Fig S1. Inhibition (%) of APEC growth by peptides at **A)** 6 mM and **B)** 12 mM concentrations. Peptides were added to the wells of the 96-well plate containing APEC suspension ($5x10^5$ CFU/mL) and incubated at 37°C in TECAN Sunrise™ absorbance microplate reader with kinetic absorbance measurement set at every 30 mins for 12 h. The inhibition (%) was calculated using the formula: (OD_{600} DMSO treated well- OD_{600} peptide treated well)/OD_{600} DMSO treated well x 100%.

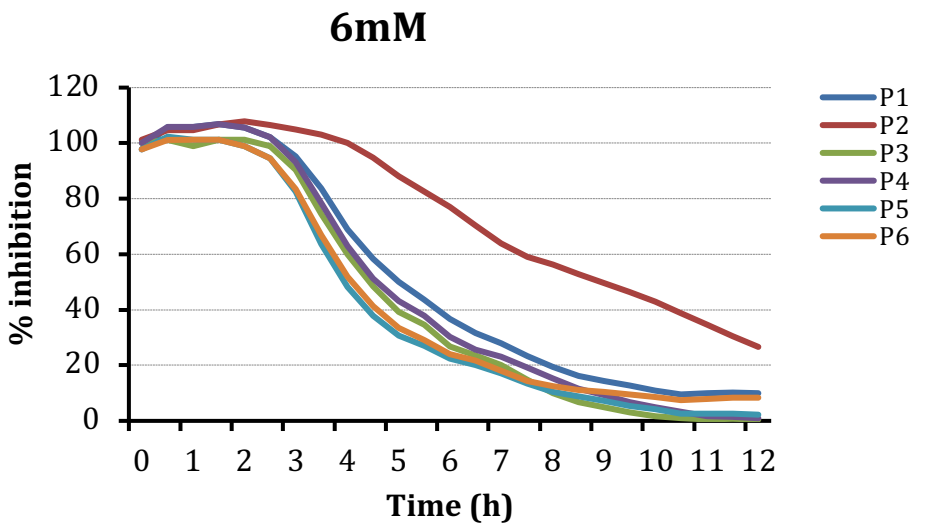
Fig. S2. Shannon's diversity index measuring the microbial richness in cecum of chickens treated with peptides at **A)** 50 mg/kg and **B)** 100 mg/kg dose, NC: non-infected and non-treated chickens, PC: infected but not treated chickens. $^{*}P<0.05$, Kruskal-Wallis test.

Fig. S3: Principal Coordinates Analysis (PCoA) plot comparing the microbial communities (weighted unifrac beta-diversity) in cecum of chickens treated with peptides at **A)** 50 mg/kg and **B)** 100 mg/kg dose, NC: non-infected and non-treated chickens, PC: infected but not treated chickens.

Fig. S4. **A)** Schematic diagram showing the experimental design to test the efficacy of peptides in commercial broiler chickens. Peptides were administered through orally twice a day from day 1 to day 7 either at 50 mg/kg or 100 mg/kg dose. On day 2, chickens were infected orally with Rif^r APEC O78 ($1\text{-}2 \times 10^9$ CFU/chicken). At day 9, chickens were euthanized, necropsied and cecum and internal organs (lung, liver, heart and kidney) were processed for quantification of APEC load. The body weight of chickens was measured at day 9.

Figure S1

A


6mM
120
100
80
60
40
20
0
% inhibition
0 1 2 3 4 5 6 7 8 9 10 11 12
Time (h)
P1
P2
P3
P4
P5
P6

B

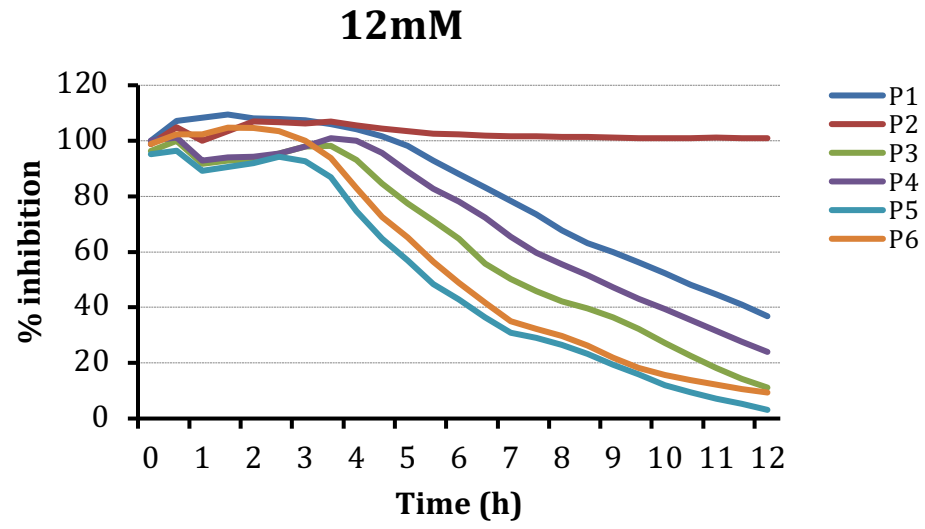
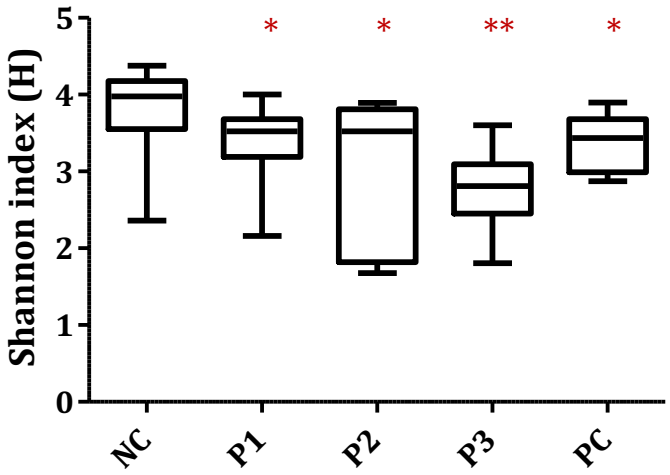

