

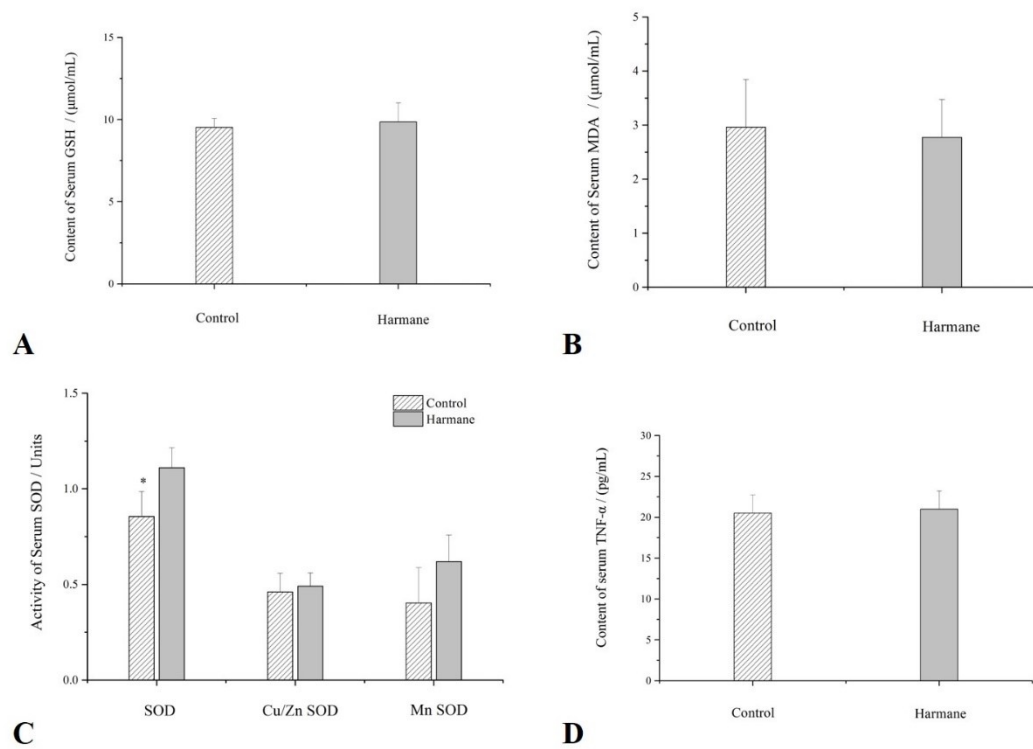
Supplementary Table 1. The pathway analysis of the identified metabolites affected in the experiment groups. Based on the selected serum metabolites, the global metabolic disorders of the most relevant pathways affected by harmene exposure were revealed using the MetaboAnalyst 4.0.

Metabolism pathway	P	-log(p)	Holm adjust	FDR	Impact
Pyruvate metabolism	0.00539	5.2232	0.45276	0.45276	0.0311
Arginine biosynthesis	0.072017	2.6308	1	1	0.06091
Selenocompound metabolism	0.10146	2.288	1	1	0
Citrate cycle (TCA cycle)	0.10146	2.288	1	1	0.04412
Glycolysis / Gluconeogenesis	0.13009	2.0395	1	1	0
Alanine, aspartate and glutamate metabolism	0.13945	1.97	1	1	0
Glutathione metabolism	0.13945	1.97	1	1	0
Glyoxylate and dicarboxylate metabolism	0.15792	1.8457	1	1	0
Arginine and proline metabolism	0.18496	1.6876	1	1	0.11063
Pyrimidine metabolism	0.18939	1.6639	1	1	0.03727
Aminoacyl-tRNA biosynthesis	0.22835	1.4769	1	1	0

Supplementary Table 2. The pathway analysis of the identified metabolites affected in the experiment groups. Based on the selected urine metabolites, the global metabolic disorders of the most relevant pathways affected by harmane exposure were revealed using the MetaboAnalyst 4.0.

