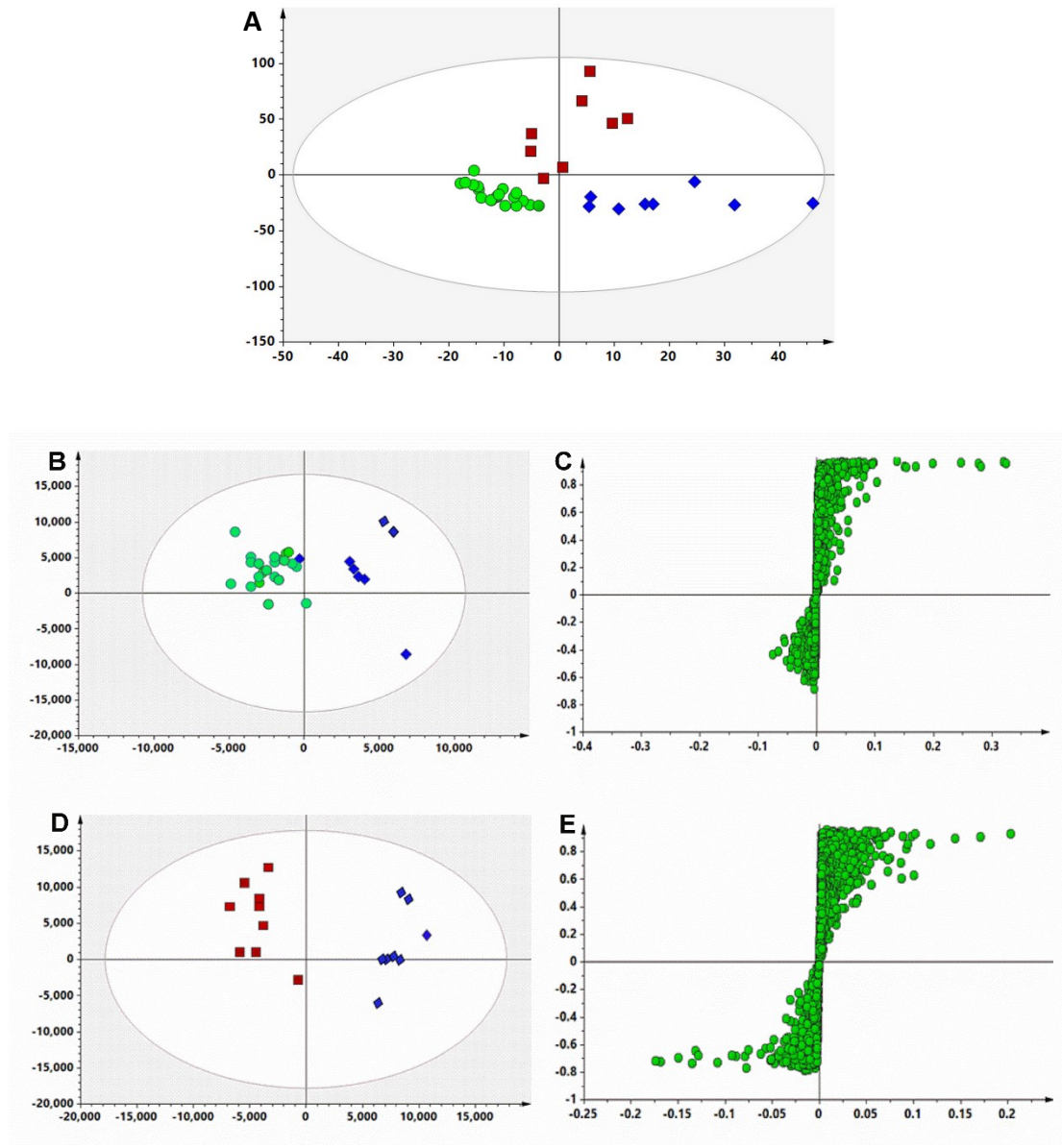
**Fig. S4. TIC of three groups of urine.**  
**Control group (A), D-gal group (B), D-gal+ GLP-1 group (C).**



**Fig. S5. PCA, O-PLS-DA and S-plot analysis of brain. PCA analysis of control group(●), D-gal group (◆) and D-gal + GLP-1 group(■) (A). O-PLS-DA score plots of of control group(●) vs D-gal group (◆) (B). S-plot analysis of control group vs D-gal group (C). O-PLS-DA score plots of of D-gal + GLP-1 group (■) vs D-gal group(◆) (D). S-plot analysis of D-gal + GLP-1 group vs D-gal group (E).**

