

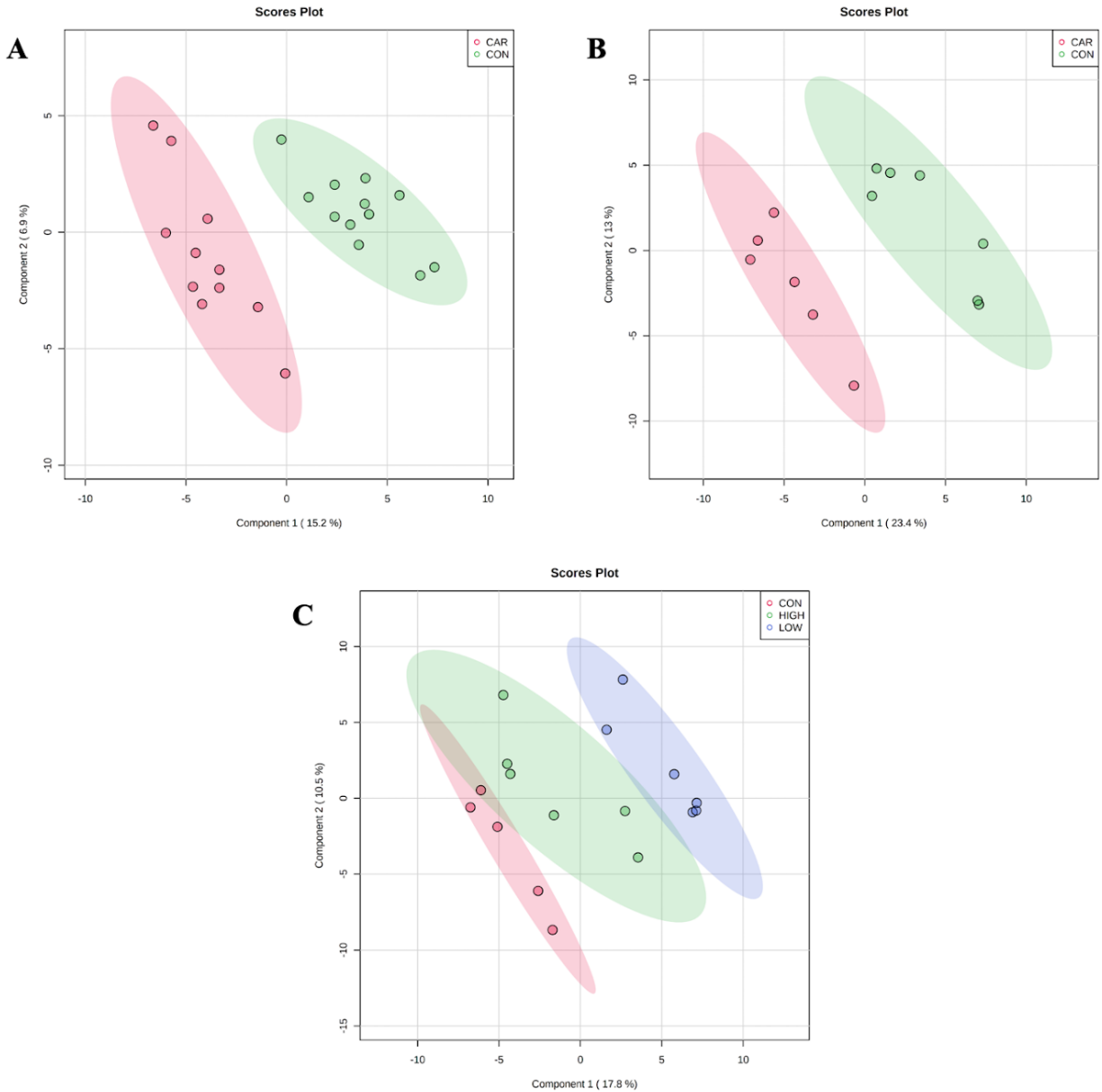


Fig. S1 Partial Least Squares Discriminant Analysis (PLS-DA) 2D score plot of the metabolites in serum showed separated clusters between the CON and CAR groups on d 5 (**A**) and d 11 (**B**) post-inoculation. Partial Least Squares Discriminant Analysis (PLS-DA) 2D score plot of the metabolites in distal colon digesta showed separated clusters between the CON and 10 or 20 mg/kg oligosaccharide-based polymer active substance groups on d 11 post-inoculation (**C**). CON = Basal nursery diet (control). LOW = Control diet supplemented with 10 mg/kg of oligosaccharide-based polymer. HIGH = Control diet supplemented with 20 mg/kg of oligosaccharide-based polymer. CAR = Control diet supplemented with 50 mg/kg carbadox. Shaded areas in different colors represent in 95% confidence interval

