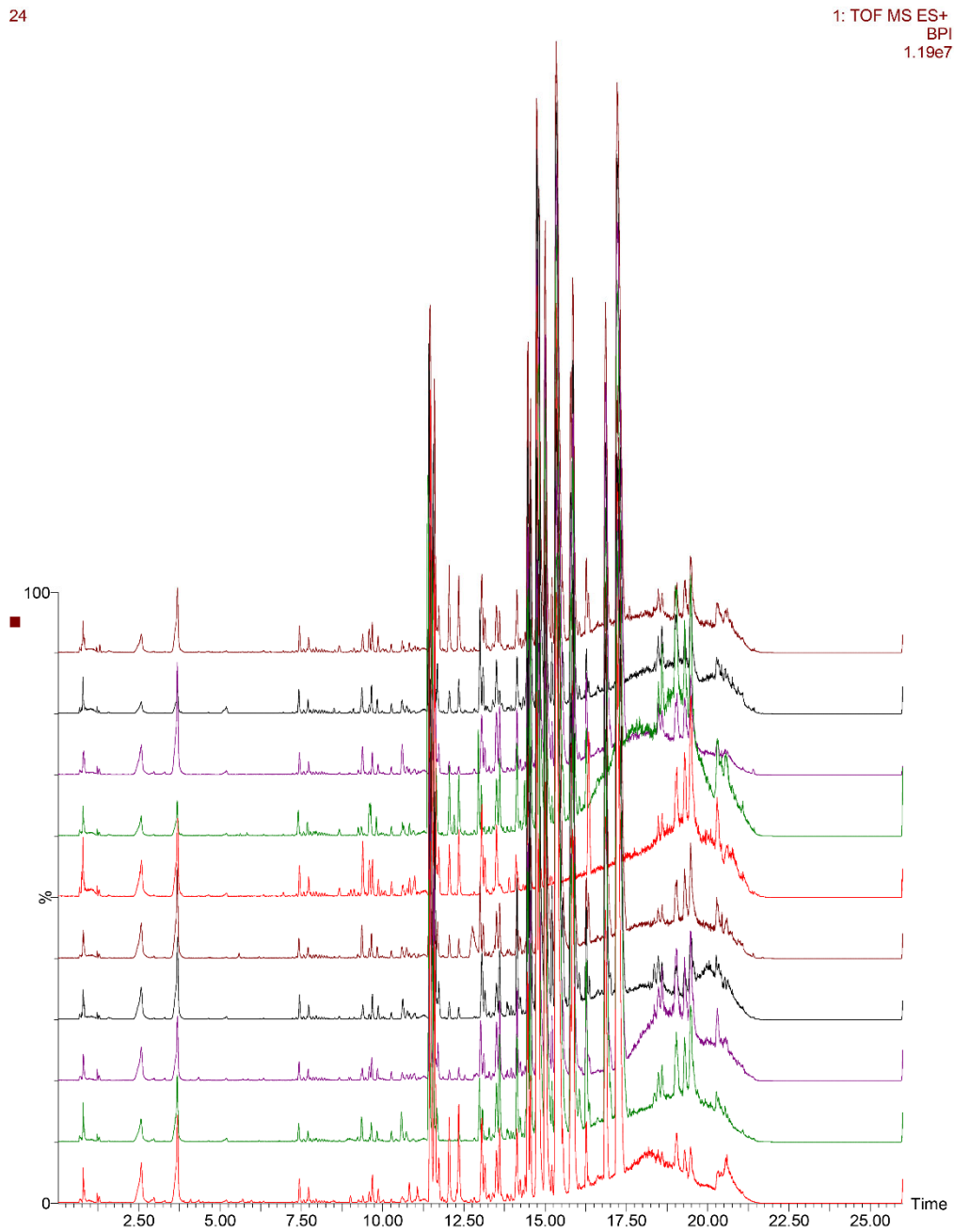


*Supplementary materials for:*

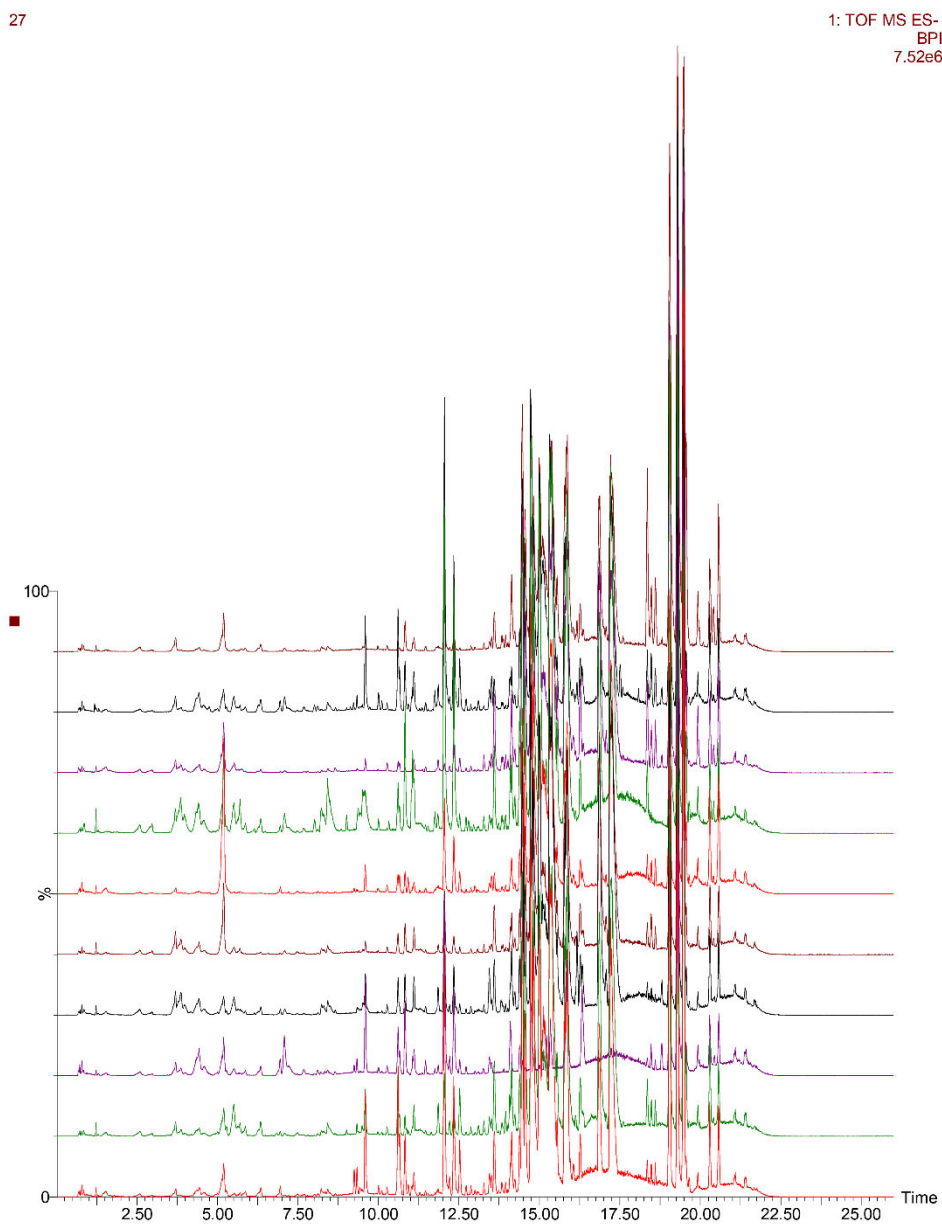
**1.LC-MS Analysis of Metabolic Profiling**

Using the optimal LC-MS, global metabolic profiling in both positive and negative ion modes were analyzed by UHPLC-MS, the base peak intensity chromatograms (BPC) of samples from the Con, Mod, ZGW, EF, PF, PE, ZL, EL, PL and PEL groups in positive and negative ion mode are presented in **Figure S1** and **Figure S2**, respectively.



**Figure S1.** The representative BPC chromatograms of samples from the Con, Mod, ZGW, PF,

EF, PE, ZL, PL, EL and PEL groups analyzed on UHPLC-QTOF/MS in ESI+ mode.

