Figure legends

Table1

Drugs	Symbol	Zone of inhibition (mm) mean ± SD
		Propionibectarium acnes
		1mm
Kaempferol alone	B1	22.9±1.5
Luteolin alone	B2	21.3±1.3
Quercetin alone	B3	24.9±1.7
Kaempferol + Luteolin	B4	25.9±1.7
Kaempferol + Quercetin	B5	26.8±1.8
Quercetin + Luteolin	B6	28.4±2.0
Clindamycin alone	B7	29.8±2.1
Quercetin + Kaempferol + Luteolin	B8	30.6±2.1

Table.1 Diameters of zones of bacterial inhibition by using Quercetin, Kaempferol, Luteolin and flavonoid combination against P acnes. Values represent mean ± SD (n >3)

Figures

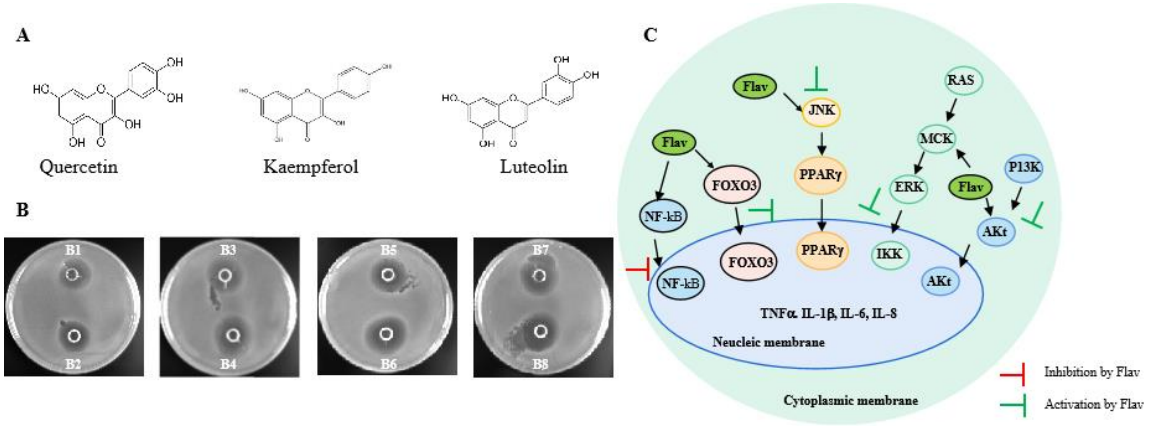

Fig. 1 Antibacterial activity of quercetin, kaempferol and luteolin against P acnes. (A) Structure of quercetin, kaempferol and luteolin; (B) The inhibitory effect of flavonoid against P acnes. (B1) kaempferol, (B2) luteolin, (B3) quercetin, (B4) kaempferol combination with luteolin, (B5) kaempferol combination with quercetin, (B6) luteolin combination with quercetin, (B8) quercetin combination with kaempferol and luteolin.（B7) Clindamycin as a positive control, respectively.（C） Major inflammatory pathways targeted by flavonoid.