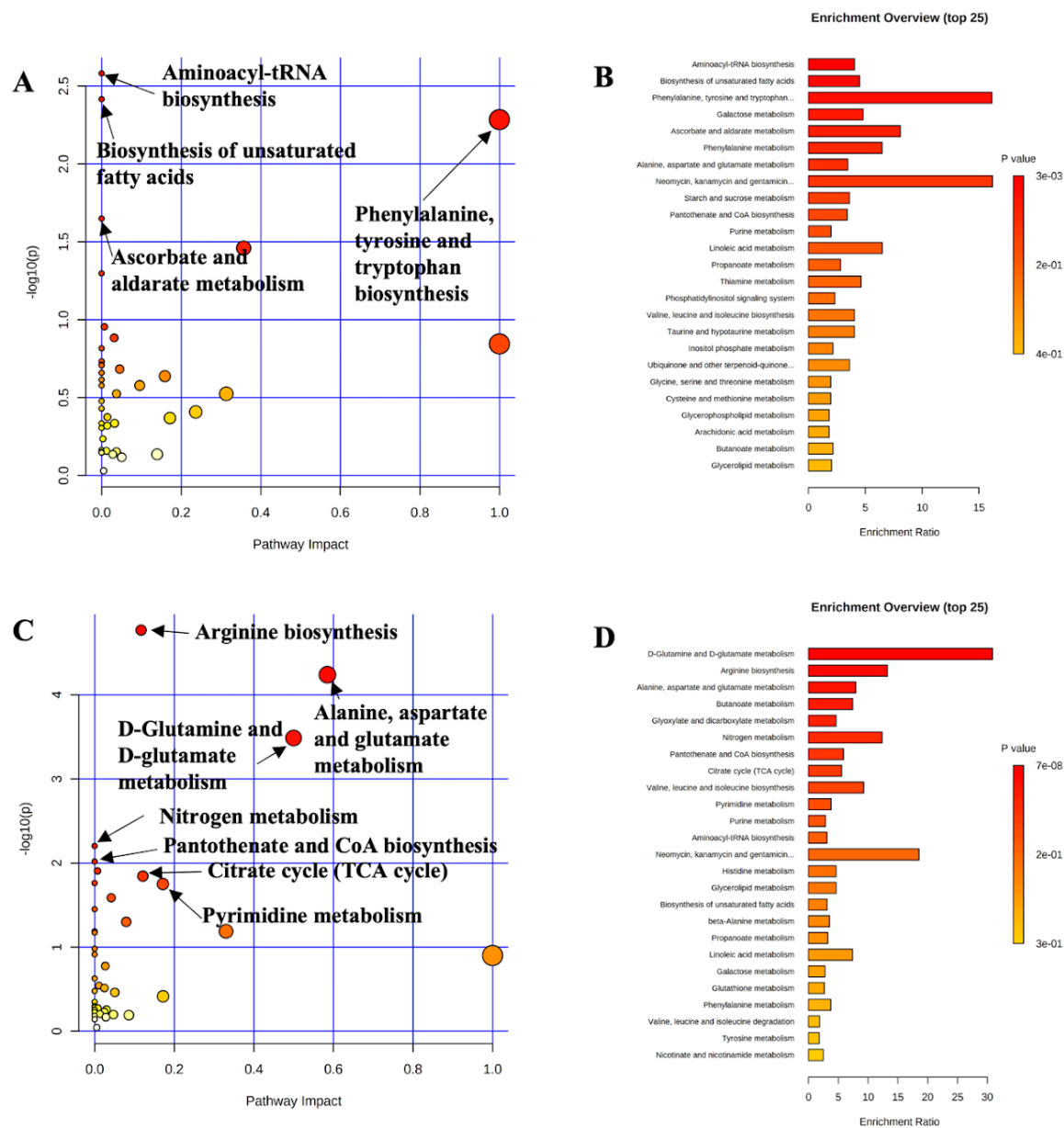


Fig. S2 Significantly changed pathways ($-\log P$ value > 1.5) in serum between the control and 50 mg/kg carbadox on d 5 (A) or d 11 (C) post-inoculation. The x-axis represents the pathway impact values and the y-axis represents the $-\log(P)$ values from the pathway enrichment analysis. Metabolite set enrichment analysis (B and D) shows the metabolic pathways were altered in control compared to 50 mg/kg carbadox on d 5 or d 11 post-inoculation, respectively. Both pathway analysis and metabolite set enrichment analysis were performed using identified metabolites with VIP > 1

