Supporting Information

A Versatile Nanoplatform with Excellent Biofilm Permeability and Spatiotemporal ROS Regulation for Peri-Implantitis Treatment

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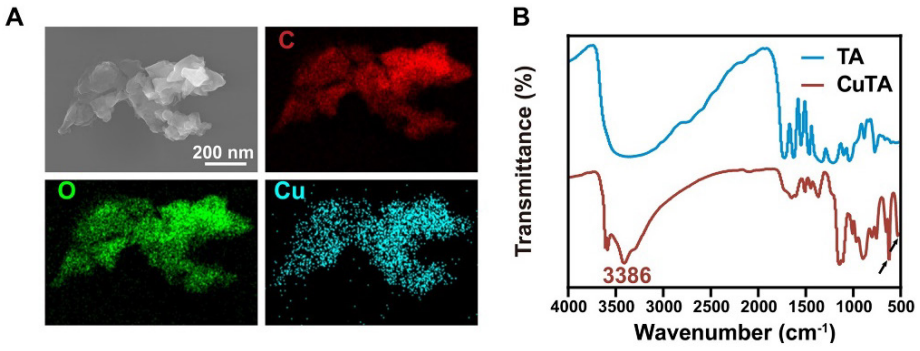

Figure S1. Characterization of CuTA. (A) SEM image and EDS-mapping analysis of CuTA. (B) FTIR of TA and CuTA.

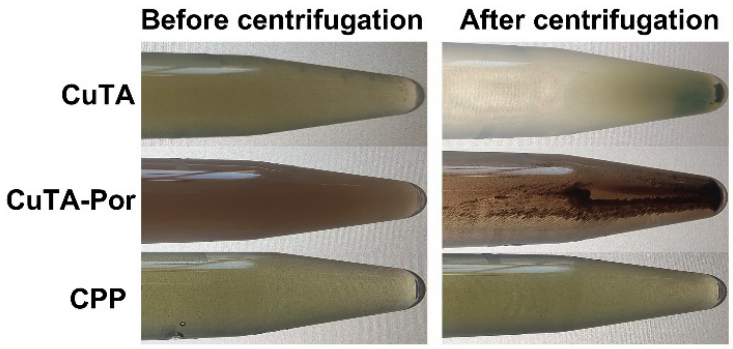

Figure S2. Images of CuTA, CuTA-Por, and CPP NPs before centrifugation and after 5 min centrifugation.

