

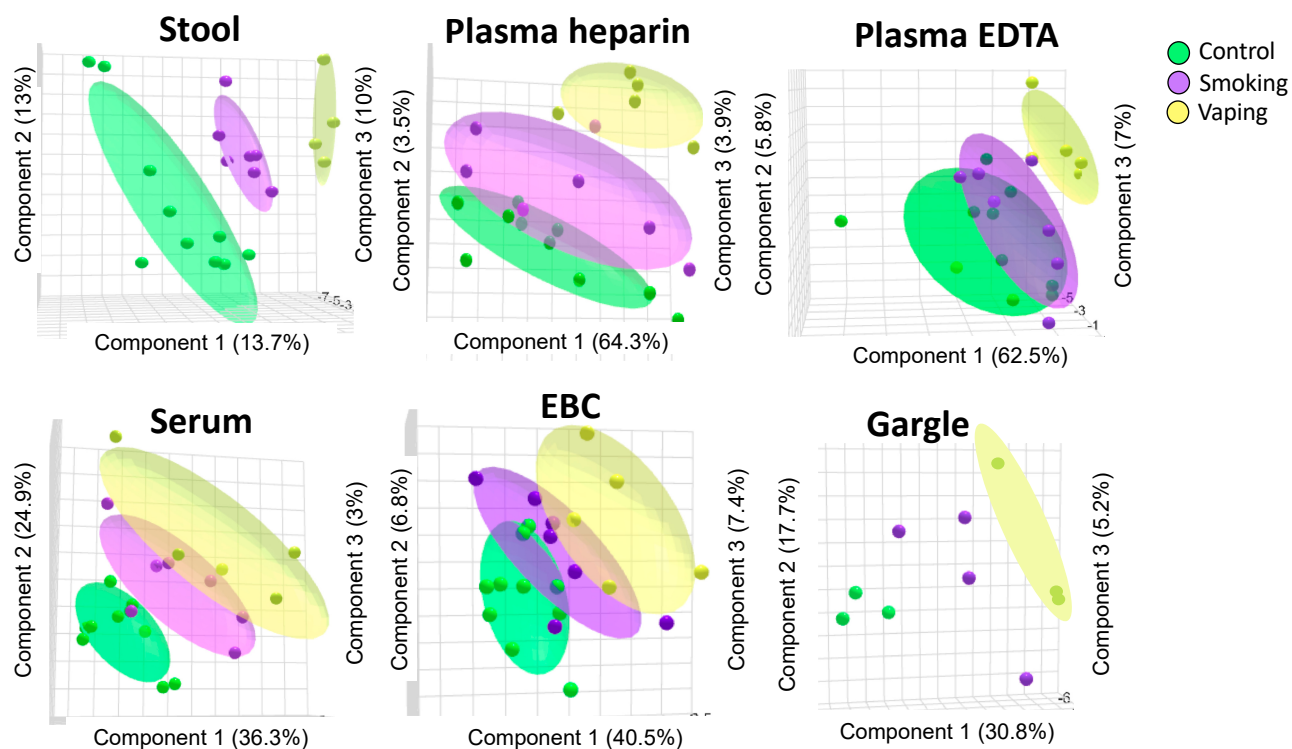


Figure S1. Vaping results in dramatic alterations to the oral, stool, and plasma metabolomes. 3D Partial Least Squares Discriminant Analysis (PLS-DA) comparing the metabolic profiles of participants who vape “vaping” (yellow), participants who do not vape “smoking” (purple), and controls (green). The smoking cohort (purple) included participants who combustible tobacco/marijuana smoke. EBC, exhaled breath condensate.