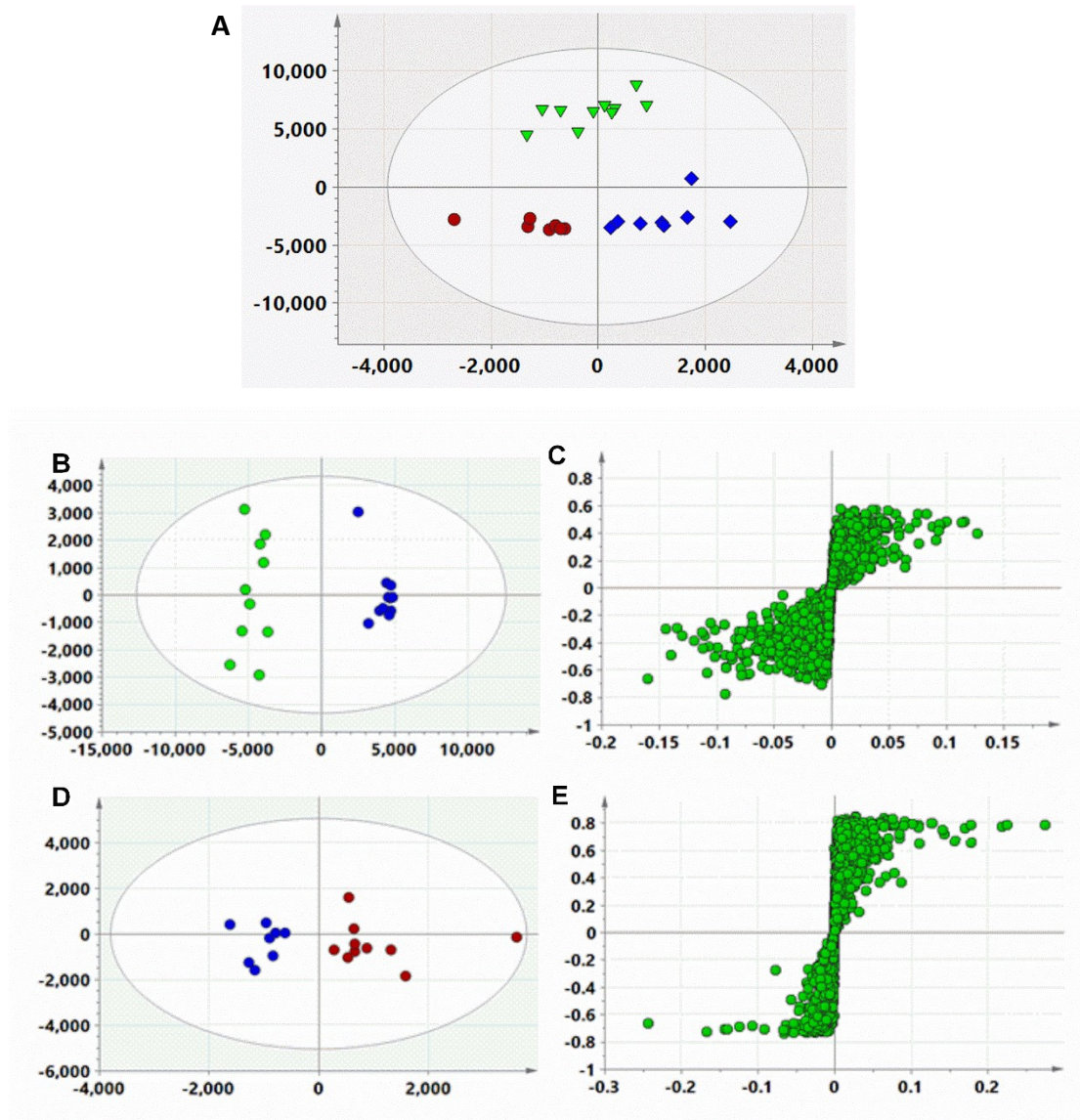


**Fig. S6. PCA, O-PLS-DA and S-plot analysis of liver. PCA analysis of control group(●), D-gal group (◆) and D-gal + GLP-1 group(■) (A). O-PLS-DA score plots of of control group(●) vs D-gal group (◆) (B). S-plot analysis of control group vs D-gal group (C). O-PLS-DA score plots of of D-gal + GLP-1 group (■) vs D-gal group(◆) (D). S-plot analysis of D-gal + GLP-1 group vs D-gal group (E).**