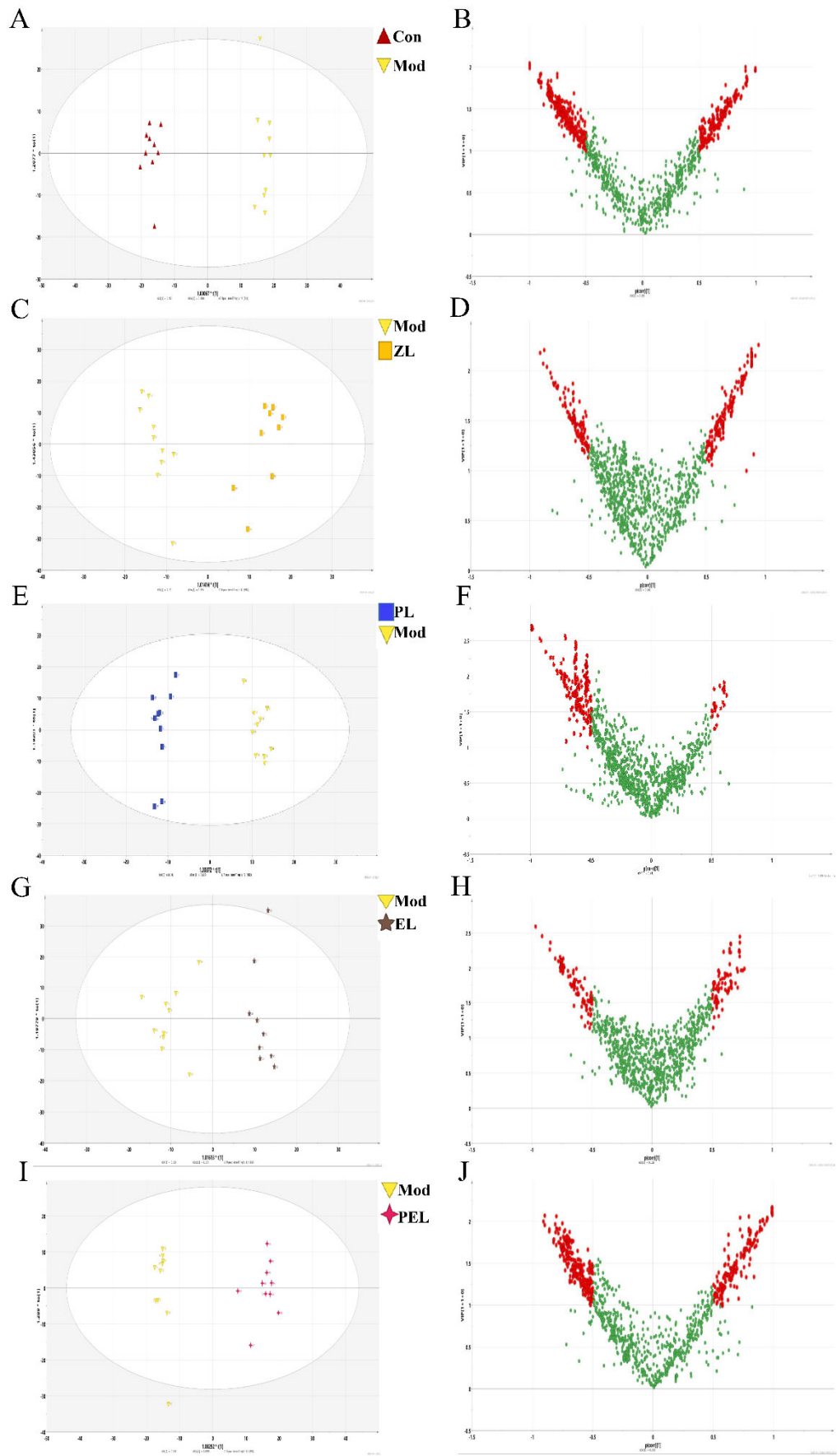


**Figure S2.** The representative BPC chromatograms of samples from the Con, Mod, ZGW, PF, EF, PE, ZL, PL, EL and PEL groups analyzed on UHPLC-QTOF/MS in ESI- mode.

