Supplementary Table S1. Animal experimental protocol

Groups	Samples	7 days treatments
Control	*n* = 6	Mice were given drinking water
Cd	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$
Cd+EDTA	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 100 mg/kg per day of EDTA
Cd+Milk	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 100 mg/kg per day of milk
Cd+L-OPs	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 100 mg/kg per day of OPs
Cd+H-OPs	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 300 mg/kg per day of OPs

Supplementary Table S2. Animal experimental protocol

Group	Samples	7 days Treatments
Control	*n* = 6	Mice were given drinking water
Cd	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$
Cd+Ala(A)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Ala
Cd+Cys(C)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Cys
Cd+Asp(D)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Asp
Cd+Glu(E)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Glu
Cd+Phe(F)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Phe
Cd+Gly(G)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Gly
Cd+His(H)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of His
Cd+Ile(I)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Ile
Cd+Lys(K)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Lys
Cd+Leu(L)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Leu
Cd+Met(M)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Met
Cd+Asn(N)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Asn
Cd+Pro(P)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Pro
Cd+Gln(Q)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Gln
Cd+Arg(R)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Arg
Cd+Ser(S)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Ser
Cd+Thr(T)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Thr
Cd+Val(V)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Val
Cd+Trp(W)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Trp
Cd+Tyr(Y)	*n* = 6	Drinking water containing 100 mg/L of $CdCl_2$ and orally administered with 40 mmol/kg per day of Tyr

Supplementary Table S3. Primer sequences of target genes

Gene name	Product length (bp)	Primer sequence (5′–3′)
ZO-1	192	Forward: CTGCACGATTTCTGCTTCCTC Reverse: CCTCCATTGCTGTGCTAGTGA
Occludin	252	Forward: CTAAATTGGCATCCAGCCCAG Reverse: TCCTTTCCACTCGGGCTCA
Plakophilin-1	274	Forward: ACTATGACTGCCCACTCCCT Reverse: CCTGATTCCCGCACCACATC
β-actin	101	Forward: TGTCCACCTTCCAGCAGATGT Reverse: AGCTCAGTAACAGTCCGCCTAGA

Supplementary Table S4. PICTUSt predicted KEGG pathways of the gut microbial community in different groups

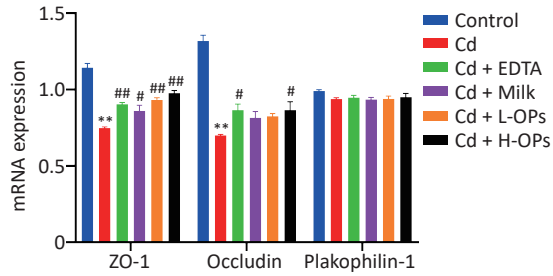
Function type	KEGG pathways	Relative abundance (%)					
		Control	Cd	Cd+EDTA	Cd+Milk	Cd+L-OPs	Cd+H-OPs
Metabolism	Amino Acid Metabolism	7.20	9.23*	8.65	8.84	8.12	7.94#
	Carbohydrate Metabolism	7.20	8.78*	8.32#	8.34#	7.87#	7.73#
	Xenobiotics Biodegradation and Metabolism	7.63	7.23	7.42	7.54	7.78	7.72
	Lipid Metabolism	8.89	9.12	8.94	8.97	8.83	8.81
	Energy Metabolism	4.24	4.94*	4.42#	4.46#	4.34#	4.32#
	Glycan Biosynthesis and Metabolism	5.08	5.34*	5.28	5.29	5.18	5.14
	Metabolism of Cofactors and Vitamins	5.93	5.96	5.88	5.92	5.76#	5.74#
	Metabolism of Terpenoids and Polyketides	4.66	4.89	4.77	4.82	4.74	4.72
	Metabolism of Other Amino Acids	3.81	4.24	4.18	4.14	4.08	3.97#
	Biosynthesis of Other Secondary Metabolites	5.08	5.17	5.14	5.16	5.12	5.10
Human Diseases	Infectious Diseases	0.43	0.41	0.44	0.45	0.42	0.46
	Neurodegenerative Diseases	0.24	0.32	0.25	0.26	0.23	0.22
Genetic Information Processing	Translation	3.82	4.18*	3.84#	3.92	3.88#	3.83#
	Folding, Sorting and Degradation	2.96	3.44*	3.21#	3.35	3.18#	3.16#

Note. *Significant difference from the control group at $P < 0.05$. #Significant difference from the Cd-exposed group at $P < 0.05$.