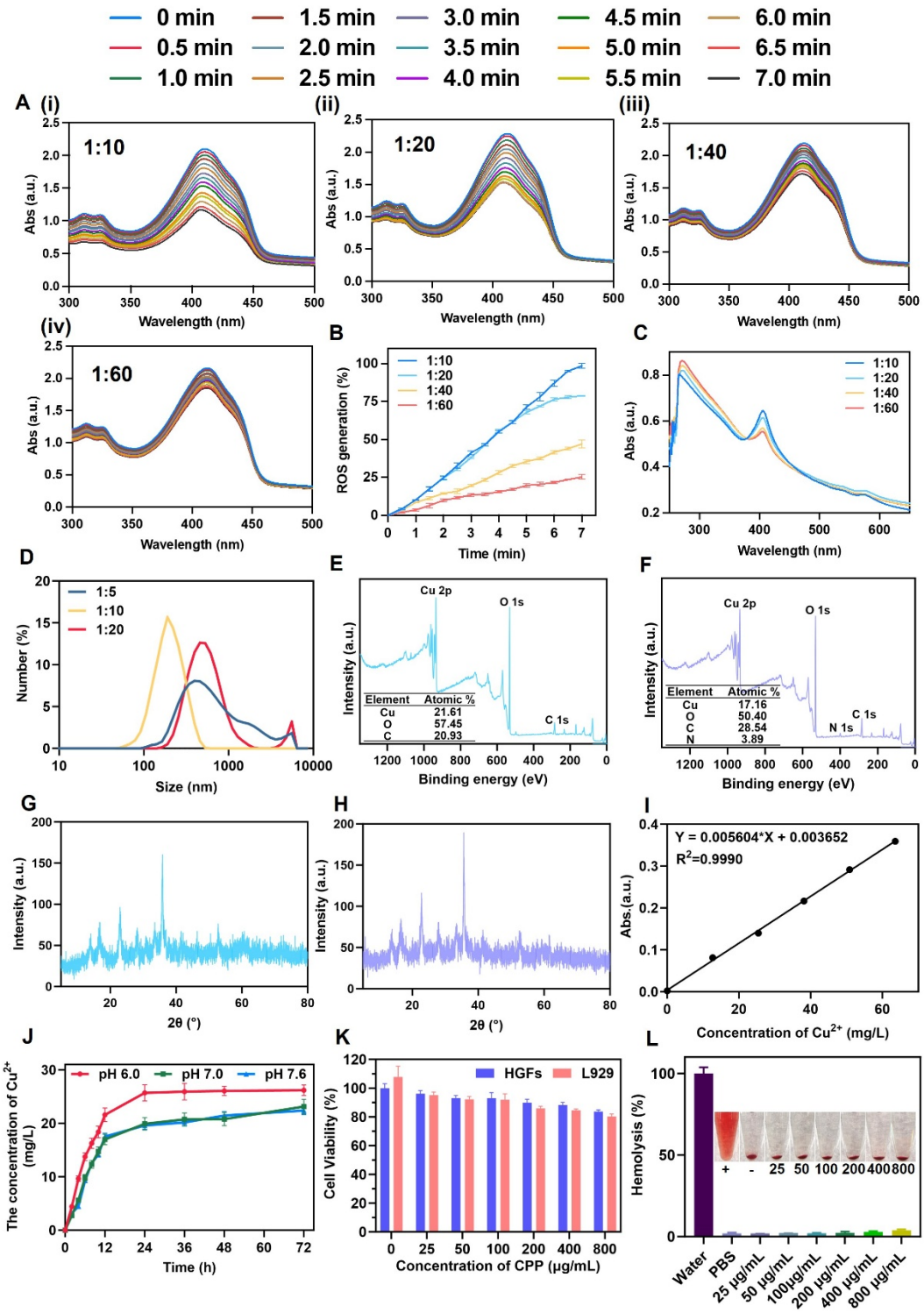

Figure S3. (A) Characterization of the *in vitro* photodynamic properties of CuTA-Por with different Por/CuTA ratios and (B) normalization analysis. (C) UV–vis spectra of CuTA-Por with different Por/CuTA ratios. (D) Hydrated particle size of CPP with different CuTA-Por/ε-PL ratios. (E) XPS spectrum of CuTA and (F) CuTA-Por. (G) XRD pattern of CuTA and (H) CuTA-Por. (I) Standard curve of Cu^{2+} and (J) the release

of Cu^{2+} from CPP at different pH. (K) CCK-8 assay of HGFs and L929 cells treated with different concentrations of CPP NPs. (L) Hemolysis assay of CPP NPs at different concentrations.

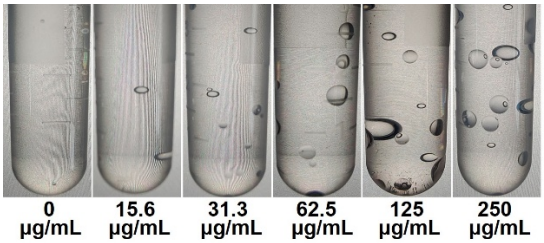

Figure S4. Images of 3% hydrogen peroxide solution after treatment with different concentrations of CPP NPs.