12mM
120
100
80
60
40
20
0
% inhibition
0 1 2 3 4 5 6 7 8 9 10 11 12
Time (h)
P1
P2
P3
P4
P5
P6

Figure S2

A


Shannon index (H)
5
4
3
2
1
0
*
*
**
*
NC
P1
P2
P3
PC

B

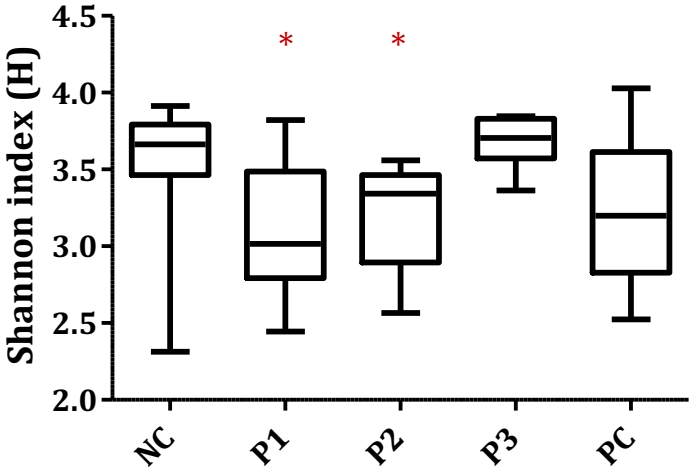
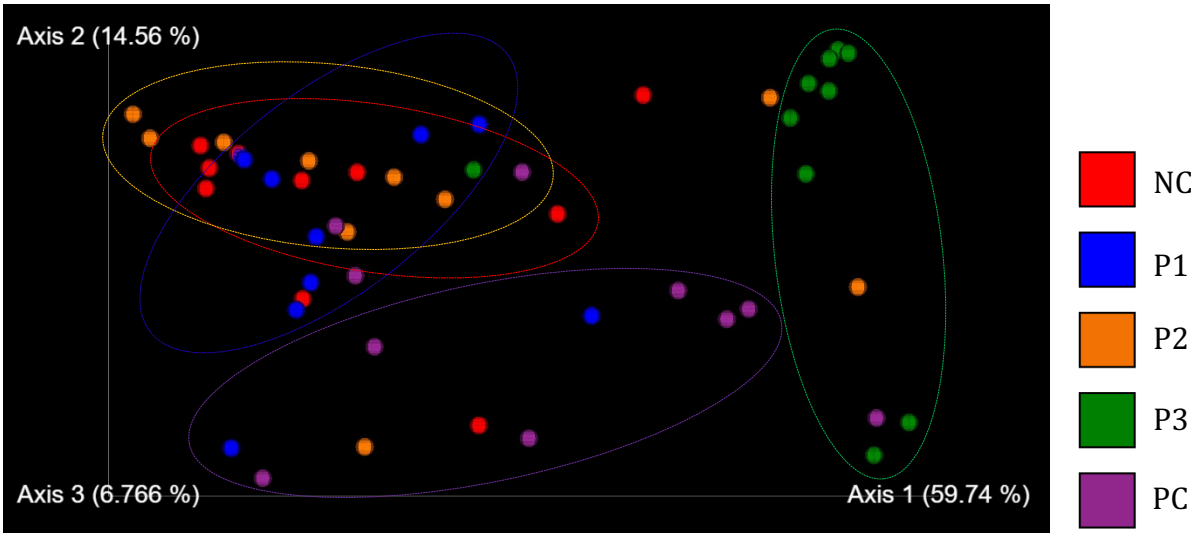