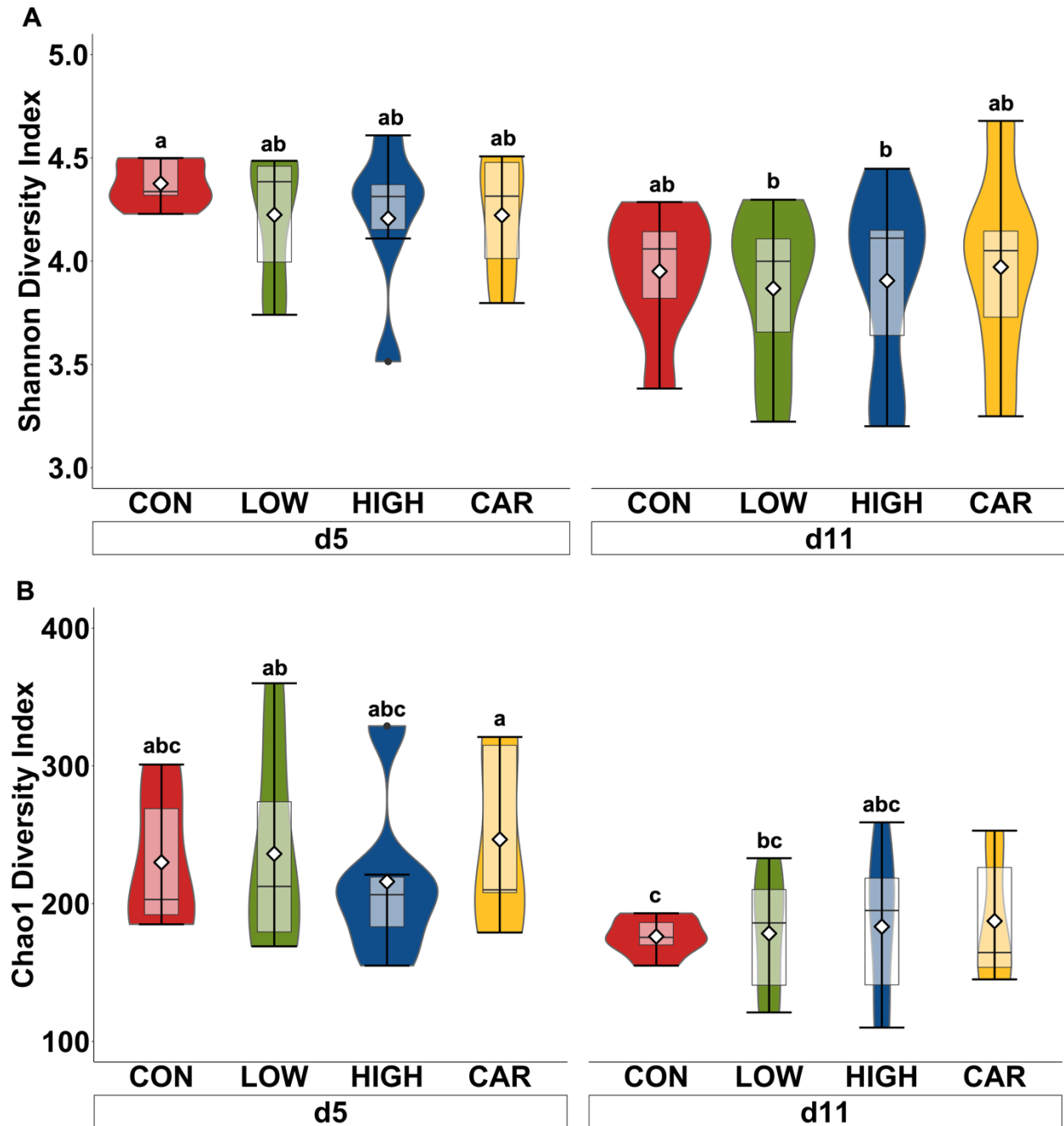


Fig. S3 Alpha diversity as indicated by Shannon (A) and Chao 1 (B) in distal colon digesta of enterotoxigenic *E. coli* F18 challenged pigs fed diets supplemented with different dose of oligosaccharide-based polymer active substance or antibiotics (carbadox) on d 5 and 11 post-inoculation. ^{a-c}Means without a common superscript are different ($P < 0.05$). Each least squares mean represents 6 observations. CON = Basal nursery diet (control); LOW = Control diet supplemented with 10 mg/kg oligosaccharide-based polymer active substance; HIGH = Control diet supplemented with 20 mg/kg

oligosaccharide-based polymer active substance; CAR = Control diet supplemented with 50 mg/kg carbadox