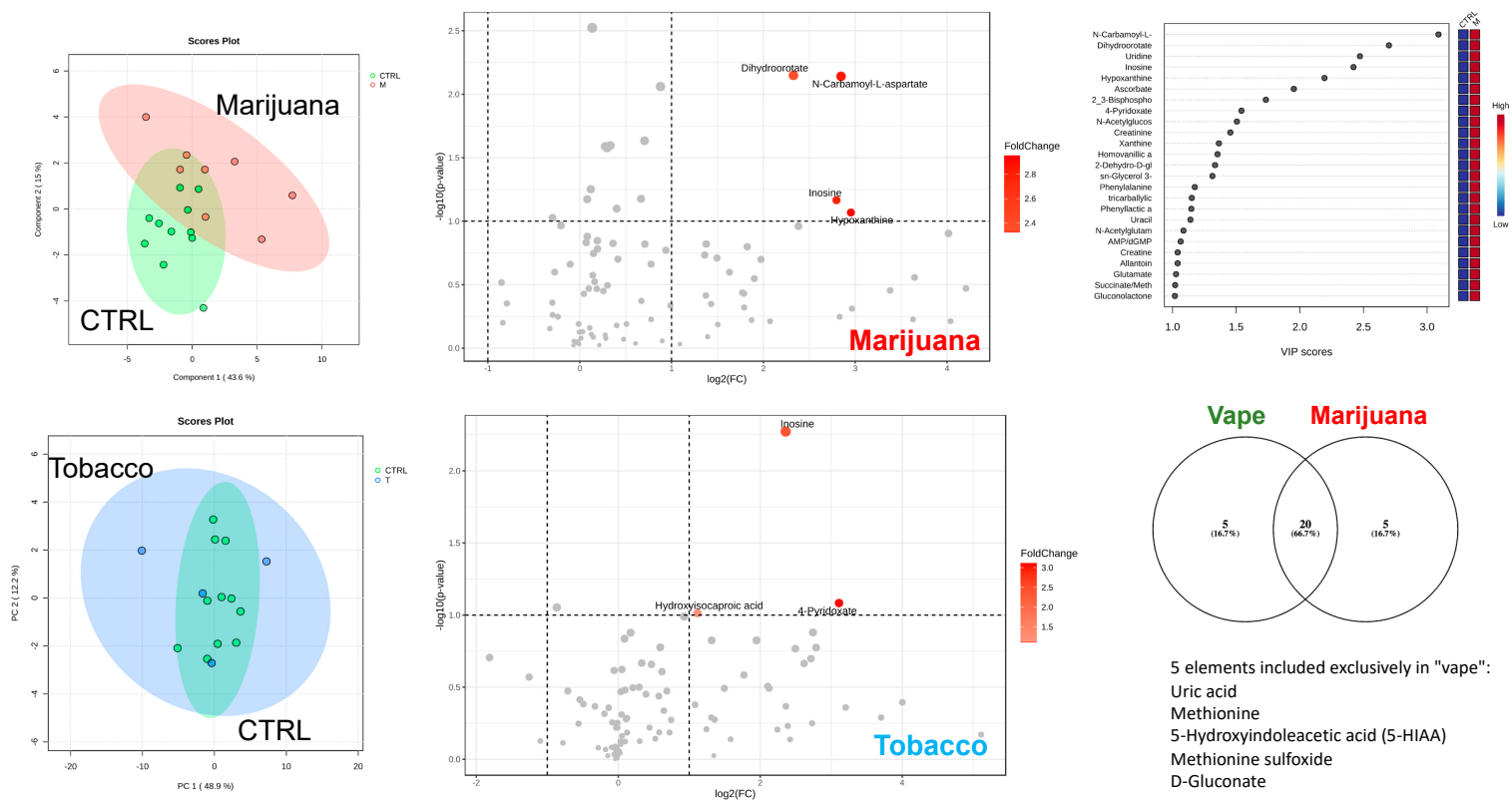


Figure S2. Combustible marijuana and tobacco smoking impact on exhaled breath condensate metabolome. Partial Least Squares Discriminant Analysis (PLS-DA) were used to assess the impact on the global metabolome. Each metabolite was assigned a variable importance in projection (VIP) score (top right) to assess its contribution to the differences in metabolic profiles. The 15 metabolites with the highest VIP scores were shown. A VIP score >1 indicates the metabolite is a significant driver of the observed separation between groups. Volcano plots were used to visualize metabolites altered in each cohort. The x-axis displays the log₂ fold change and the y-axis displays significance. VIP scores were not analyzed for the Tobacco vs control cohort since the groups overlap. Metabolites with a VIP score >1 for each pairwise comparison were used to identify metabolites altered only by vaping. The Venn diagram (bottom right) comparing these metabolites shows 5 unique markers for vaping.

