Supporting information

Nanoparticle-encapsulated baicalein markedly modulates pro-inflammatory response in gingival epithelial cells

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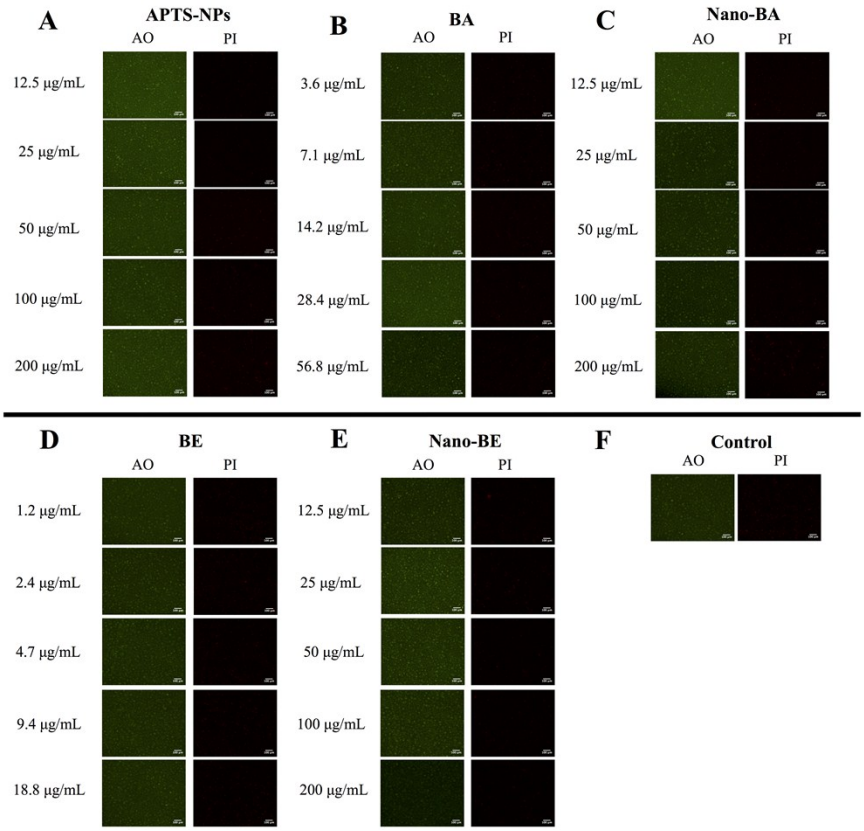

Fig. S1 Fluorescent images showing the viable cells (stained in green by AO) and dead cells (stained in red by PI) after 24-h treatments of APTS-NPs (12.5-200 μg/mL) (A), BA (3.6-56.8 μg/mL) (B), Nano-BA (12.5-200 μg/mL) (C), BE (1.2-8.8 μg/mL) (D) and Nano-BE (12.5-200 μg/mL) (E) with reference to controls (F). The scale bars are 100 μm.