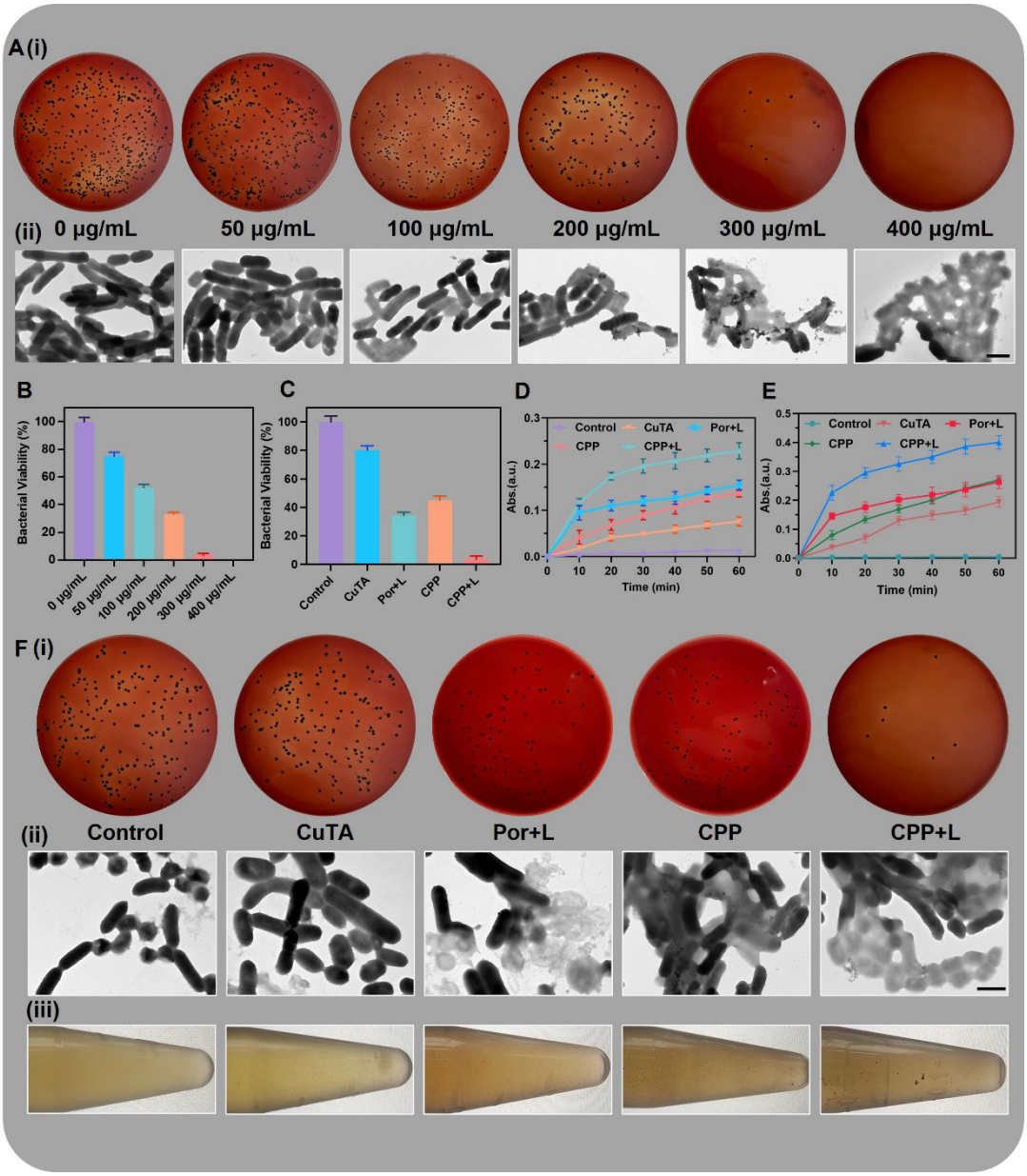

Figure S5. (A) (i) Images of colonies, (ii) TEM images, and (B) quantitative analysis of *P. gingivalis* after treatment with different concentrations of CPP NPs. Scale bar: 1 μm. (C) Quantitative analysis of *P. gingivalis* after different treatments. (D) Nucleic acid leak assay of *P. gingivalis*, the absorbance curves of *P. gingivalis* suspensions after treated with various NPs at 260 nm. (E) Protein leak assay of *P. gingivalis*. (F) (i) Images of colonies, (ii) TEM images, and (iii) photos of *P. gingivalis* after different treatments. Scale bar: 1 μm.