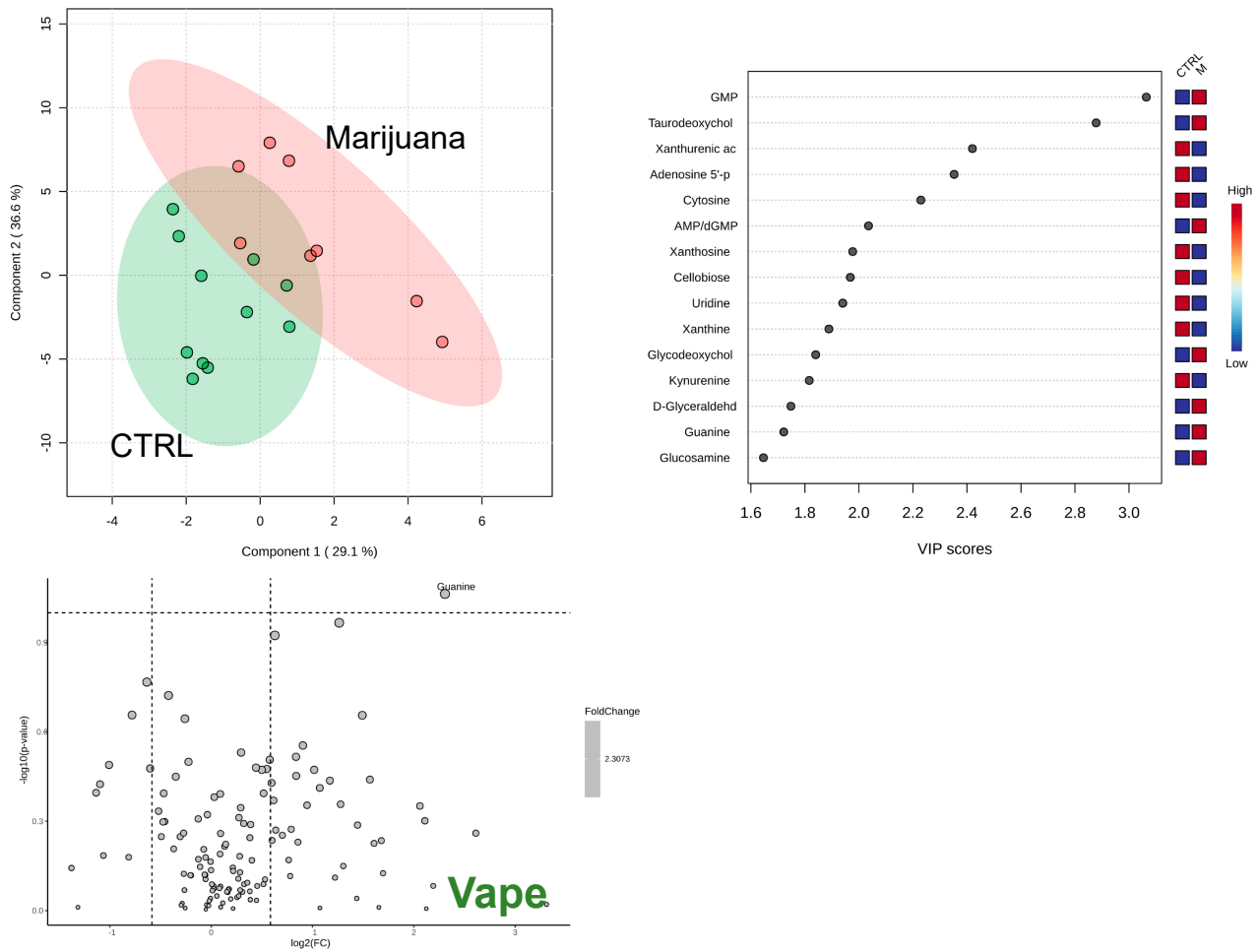


Figure S3. Vaping and combustible marijuana smoking impact on serum metabolome. Partial Least Squares Discriminant Analysis (PLS-DA) were used to assess the impact on the global metabolome. Each metabolite was assigned a variable importance in projection (VIP) score (top right) to assess its contribution to the differences in metabolic profiles. The 15 metabolites with the highest VIP scores were shown. A VIP score >1 indicates the metabolite is a significant driver of the observed separation between groups. Volcano plots were used to visualize metabolites altered in each cohort. The x-axis displays the log₂ fold change and the y-axis displays significance.