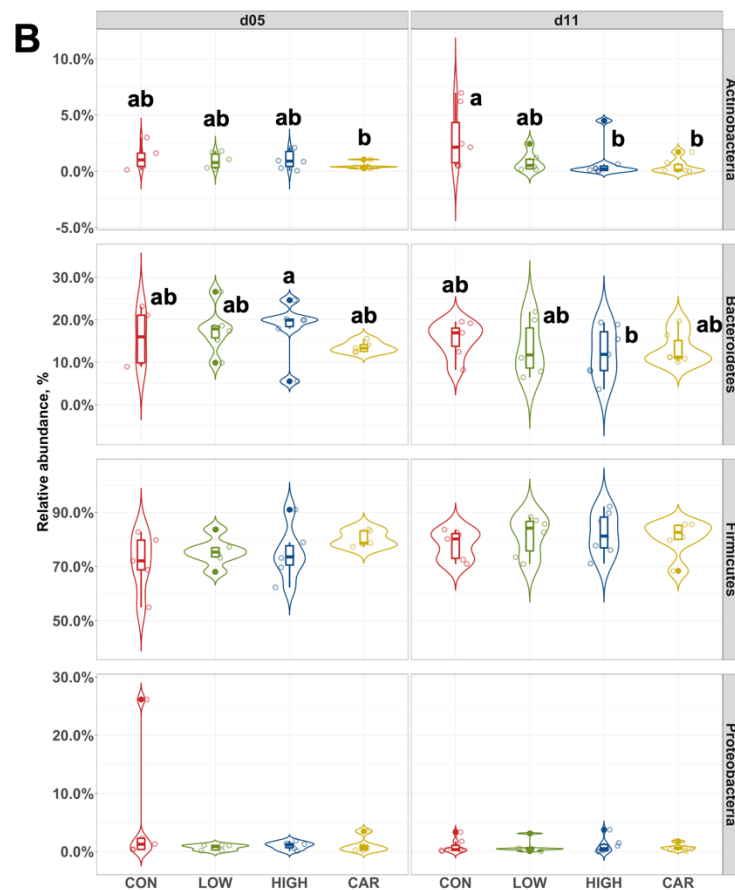
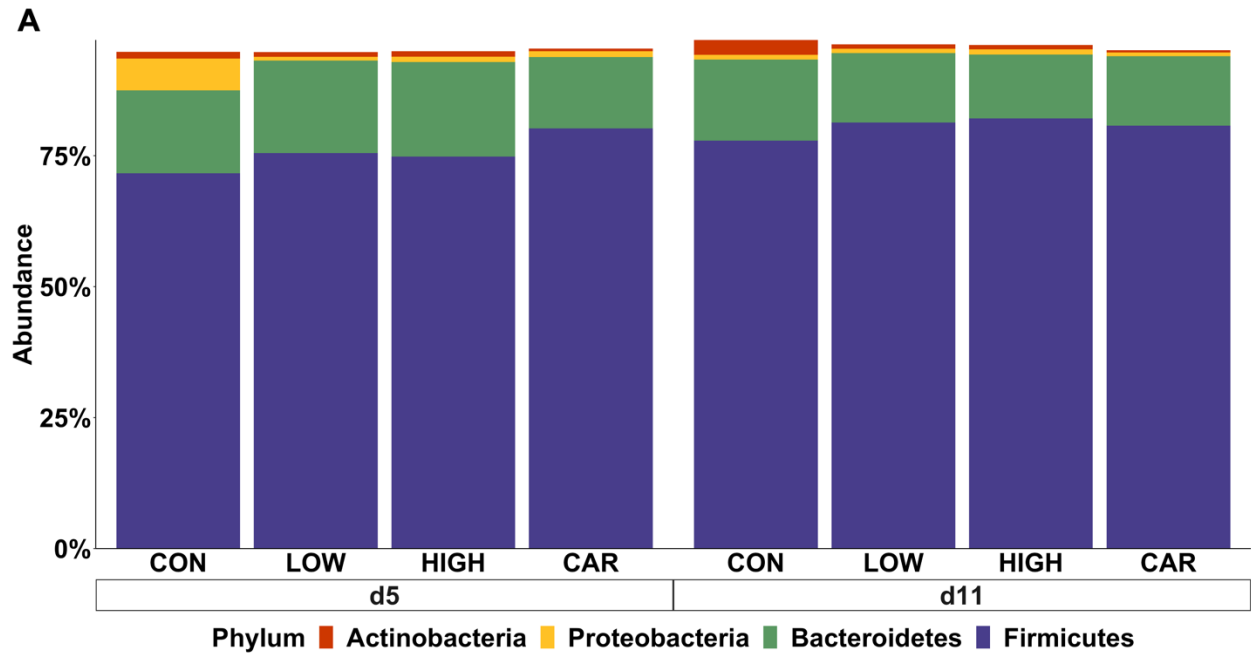


Fig. S4 Stacked bar plot showing the relative abundance of bacterial phyla in colon digesta of enterotoxigenic *E. coli* F18 challenged pigs fed diets supplemented with different dose of oligosaccharide-based polymer active substance or antibiotics (carbadox) on d 5 and 11 post-inoculation

(A). Violin plot showing the relative abundance of individual bacterial phylum (B). ^{a,b}Means without a common superscript are different ($P < 0.05$). Each least squares mean represents 6 observations. CON = Basal nursery diet (control); LOW = Control diet supplemented with 10 mg/kg oligosaccharide-based polymer active substance; HIGH = Control diet supplemented with 20 mg/kg oligosaccharide-based polymer active substance; CAR = Control diet supplemented with 50 mg/kg carbadox