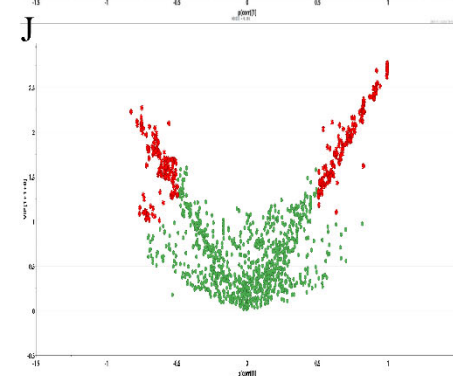
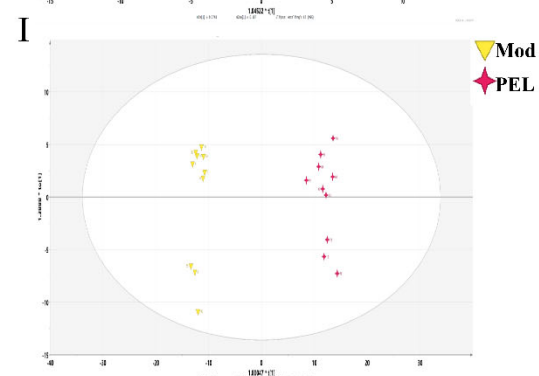
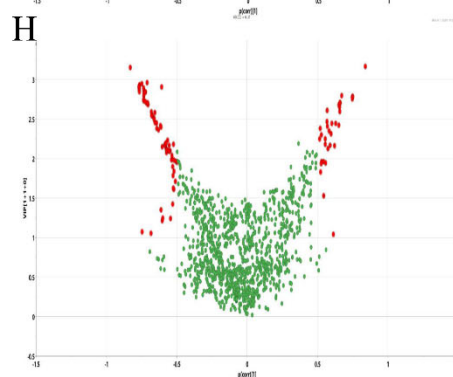
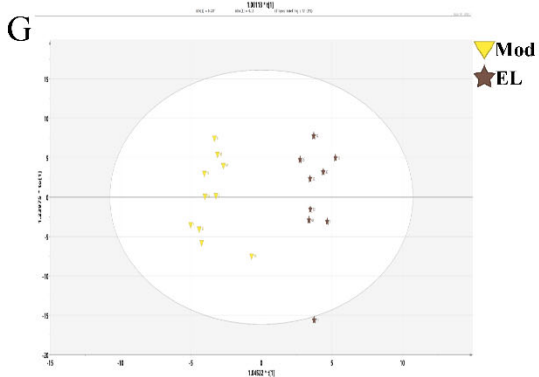
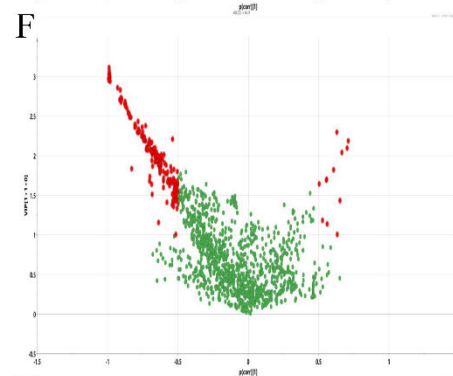
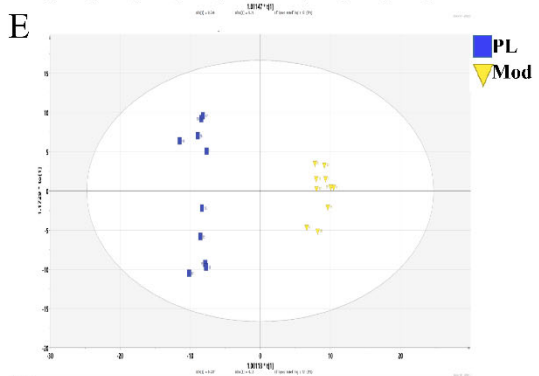
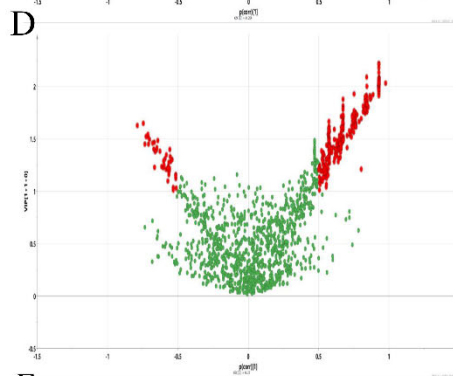
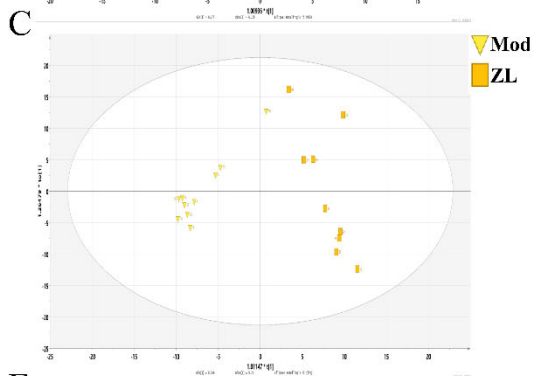
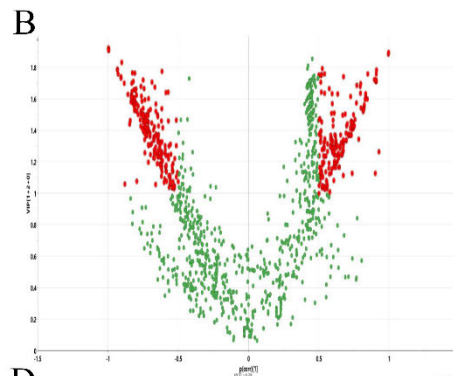
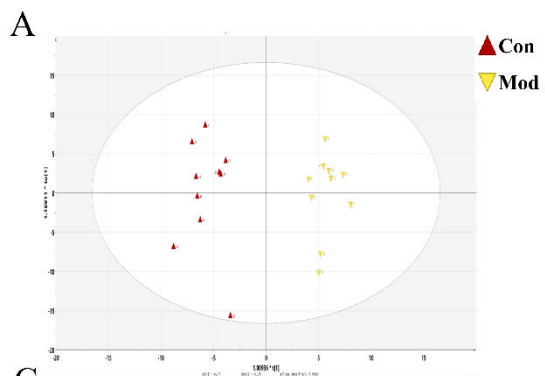
**2. Parameters of PCA and OPLS-DA models and the results of OPLS-DA analysis based on data derived from ESI+ mode and ESI- mode**