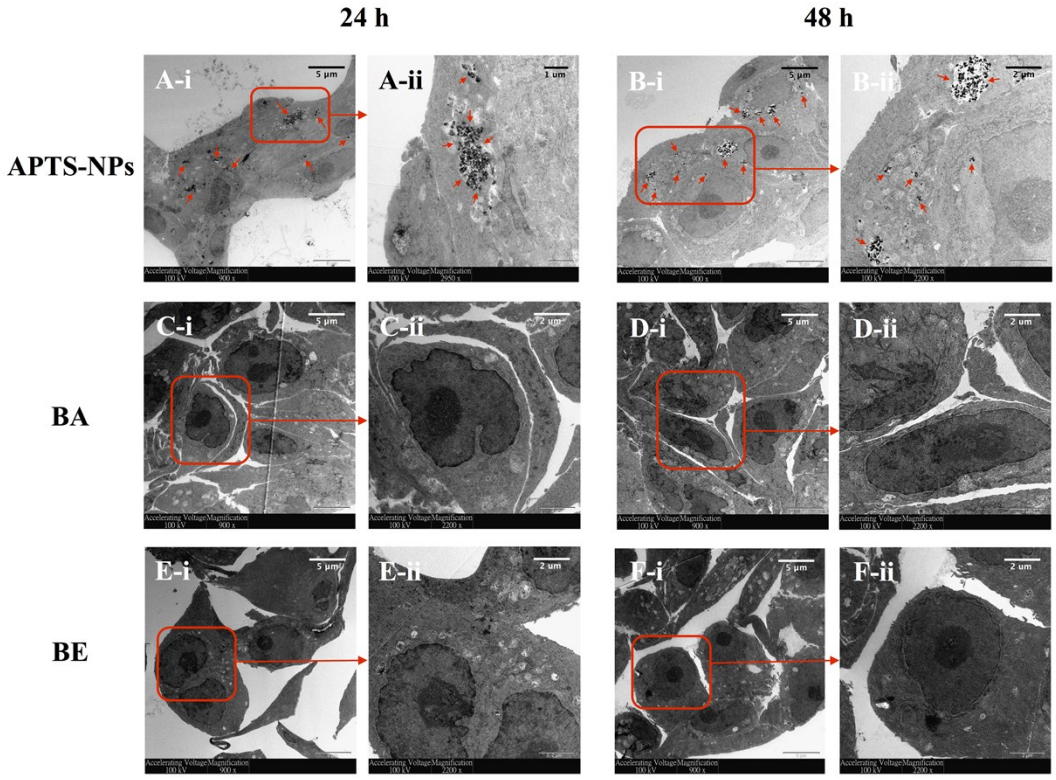

Fig. S2 TEM images of hGECs incubated with APTS-NPs (50 μg/mL) (A), BA (14.2 μg/mL) (C) and BE (4.7 μg/mL) (E) for 24 h, and then cultured in the nanoparticle-free media with IL-1β (1 ng/mL) for another 24 h (B, D and F). Afterwards, a large amount of APTS-NPs (black dots pointed by red arrows) appears in the cells (A and B). Following another 24 h incubation in the nanoparticle-free media containing IL-1β, there exists a small amount of APTS-NPs (black dots pointed by red arrows) within the cells. For the cells pretreated by BA and BE, there is no notable difference before and after the stimulation of IL-1β.

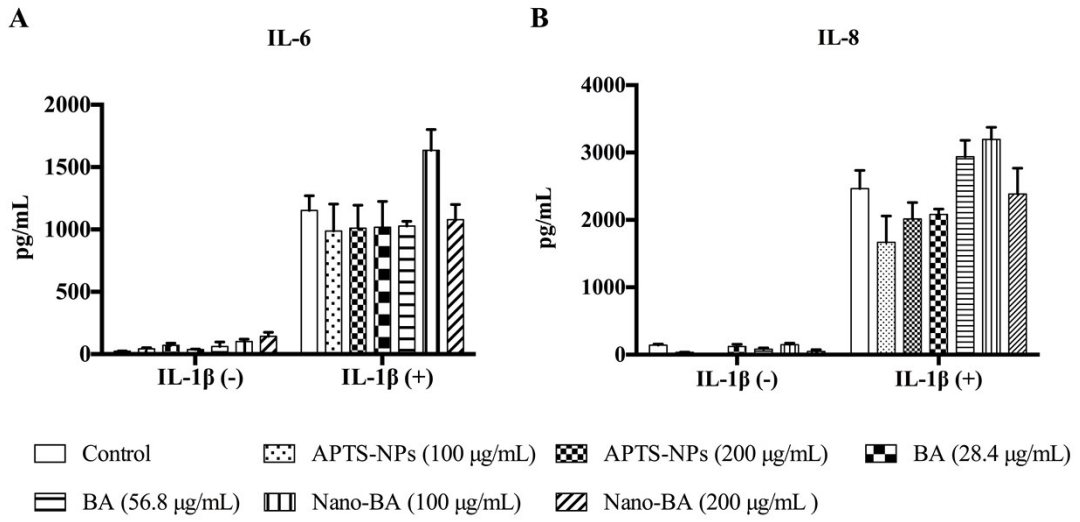

Fig. S3 The levels of IL-6 and IL-8 in the supernatants from the control cells and those with pre-treatment of APTS-NPs (100 and 200 μg/mL), BA (28.4 and 56.8 μg/mL) and Nano-BA (100 and 200 μg/mL), with (+) or without (-) follow-up IL-1β stimulation (1 ng/mL). All data are collected from one biological repeat in triplicate and presented as mean±SD.