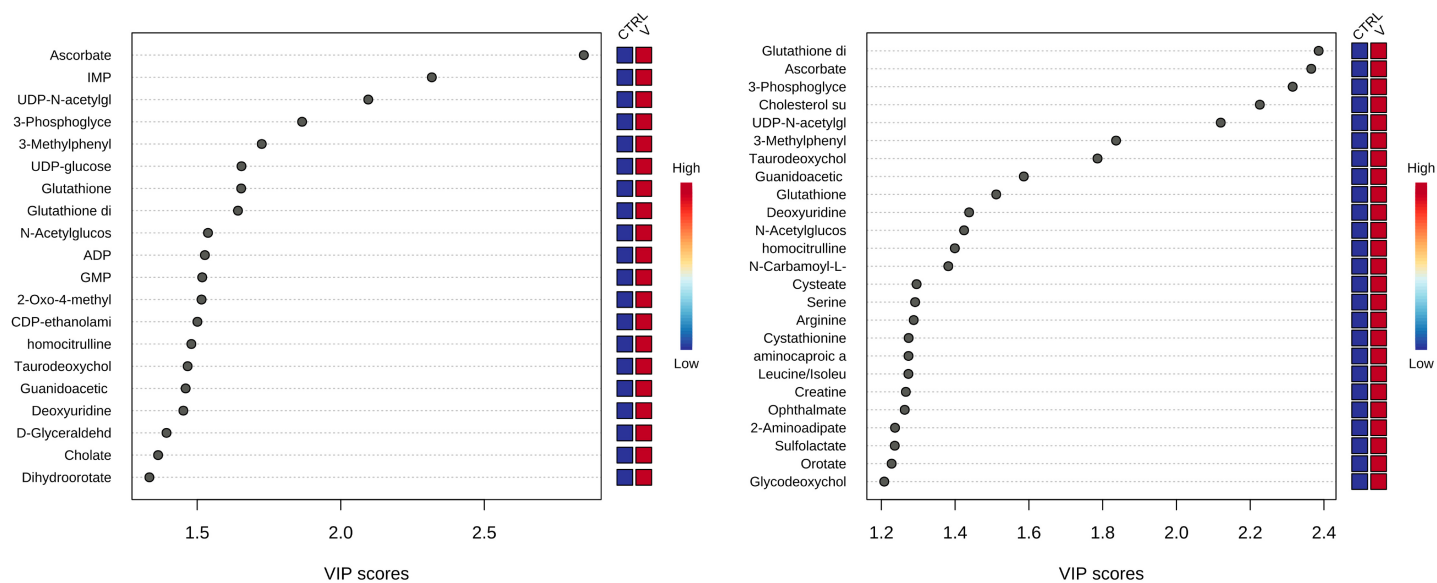


Figure S4. Top 15 metabolites driving metabolic profile differences induced by vaping in plasma EDTA (left) and plasma heparin (right). Each metabolite was assigned a variable importance in projection (VIP) score to assess its contribution to the differences in metabolic profiles in the PLS-DA model. The 15 metabolites with the highest VIP scores were shown. A VIP score >1 indicates the metabolite is a significant driver of the observed separation between groups.