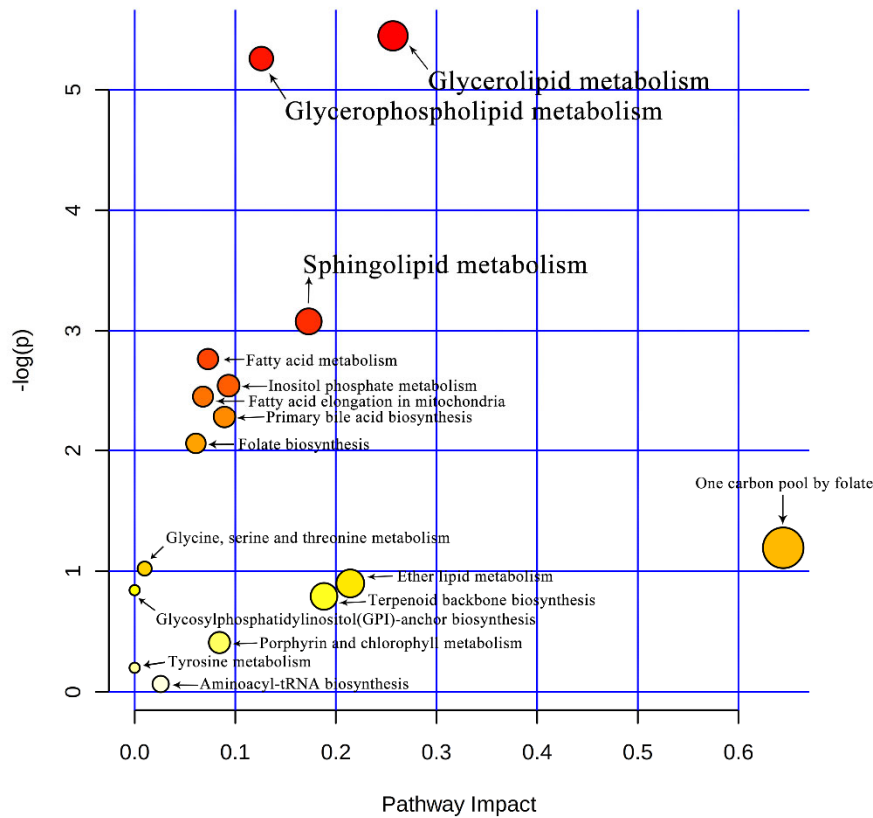
**Figure S3.** PCA score plot derived from the LC-MS analysis of rats from Con, Mod, ZGW, PF, EF, PE, ZL, PL, EL and PEL groups in ESI+ mode (A) and ESI- mode (B).



**Figure S4.** OPLS-DA analysis of data derived from ESI+ mode. OPLS-DA score plots for pair-wise comparisons between Con and Mod (**A**), Mod and ZL (**C**), Mod and PL (**E**), Mod and EL (**G**), Mod and PEL (**I**). S-plot of OPLS-DA model for Con and Mod (**B**), Mod and ZL (**D**), Mod and PL (**F**), Mod and EL (**H**), Mod and PEL (**J**), the points in red stands for the identified biomarkers.



**Figure S5.** OPLS-DA analysis of data derived from ESI- mode. OPLS-DA score plots for pair-wise comparisons between Con and Mod (A), Mod and ZL (C), Mod and PL (E), Mod and EL (G), Mod and PEL (I). S-plot of OPLS-DA model for Con and Mod (B), Mod and ZL (D), Mod and PL (F), Mod and EL (H), Mod and PEL (J), the points in red stands for the identified biomarkers.



**Figure S6.** The most perturbed pathway induced by *Epimedii Folium* and/or *Psoraleae Fructus* were revealed by MetaboAnalyst 4.0 software. The pathway with high  $-\log(p)$  and pathway impact value is greatly perturbed.