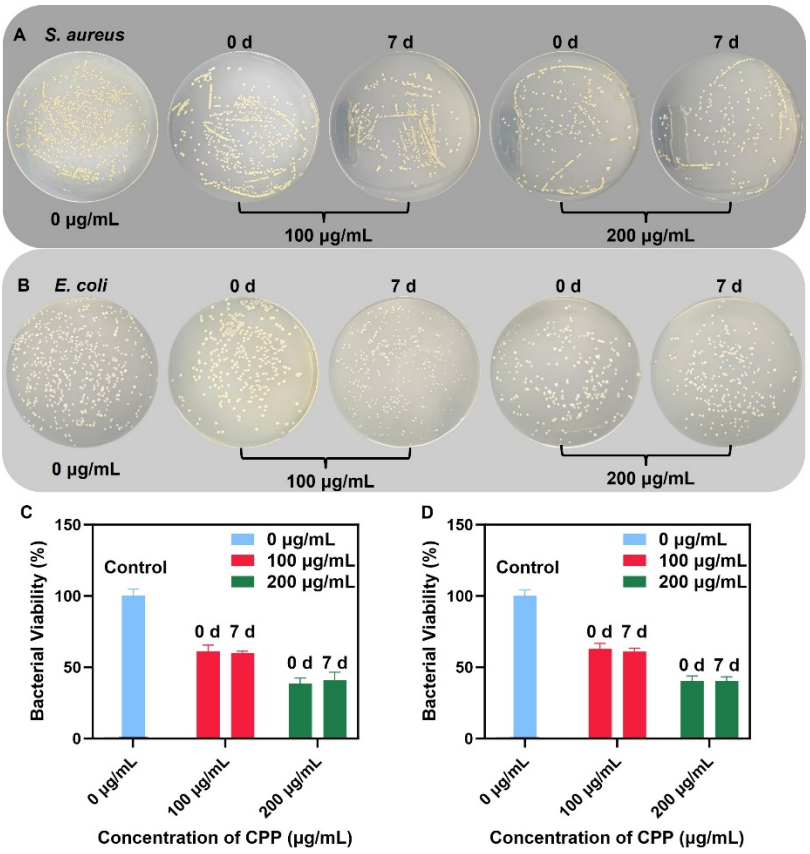

Figure S6. Evaluation of the antibacterial stability of CPP against *S. aureus* and *E. coli* after 7 days of incubation. (A) Images of *S. aureus* colonies and (C) quantitative analysis. (B) Images of *E. coli.* colonies and (D) quantitative analysis.

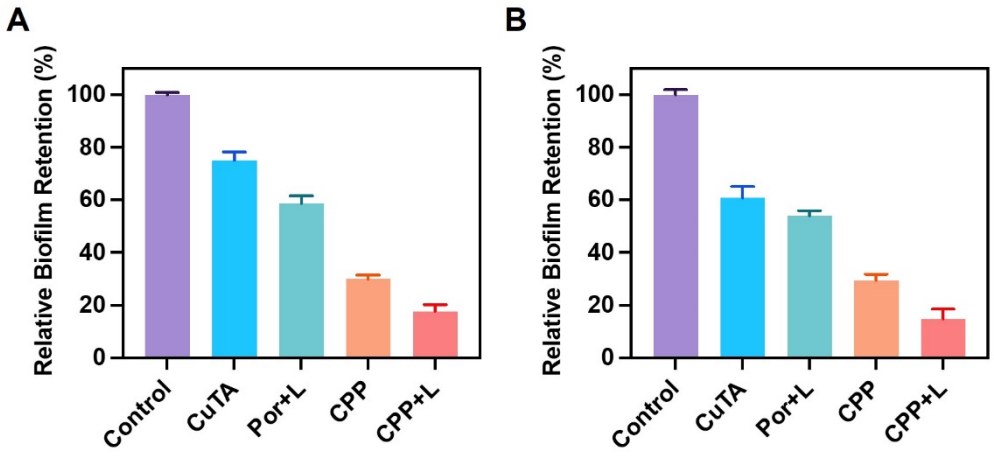

Figure S7. Quantitative analysis of the crystal violet-stained (A) established biofilms and (B) forming biofilms treated with different NPs.