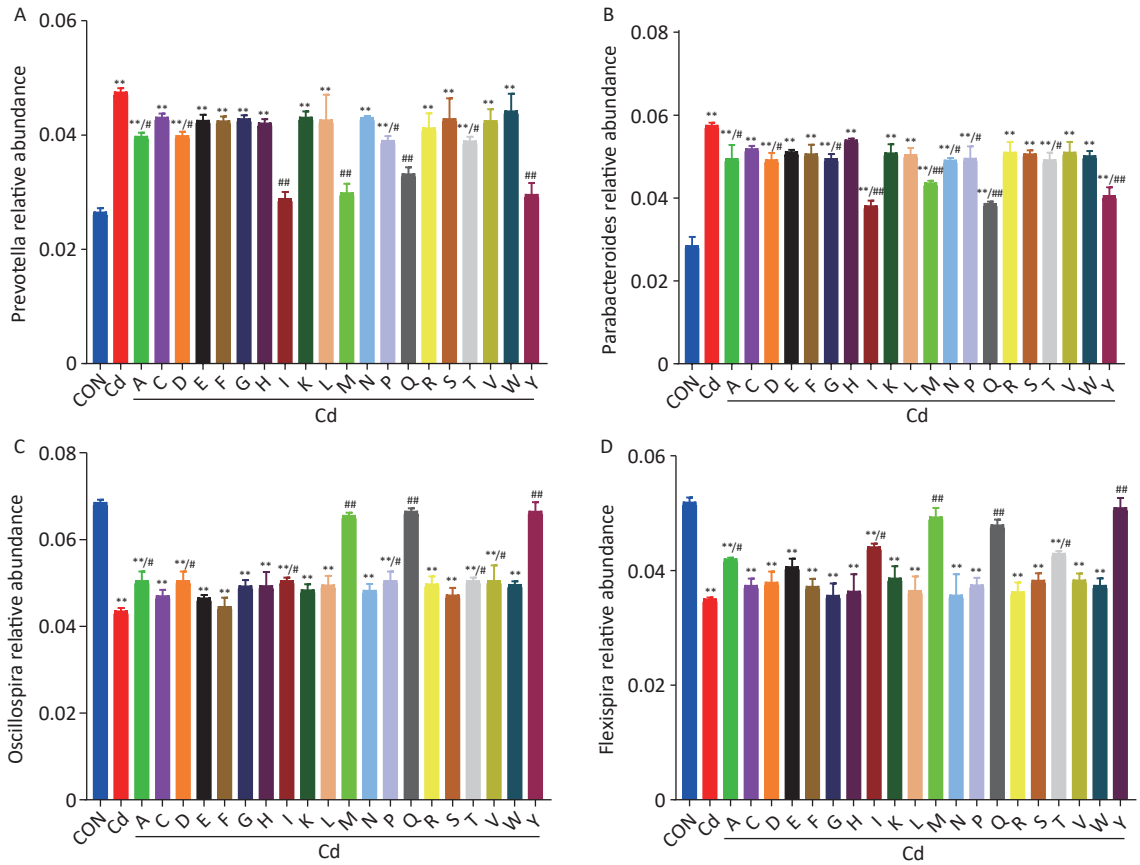
Supplementary Table S5. Composition and contents of amino acids of OPs and milk (μg/g)

Amino acids	Contents in milk	Contents in OPs
Ala#	3.45 ± 0.14	1499.88 ± 119.08
Cys	ND	24.24 ± 10.71
Asp	0.47 ± 0.08	136.22 ± 10.71
Glu	13.98 ± 0.01	1267.78 ± 72.61
Phe*#	2.27 ± 0.05	1652.84 ± 176.83
Gly	ND	ND
His	3.83 ± 0.17	1463.54 ± 86.01
Ile*#	3.86 ± 0.05	8964.73 ± 489.29
Lys*	6.17 ± 0.11	598.17 ± 301.07
Leu*#	4.91 ± 0.11	991.21 ± 26.48
Met*#	0.88 ± 0.01	4899.66 ± 148.11
Asn	6.84 ± 0.02	529.08 ± 63.47
Pro#	3.18 ± 0.08	1409.75 ± 32.95
Gln	1.61 ± 0.04	2327.62 ± 96.69
Arg	1.46 ± 0.02	ND
Ser	0.51 ± 0.01	288.53 ± 35.01
Thr*	0.32 ± 0.02	820.61 ± 43.03
Val*#	8.89 ± 0.26	877.9 ± 134.03
Trp	1.69 ± 0.03	1142.69 ± 28.61
Tyr#	6.12 ± 0.27	10236.49 ± 270.07
Total amino acids	70.55 ± 0.91	39131.02 ± 2083.37
Essential amino acid	27.35 ± 0.37	18805.14+1265.91
Hydrophobic amino acids	33.60 ± 0.84	30532.49 ± 1343.91

Note. *Essential amino acid. #Hydrophobic amino acids.



Supplementary Figure S1. Gut mRNA levels of tight junction genes (occludin, ZO-1, and plakophilin-1) determined by quantitative real-time PCR. ZO-1 (zonula occludens-1). $^{**}P < 0.01$; significant difference from the control group. $^{\#}P < 0.05$ and $^{\#\#}P < 0.01$; significant difference from the Cd-treated group.



Supplementary Figure S2. Effects of amino acids on the relative abundance of key gut microbiota (A–D: *Prevotella*, *Parabacteroides*, *Oscillospira*, and *Flexispira*) in mice. A (Alanine); C (Cysteine); D (Aspartic acid); E (Glutamic acid); F (Phenylalanine); G (Glycine) ; H (Histidine); I (Isoleucine); K (Lysine); L (leucine); M (Methionine); N (Asparagine); P (Proline); Q (Glutamine); R (Arginine); S (Serine); T (Threonine); V (Valine); W (Tryptophan); Y (Tyrosine). $^{**}P < 0.01$; significant difference from the control group. $^{\#}P < 0.05$ and $^{\#\#}P < 0.01$; significant difference from the Cd-treated group.