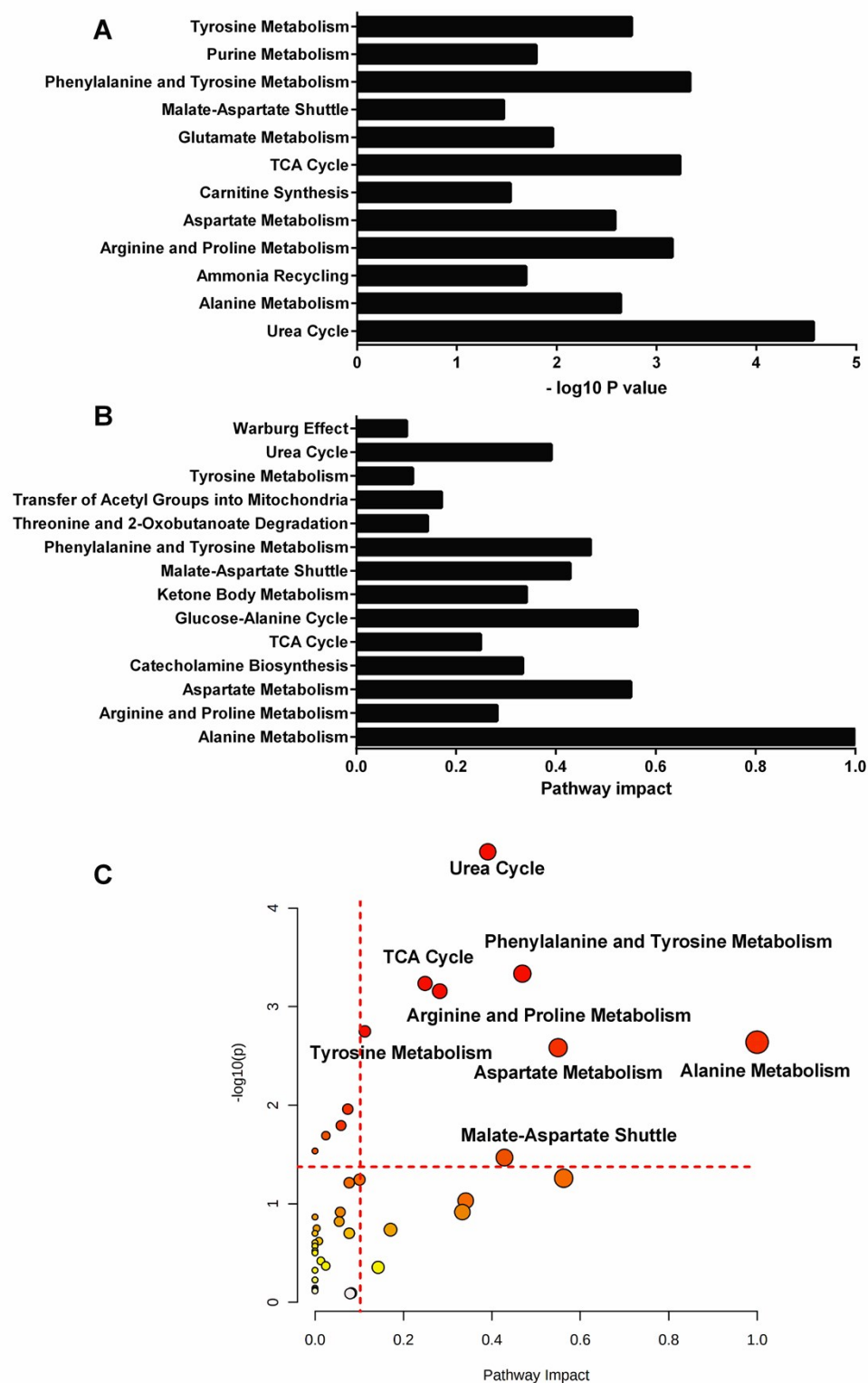


**Fig. S7. PCA, O-PLS-DA and S-plot analysis of blood. PCA analysis of control group(●), D-gal group (◆) and D-gal + GLP-1 group(■) (A). O-PLS-DA score plots of of control group(●) vs D-gal group (◆) (B). S-plot analysis of control group vs D-gal group (C). O-PLS-DA score plots of of D-gal + GLP-1 group (■) vs D-gal group(◆) (D). S-plot analysis of D-gal + GLP-1 group vs D-gal group (E).**





**Fig. S8. PCA, O-PLS-DA and S-plot analysis of urine. PCA analysis of control group(▼), D-gal group (◆) and D-gal + GLP-1 group(●) (A). O-PLS-DA score plots of of control group(●) vs D-gal group (●) (B). S-plot analysis of control group vs D-gal group (C). O-PLS-DA score plots of of D-gal + GLP-1 group (●) vs D-gal group(●) (D). S-plot analysis of D-gal + GLP-1 group vs D-gal group (E).**



**Fig. S9. Pathway analysis of metabolomics. Pathways of -Log<sub>10</sub> P value more than 1.30 ( P value less than 0.05) (A). Pathways of impact more than 0.10 (B). Topological analysis of all pathways (C).**