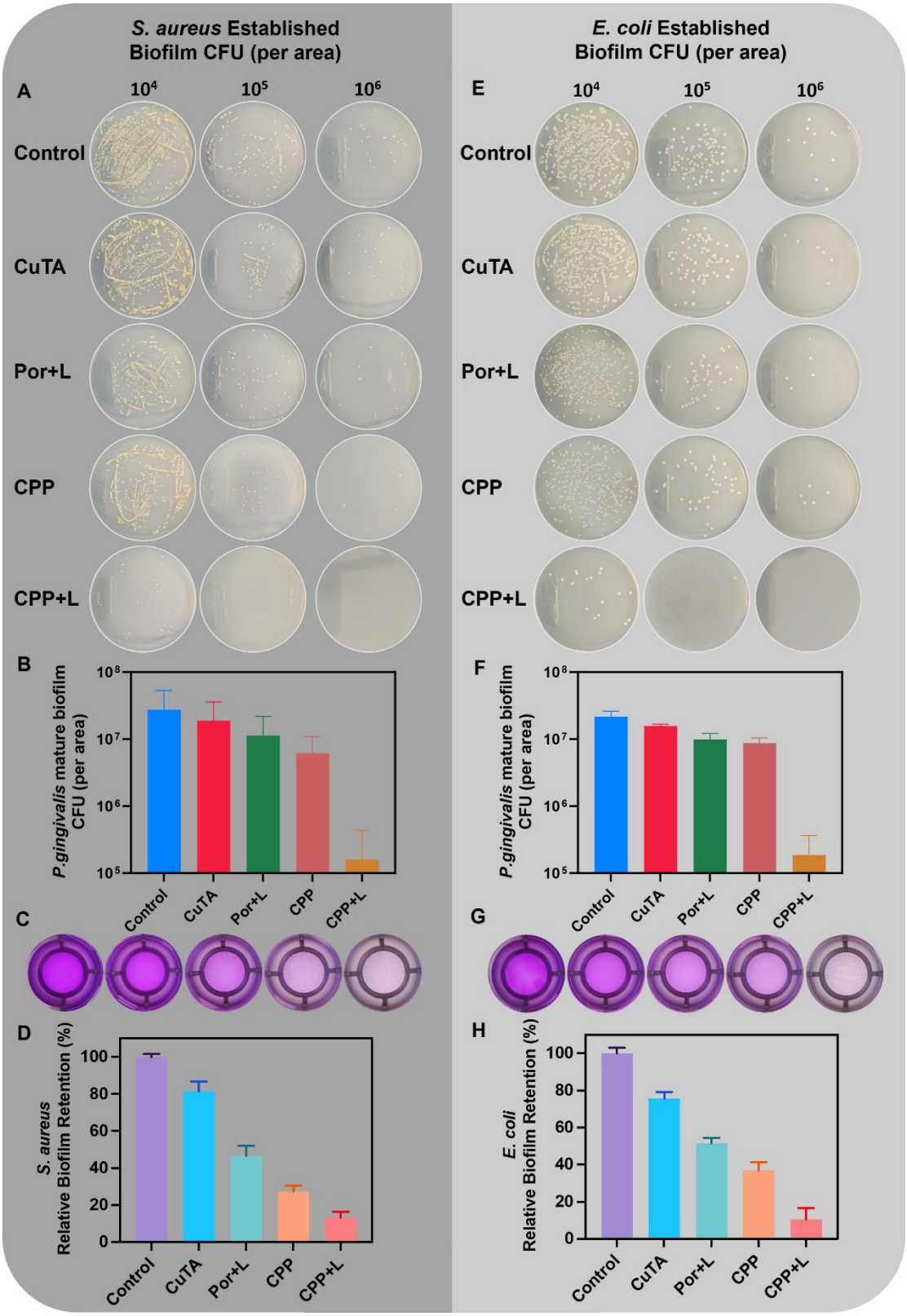

Figure S8. Antibacterial effects on established biofilms of *S. aureus* and *E. coli.* (A) Images of *S. aureus* colonies and (B) quantitative analysis. (C) Images and (D) corresponding quantitative analysis of the *S. aureus* biofilm after crystal violet staining.

(E) Images of *E. coli.* colonies and (F) quantitative analysis. (G) Images and (H) corresponding quantitative analysis of the *E. coli.* biofilm after crystal violet staining.