Shannon index (H)
4.5
4.0
3.5
3.0
2.5
2.0
*
*
NC
P1
P2
P3
PC

Figure S3

A


Axis 2 (14.56 %)
Axis 3 (6.766 %)
Axis 1 (59.74 %)
NC
P1
P2
P3
PC

B

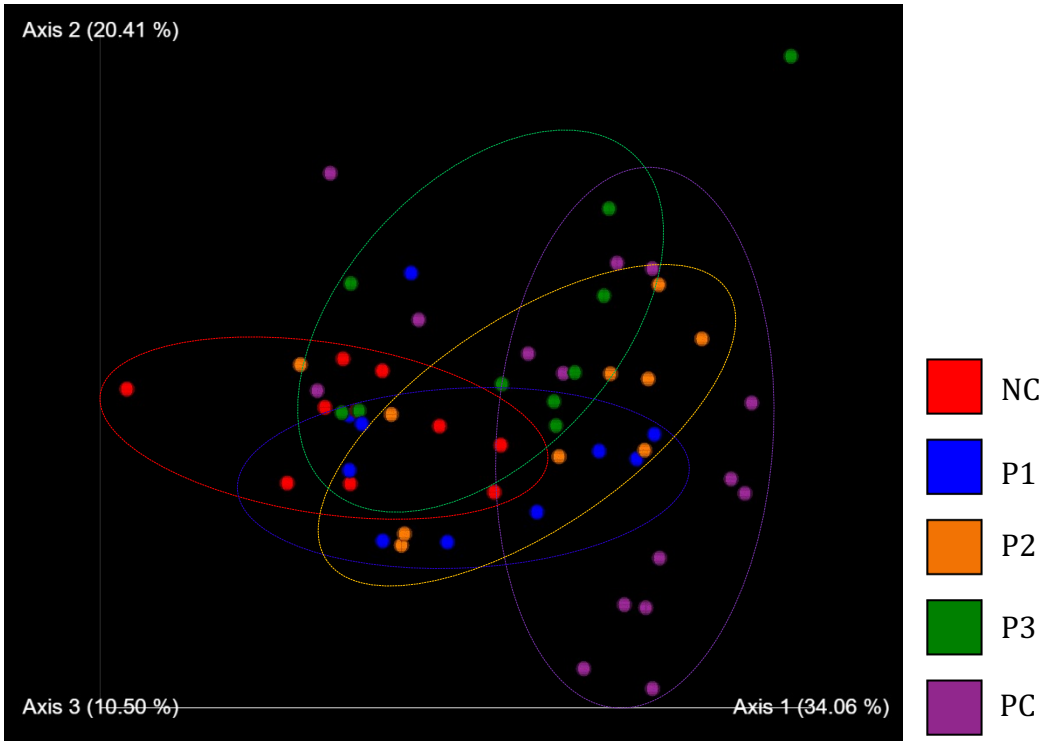

Axis 2 (20.41 %)
Axis 3 (10.50 %)
Axis 1 (34.06 %)
NC
P1
P2
P3
PC

Figure S4

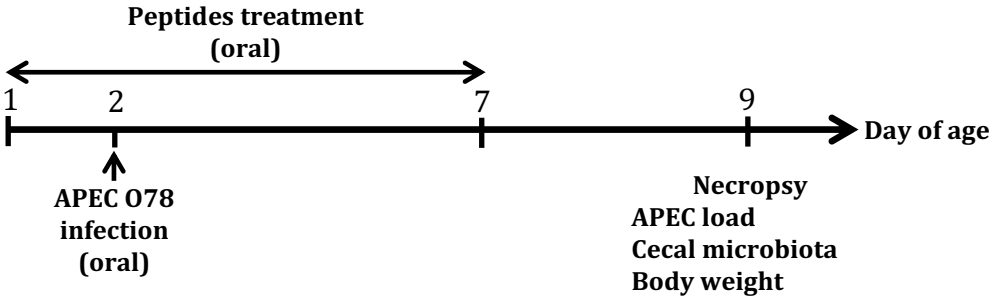

Peptides treatment
(oral)
1
2
7
9
Day of age
APEC O78
infection
(oral)
Necropsy
APEC load
Cecal microbiota
Body weight

Table S1. MIC_{50} concentrations of peptides against APEC O78**.**

Peptide	MIC_{50} (mM)
P1	14.7
P2	9.5
P3	16.2
P4	20.0

Table S2. Sequence of alanine analogues of peptides.

Peptide	Sequence
P1-1	**A**PSRQERR
P1-2	N**A**SRQERR
P1-3	NP**A**RQERR
P1-4	NPS**A**QERR
P1-5	NPSR**A**ERR
P1-6	NPSRQ**A**RR
P1-7	NPSRQE**A**R
P1-8	NPSRQER**A**
P2-1	**A**DENK
P2-2	P**A**ENK
P2-3	PD**A**NK
P2-4	PDE**A**K
P2-5	PDEN**A**
P3-1	**A**HTAPK
P3-2	V**A**TAPK
P3-3	VH**A**APK
P3-4	VHTA**A**K
P3-5	VHTAP**A**