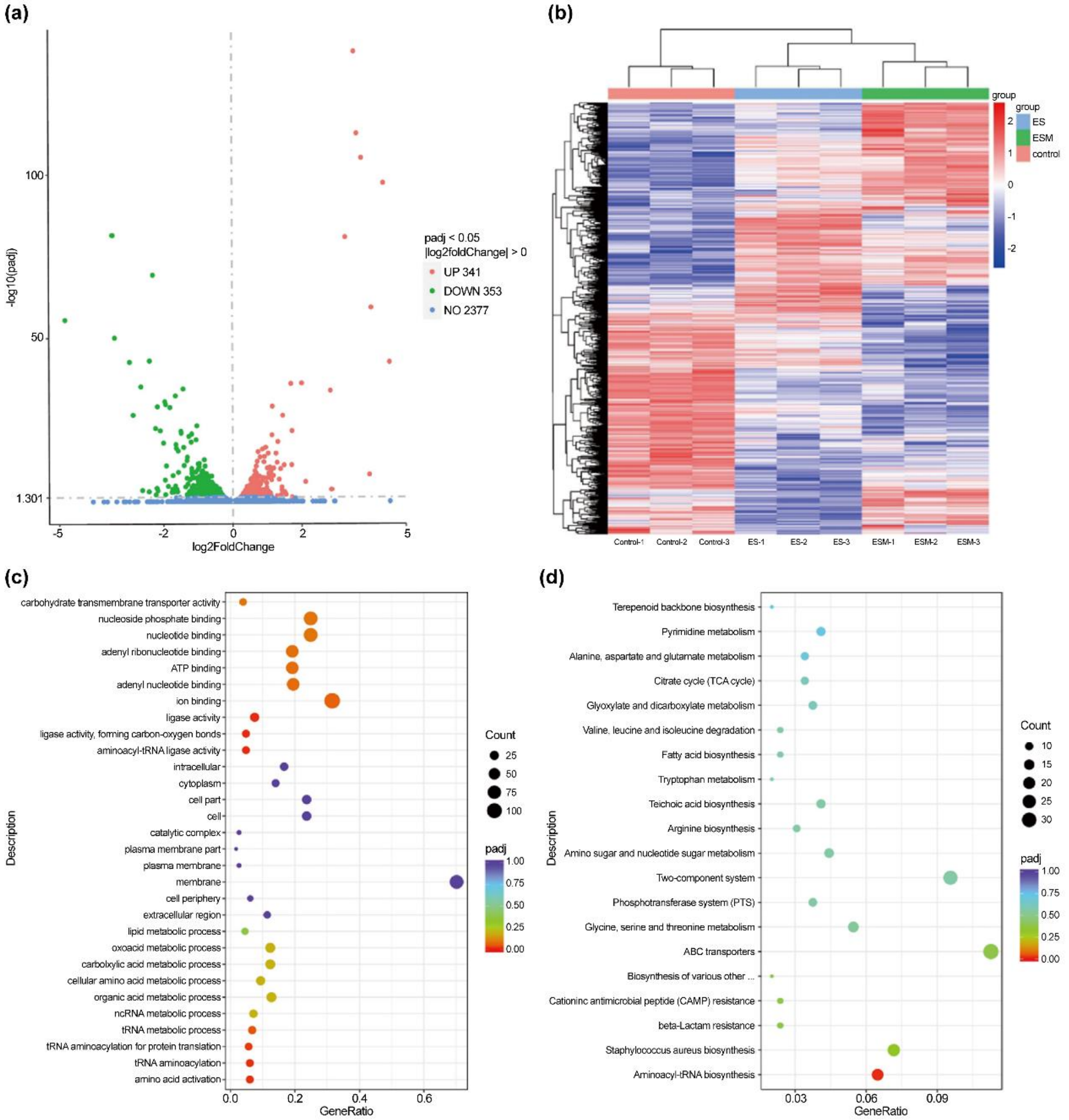

Fig. S6. ESM and ES transcriptome data. (a) Volcano plot of differentially expressed genes (DEGs) for **ESM** and **ES** groups. In comparison to the **ES** treatment group, the ESM treatment group contained 694 DEGs, of which 341 were highly upregulated and 353 were significantly downregulated. (b) Cluster heatmap of DEGs between **ESM** and **ES** groups. The DEG clustering heatmap, which displays the similarities in gene expression amongst different groups, revealed that most genes had significantly different expression levels in the ESM, ES, and control groups. (c) Bubble diagram of GO enrichment analysis of DEG between **ESM**

and **ES** groups. The GO enrichment analysis of DEGs revealed that most DEGs were connected to tRNA aminoacylation, tRNA metabolism, and amino acid activation. (d) The KEGG enrichment analysis bubble diagram of DEGs between ESM and ES groups. It revealed that following **ESM** treatment, significantly different genes were primarily enriched in pathways related to phosphotransferase system, fatty acid biosynthesis, amino acid degradation, citric acid cycle (TCA cycle), secondary metabolite biosynthesis, fatty acid degradation, and arginine biosynthesis.

ES, esculetin; ESM, esculetin-manganese complex.