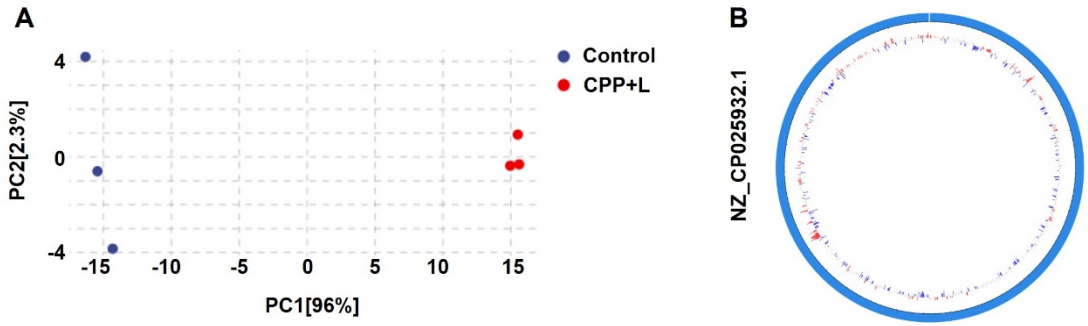

Figure S9. (A) Principal component analysis was performed based on DEGs in the *P. gingivalis* biofilm in Control and CPP+L groups. (B) Genomic cycle map based on DEGs in the *P. gingivalis* biofilm in Control and CPP+L groups.

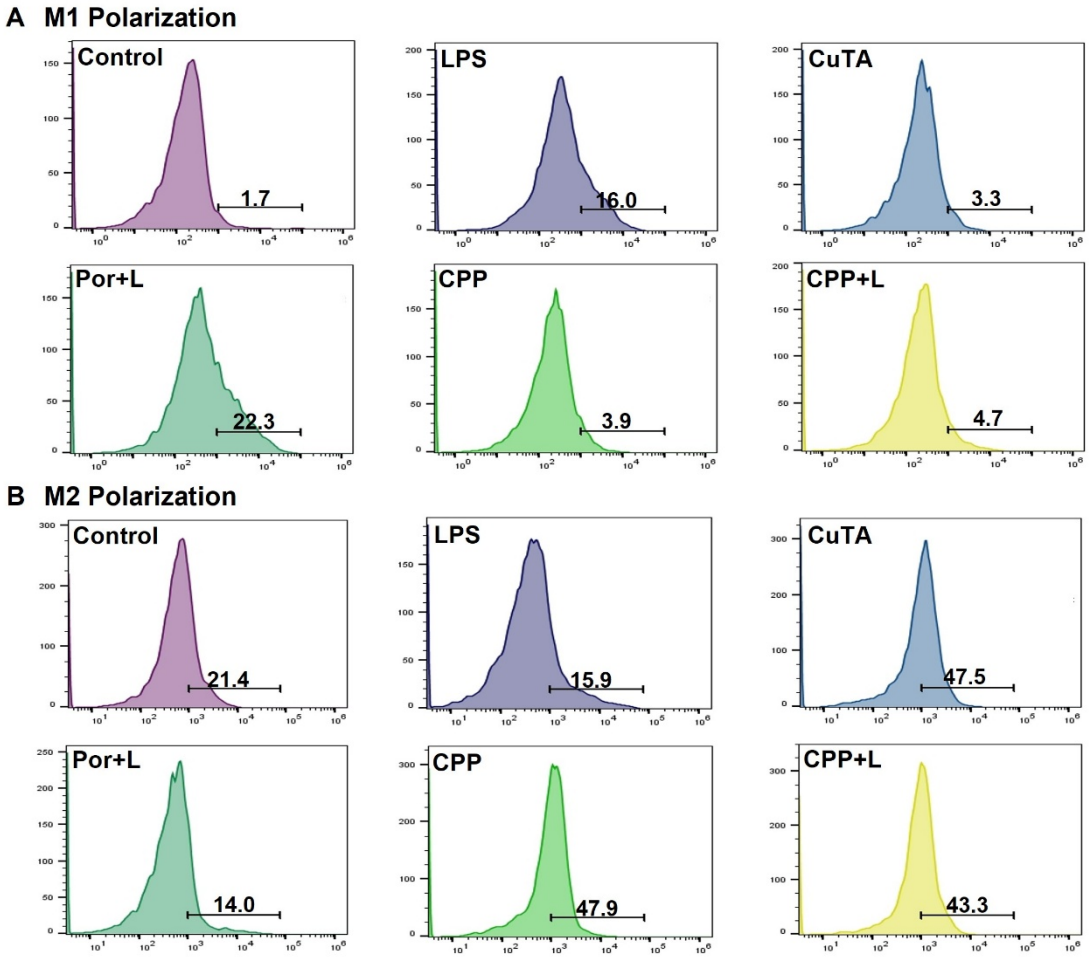

Figure S10. (A) Flow cytometry analysis of specific marker of M1 macrophage CD86

and (B) specific marker of M2 macrophage CD206.