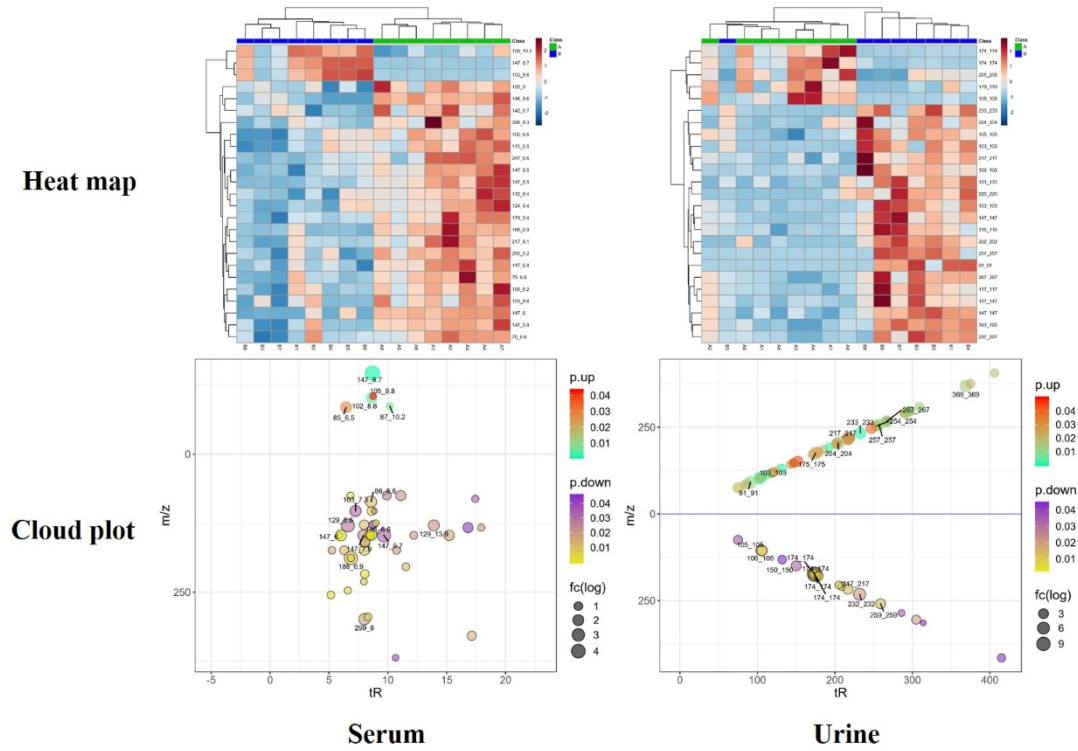
Metabolism pathway	P	-log(p)	Holm adjust	FDR	Impact
Phenylalanine metabolism	0.005005	5.2973	0.42044	0.42044	0
Vitamin B6 metabolism	0.080673	2.5174	1	1	0
Ascorbate and aldarate metabolism	0.089253	2.4163	1	1	0
Biotin metabolism	0.089253	2.4163	1	1	0
Butanoate metabolism	0.13105	2.0322	1	1	0.03175
Fructose and mannose metabolism	0.15527	1.8626	1	1	0
Citrate cycle (TCA cycle)	0.17106	1.7657	1	1	0.05003
Lysine degradation	0.20936	1.5637	1	1	0
Alanine, aspartate and glutamate metabolism	0.23154	1.463	1	1	0.08654
Glyoxylate and dicarboxylate metabolism	0.26021	1.3463	1	1	0.02381
Amino sugar and nucleotide sugar metabolism	0.29466	1.2219	1	1	0
Arginine and proline metabolism	0.30137	1.1994	1	1	0.02385

Aminoacyl-tRNA biosynthesis	0.36527	1.0071	1	1	0
Purine metabolism	0.46682	0.76181	1	1	0.00012



Supplementary Figure 1. Serum oxidative stress and inflammation stress level including the content of GSH (A), MDA (B), TNF- α (D), and the activity of SOD (C).

*: $p < 0.05$ versus control group.



Supplementary Figure 2. Heat map visualizing the changes in the concentration of potential biomarkers in the serum and urine samples of harmane exposure. Rows: samples. Columns: biomarkers extracted from the volcano plot in the serum and urine samples of the control group and CML group. Color key indicates the concentration of metabolites: blue, lowest; red, highest. And cloud map visualizing the p -value, the directional fold change, the retention time, and the mass-to-change ratio features of metabolites in the serum and urine samples.