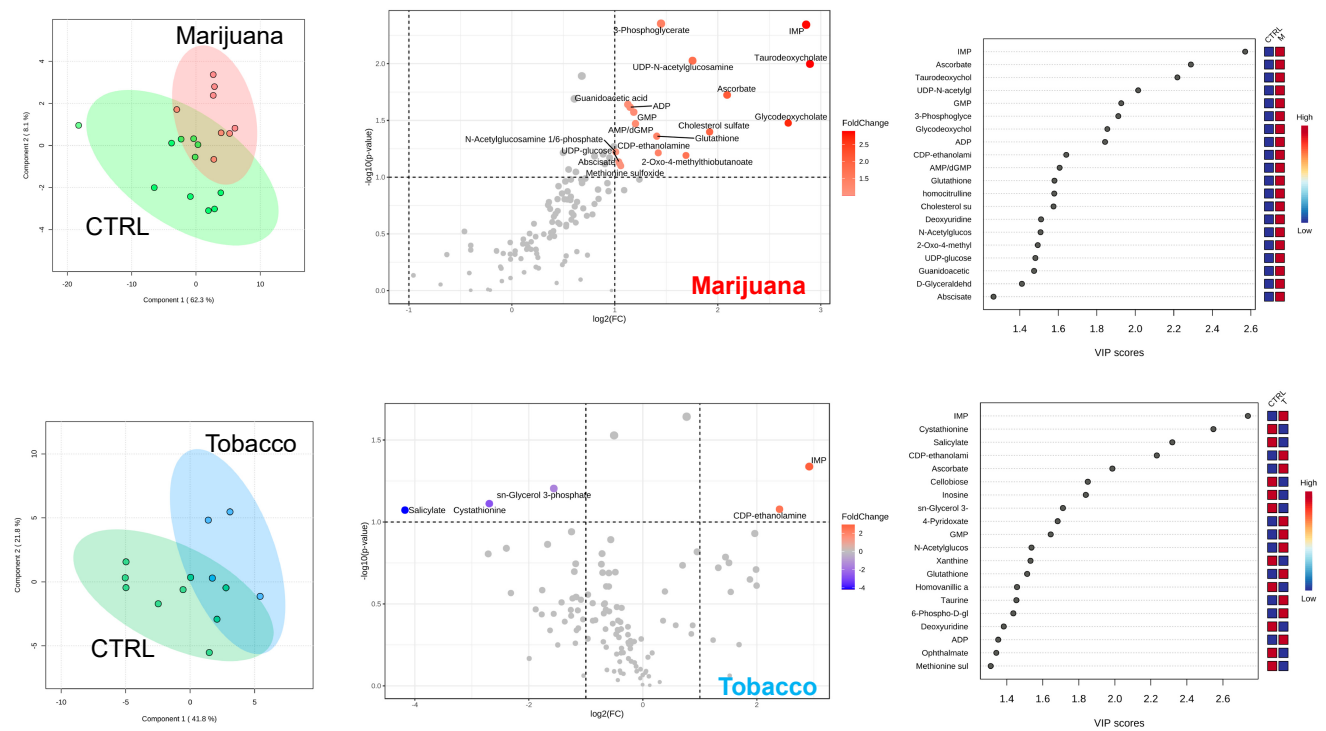


Figure S5. Combustible marijuana and tobacco smoking impact on plasma EDTA metabolome. Partial Least Squares Discriminant Analysis (PLS-DA) were used to assess the impact on the global metabolome. Each metabolite was assigned a variable importance in projection (VIP) score to assess its contribution to the differences in metabolic profiles. The 15 metabolites with the highest VIP scores were shown. A VIP score >1 indicates the metabolite is a significant driver of the observed separation between groups. Volcano plots were used to visualize metabolites altered in each cohort. The x-axis displays the $\log_2$ fold change and the y-axis displays significance.