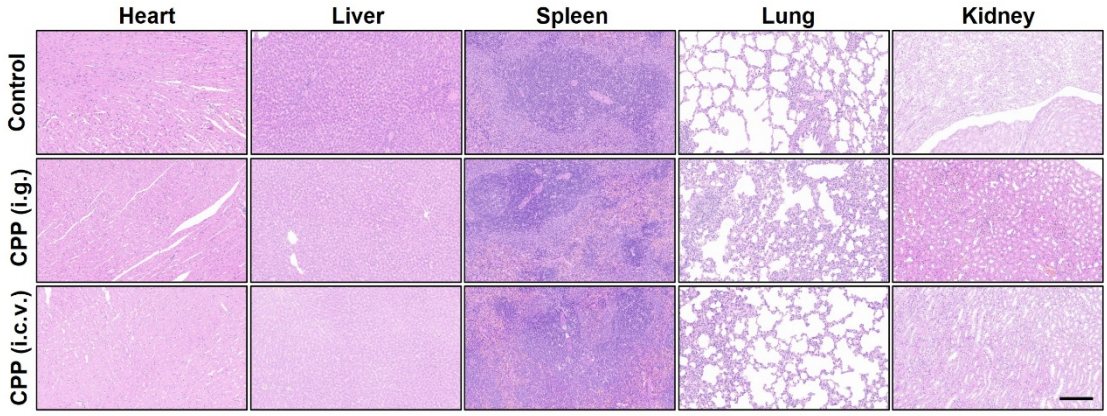

Figure S11. H&E staining of major organs of rats after different treatments. Scale bar: 200 μm.

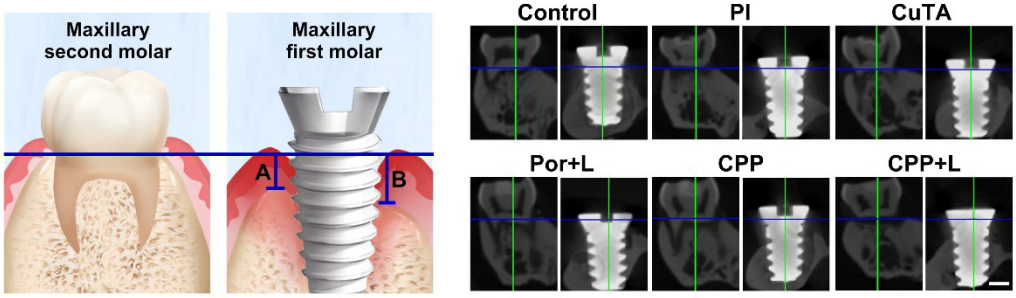

Figure S12. Scheme of the measurement of bone resorption height. Scale bar: 1 mm.

Table S1. Primer sequences used in this study.

Gene	Forward sequence (5' to 3')	Reverse sequence (5' to 3')
16s rRNA	TGTAGATGACTGATGGTGAAA	ACTGTTAGCAACTACCGATGT
Rgp A	CTGCGAGCGGTATTAGTGGT	CTACCAGCCCGTTTCCAACT
Rgp B	TCGGGACAAGTGTACGAACG	AACCAGTCTTGGGCTTCTCC
Kgp	AGCTGACAAAGGTGGAGACCAAAGG	TGTGGCATGAGTTTTTCGGAACCGT
Fim II	ACAACTATACTTATGACAATGG	AACCCCGCTCCCTGTATTCCGA
Fim IV	CTATTCAGGTGCTATTACCCAA	AACCCCGCTCCCTGTATTCCGA

Table S2. Primer sequences used in this study.

Gene	Forward sequence (5' to 3')	Reverse sequence (5' to 3')
β-Actin	CATCCGTAAAGACCTCTATGCCAAC	ATGGAGCCACCGATCCACA

IL-1β	TCCAGGATGAGGACATGAGCAC	GAACGTCACACACCAGCAGGTTA
IL-6	CCACTTCACAAGTCGGAGGCTTA	CCAGTTTGGTAGCATCCATCATTTC
TNF-α	ACTCCAGGCGGTGCCTATGT	GTGAGGGTCTGGGCCATAGAA
IL-10	CCAGTACAGCCGGGAAGACA	GAAGGCAGTCCGCAGCTCTA
TGF-β	CTTCAGCCTCCACAGAGAAGAACT	TGTGTCCAGGCTCCAAATATAG
Arg-1	TCATGGAAGTGAACCCAACTCTTG	TCAGTCCCTGGCTTATGGTTACC

Table S3. Routine blood test of rats after 7 days of treatments.