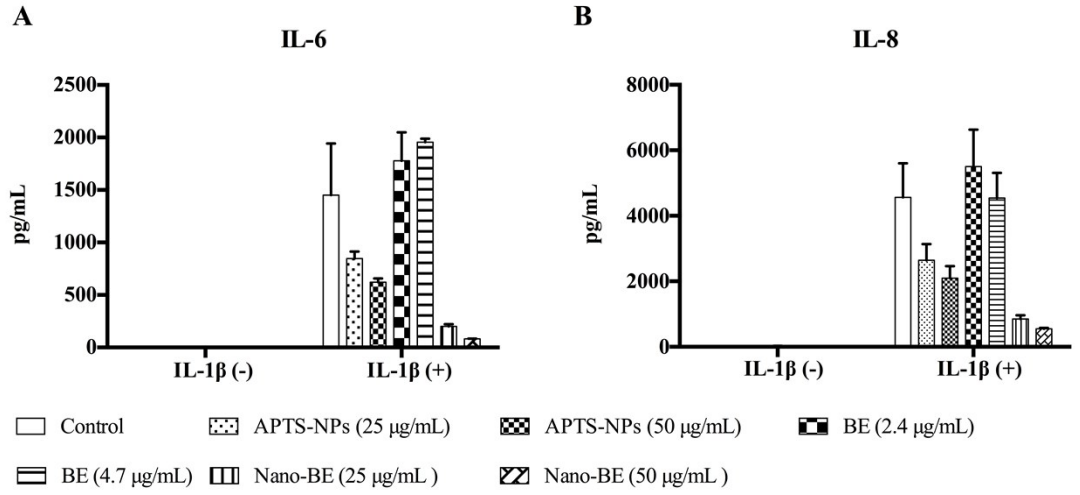

Fig. S4 The levels of IL-6 and IL-8 in the supernatants from the control cells and those with pre-treatment of APTS-NPs (25 and 50 μg/mL), BE (2.4 and 4.7 μg/mL) and Nano-BE (25 and 50 μg/mL), with (+) or without (-) follow-up IL-1β stimulation (1 ng/mL). All data are collected from one biological repeat in triplicate and presented as mean±SD.

Table S1 The fold changes of 105 cytokines in the supernatants of cultured hGECs with pre-treatments of Nano-BA and Nano-BE followed up IL-1β stimulation with reference to the controls.