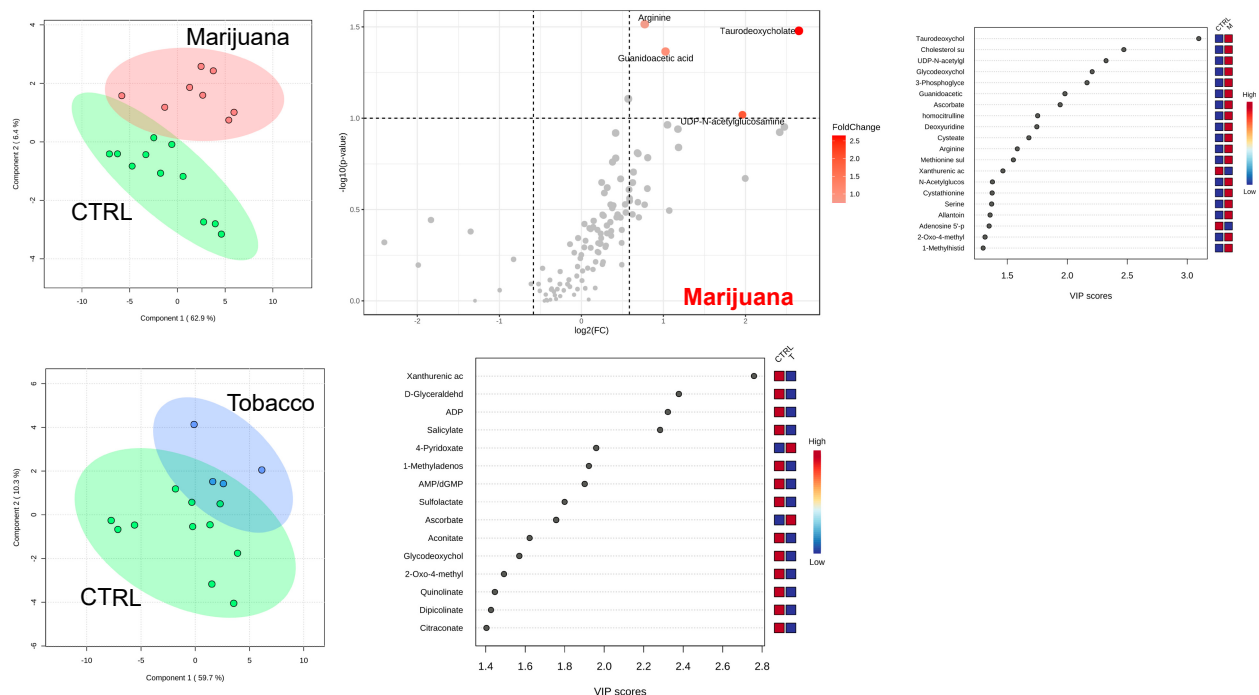


Figure S6. Combustible marijuana and tobacco smoking impact on plasma heparin metabolome. Partial Least Squares Discriminant Analysis (PLS-DA) were used to assess the impact on the global metabolome. Each metabolite was assigned a variable importance in projection (VIP) score to assess its contribution to the differences in metabolic profiles. The 15 metabolites with the highest VIP scores were shown. A VIP score >1 indicates the metabolite is a significant driver of the observed separation between groups. Volcano plots were used to visualize metabolites altered in each cohort. The x-axis displays the $\log_2$ fold change and the y-axis displays significance.

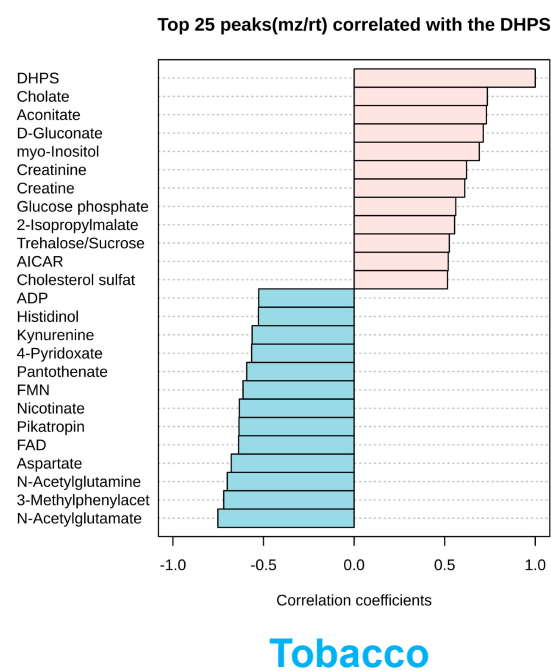
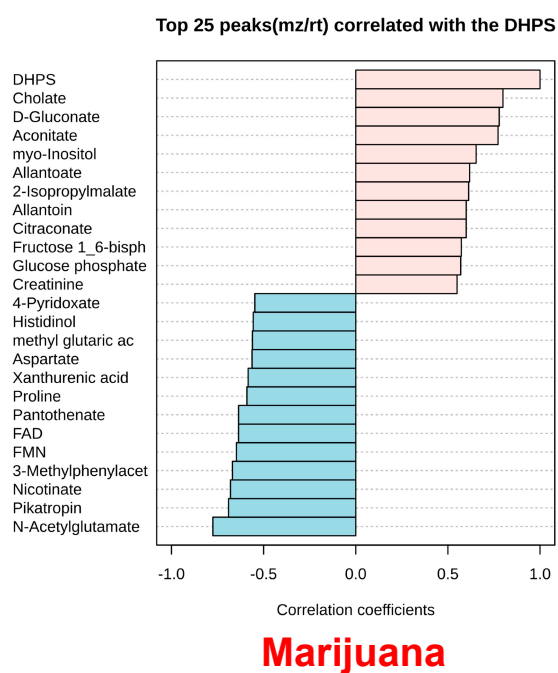


Figure S7. Stool metabolites correlated with DHPS in combustible marijuana and tobacco smoking cohorts using Pearson's r correlation coefficients. DHPS, 2,3-dihydroxypropane-1-sulfonate