	Normal range	Control	CPP (i.g.)	CPP (i.c.v.)
WBC	1.90-16.80 (10^9/L)	4.49±0.35	4.66±0.40	4.61±0.56
Neu#	0.35-6.30 (10^9/L)	0.52±0.04	0.47±0.33	0.55±0.07
Lym#	0.91-12.20 (10^9/L)	3.50±0.25	3.94±1.92	3.80±0.49
Mon#	0.08-2.30 (10^9/L)	0.33±0.03	0.17±0.10	0.20±0.00
Eos#	0.00-0.60 (10^9/L)	0.11±0.06	0.08±0.04	0.06±0.01
Bas#	0.00-0.10 (10^9/L)	0.04±0.01	0.01±0.01	0.00±0.00
Neu%	7.30-50.00 (%)	11.55±0.05	8.65±2.65	11.80±0.20
Lym%	40.00-88.90 (%)	77.90±0.60	86.15±1.15	82.50±0.70
Mon%	2.00-18.00 (%)	7.40±1.10	3.35±0.55	4.20±0.50
Eos%	0.50-6.00 (%)	2.35±0.95	1.75±0.05	1.45±0.45
Bas%	0.00-1.00 (%)	0.80±0.08	0.10±0.00	0.05±0.05
RBC	5.00-9.80 (10^{12}/L)	5.89±0.81	7.91±0.66	7.47±0.15
HGB	120.00-170.00 (g/L)	125.50±8.50	155.00±3.00	146.50±2.50
HCT	32.00-53.00 (%)	39.65±5.25	50.70±2.30	48.00±0.30
MCV	50.00-67.00 (fL)	67.35±0.35	64.25±2.45	64.30±0.80
MCH	16.00-23.00 (pg)	21.55±1.55	19.70±1.30	19.60±0.00
MCHC	300.00-370.00 (g/L)	320.00±21.00	306.00±8.00	305.00±4.00
RDW-CV	11.00-16.00 (%)	15.45±0.15	12.90±0.20	13.90±0.10
RDW-SD	30.00-50.00 (fL)	39.05±0.45	31.65±1.95	34.00±0.65
PLT	250.00-1500.00 (10^9/L)	840.00±98.00	871.50±10.50	962.50±30.50
MPV	4.80-7.50 (fL)	10.85±0.55	9.40±1.00	9.20±0.20
PDW	12.00-17.50	15.90±0.10	15.75±0.15	15.65±0.15
PCT	0.20-0.78 (%)	0.71±0.06	0.72±0.09	0.79±0.01

Table S4. Liver and kidney functions test of rats after 7 days of treatments.

	Normal range	Control	CPP (i.g.)	CPP (i.c.v.)
Liver Function				
ALT	21.53-61.75 (U/L)	30.62±3.16	35.06±4.77	31.61±1.12
AST	41.47-195.65 (U/L)	104.40±18.00	176.67±0.95	159.39±7.74
ALB	21.16-34.77 (g/L)	33.76±0.26	38.97±1.98	33.72±0.76
ALP	12.04-610.97 (U/L)	198.44±67.21	229.96±66.64	103.54±2.27
γ-GT	0.58-6.81 (U/L)	4.53±0.18	3.07±1.41	4.55±0.03
DBIL	2.24-16.892 (μM)	9.27±1.49	10.08±2.17	6.68±0.71
TBIL	2.57-36.85 (μM)	21.11±7.45	24.47±5.34	19.62±0.25

TBA	9.03-14.54 (μM)	12.77±0.23	12.14±1.39	12.20±0.65
Renal Function				
BUN	9.75-22.71 (mg/dL)	16.79±3.59	18.07±1.73	14.14±0.04
CREA	10.90-118.07 (mM)	26.54±6.42	27.25±7.70	20.96±2.09
UA	58.38-122.65 (μM)	68.77±3.85	76.97±6.45	71.52±4.21