Cytokines	Fold Change			Cytokines	Fold Change			Cytokines	Fold Change		
	Controls/ IL-1β	Nano-BA/ IL-1β	Nano-BE/ IL-1β		Controls / IL-1β	Nano-BA/ IL-1β	Nano-BE/ IL-1β		Controls / IL-1β	Nano-BA/ IL-1β	Nano-BA/ IL-1β
Adiponectin	0	0	3.30	IGFBP-2	1.70	1.07	0.83	MCP-3	0.80	1.63	0.14
Apolipoprotein A-I	0	0	3.83	IGFBP-3	0.49	2.01	0.65	M-CSF	0.74	1.50	0.20
Angiogenin	0	0	0.32	IL-1α	0.79	1.73	0.70	MIF	0.92	1.73	0.86
Angiopoietin-1	0	0	4.96	IL-1β	2.35	1.88	1.44	MIG	1.04	1.37	0.34
Angiopoietin-2	0.06	1.21	1.07	IL-1ra	1.52	1.08	1.53	MIP-1α/MIP-1β	1.35	1.26	0.57
BAFF	0.44	1.77	2.21	IL-2	1.07	0.95	1.34	MIP-3α	7.26	0.86	0.59
BDNF	0.65	0.66	0.50	IL-3	1.12	1.42	2.08	MIP-3β	1.23	1.13	1.17
Complement Component C5/C5a	1.41	1.15	1.44	IL-4	0.00	0.00	0.23	MMP-9	1.89	0.72	1.30
CD14	1.12	0.94	1.19	IL-5	0.00	0.00	18.66	Myeloperoxidase	0.43	0.00	0.31
CD30	0.70	1.18	1.22	IL-6	3.10	3.02	1.24	Osteopontin	0.37	0.03	0.52
CD40 ligand	0.19	0	1.05	IL-8	2.40	3.15	1.84	PDGF-AA	0.49	0.01	0.40
Chitinase 3-like 1	0	0	1.35	IL-10	0.57	1.88	0.30	PDGF-AB/BB	0.00	0.00	0.00
Complement Factor D	0	0	0.98	IL-11	0.58	1.95	0.18	Pentraxin-3	2.61	3.06	2.15
C-Reactive Protein	0	0.01	1.00	IL-12 p70	0.73	1.60	0.31	PF4	1.12	0.91	0.00
Cripto-1	0	0.50	3.97	IL-13	0.61	1.23	1.13	RAGE	0.97	0.54	0.13
Cystatin C	0.80	1.49	1.42	IL-15	0.87	1.13	1.00	RANTES	1.04	0.81	0.82
Dkk-1	0.97	0.52	0.34	IL-16	1.07	0.69	1.72	RBP-4	0.93	1.34	0.70
DPPIV	0.98	1.36	1.60	IL-17A	1.43	1.58	1.05	Relaxin-2	1.20	0.91	0.94
EGF	0.99	1.21	1.05	IL-18 BPa	0.91	1.09	2.43	Resistin	1.32	1.01	1.04

EMMPRIN	1.64	1.18	1.07	IL-19	0.00	0.00	0.37	SDF-1α	1.38	1.07	0.94
ENA-78	2.00	1.32	0.56	IL-22	0.05	0.00	0.29	Serpin E1	1.04	1.17	0.97
Endoglin	0	0	1.85	IL-23	0.00	0.00	0.52	SHBG	0.46	0.42	0.32
Fas Ligand	0	0	1.42	IL-24	1.97	4.64	1.49	ST2	0.17	0.26	0.72
FGF basic	0.17	0.60	0.85	IL-27	0.97	3.08	0.19	TARC	0.43	1.63	0.35
FGF-7	0.00	4.13	11.63	IL-31	0.00	3.49	0.00	TFF3	1.27	1.97	0.64
FGF-19	0.89	1.16	0.64	IL-32	0.82	2.05	0.35	TfR	1.22	1.37	0.04
Flt-3 Ligand	0.19	0.77	1.21	IL-33	1.76	3.11	0.72	TGF-α	1.84	2.10	0.61
G-CSF	3.57	4.19	2.05	IL-34	2.15	2.57	1.31	Thrombospondin-1	1.15	1.01	0.94
GDF-15	1.13	1.06	1.48	IP-10	4.18	0.97	0.92	TNF-alpha	0.64	0.79	0.70
GM-CSF	4.87	3.96	1.20	I-TAC	1.91	1.77	2.07	uPAR	1.36	1.58	1.11
GRO-α	7.55	0.54	4.03	Kallikrein 3	1.38	1.23	1.78	VEGF	3.64	1.58	2.80
Growth Hormone	0	0	1.85	Leptin	0.00	0.00	0.00	Vitamin D BP	0.50	0.71	0.47
HGF	0	0	1.23	LIF	0.00	0.00	0.00	CD31	0.23	1.13	0.07
ICAM-1	1.07	1.31	1.37	Lipocalin-2	0.17	0.00	0.73	TIM-3	1.28	1.74	0.00
IFN-γ	0.21	1.23	0.61	MCP-1	3.32	1.54	0.56	VCAM-1	1.29	1.54	0.08

Notes: The mean pixel densities of the cytokines were calculated from array membranes using HLImage++, and the values were normalized to the reference spots.