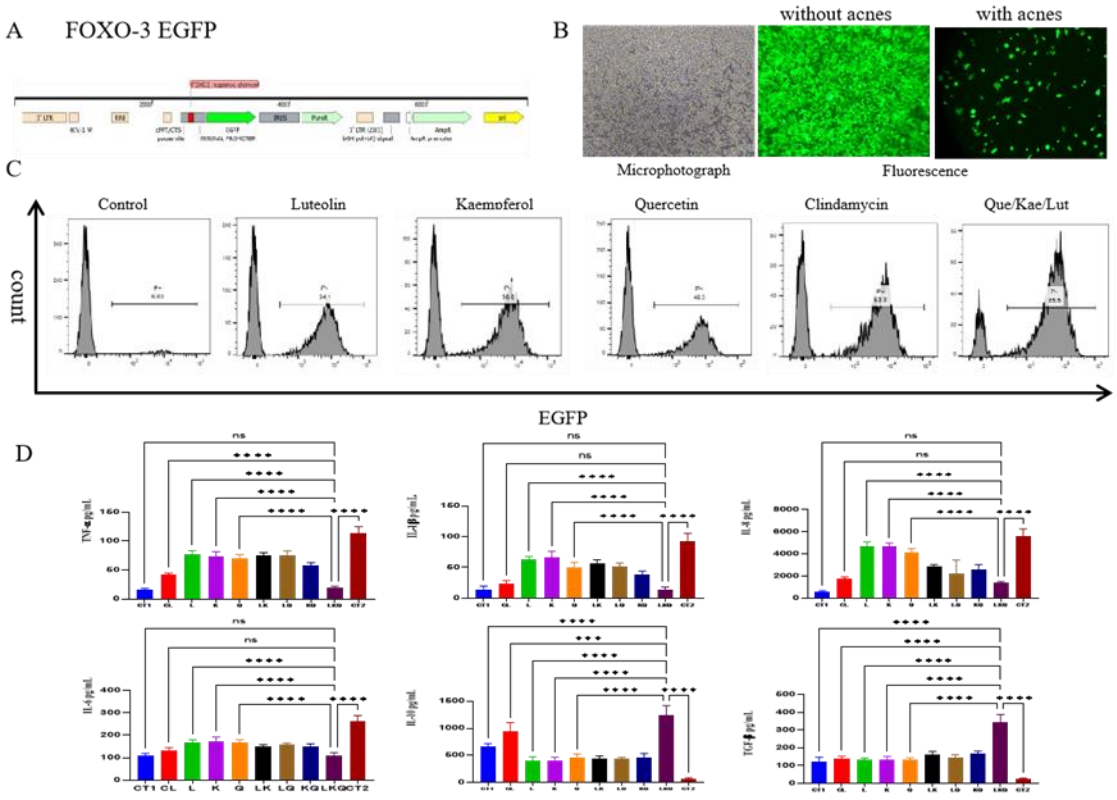

Fig.2 Generation and characterization of the lentivirus-based FOXO3 signaling pathway activation fluorescence reporter system. A) Schematic illustration of reporter constructs encoding FOXO-3 EGFP with restriction enzyme recognition sites. B) Fluorescent inverted microscope results of CP-H113 cells, FOXO-3 signaling pathway was activated by 10μm triciribine for 1hr. After incubation, stimulated with or without 1.0×10^7 CFU/well of P acnes for 18 h. C) Histogram representation to measure the effect on the transcription factor activation of FOXO3 signaling pathway. Numbers show geometric mean of fluorescence intensity (EGFP). D) Effect of flavonoid against P acnes-induced cytokines in CP-H113 cells. (CT1) control, (L) luteolin, (K) kaempferol, (Q)quercetin, (LK) luteolin combination with kaempferol, (LQ) luteolin combination with quercetin, (KQ)kaempferol combination with quercetin, (LKQ) quercetin combination with kaempferol and luteolin. A control experiment without P acnes-stimulation was conducted in CT2, and CL(Clindamycin) as a positive control, respectively. Data were analyzed by one-way ANOVA test (* $p < 0.05$ versus control and ** $p < 0.05$ versus P acnes alone, n=5 each group). Abbreviation: ns, no statistically significant.

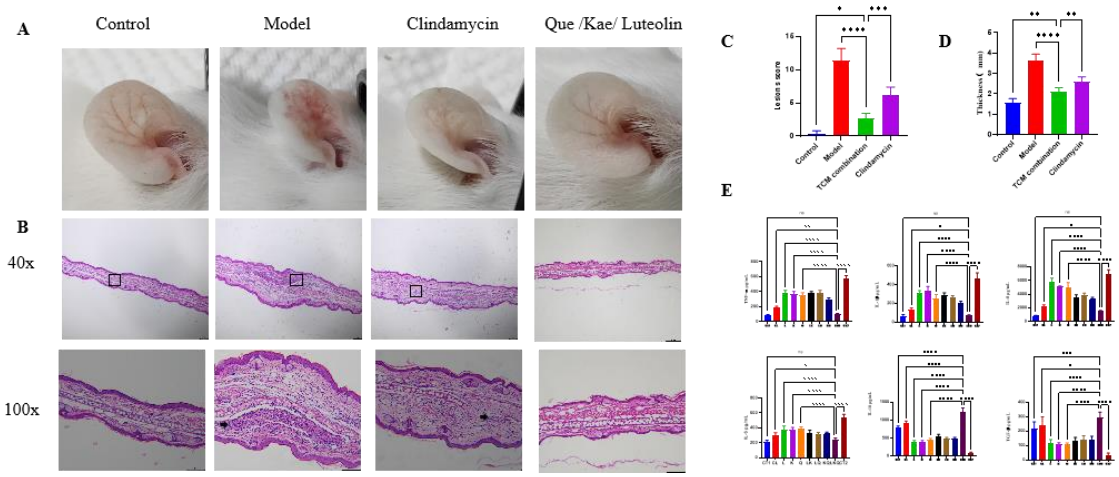

Figure 3. Effect of flavonoid combination therapy on P acnes-induced skin inflammation in vivo. P acnes were intradermally injected into the ears for 24 h. Control (non-treatment) mice were similarly treated with PBS and without P acnes inflammation, while the model group with P acnes. Clindamycin as a positive control, respectively. (A) Effect of flavonoid combination therapy on P acnes-induced skin inflammation. Ear thickness, swelling, erythema, and inflammatory response after treatment; (B) Paraffin sections of left ear were stained with hematoxylin and eosin observed by microscope (40× and 100× magnified); (C) Lesions score, and (D) Auricle thickness. (E) Effect of flavonoid compounds against P acnes-induced cytokines in ears models. Data were analyzed by one-way ANOVA test (* $p < 0.05$ versus control and ** $p < 0.05$ versus P. acnes alone, n=5 each group). Abbreviation: ns, no statistically significant.)

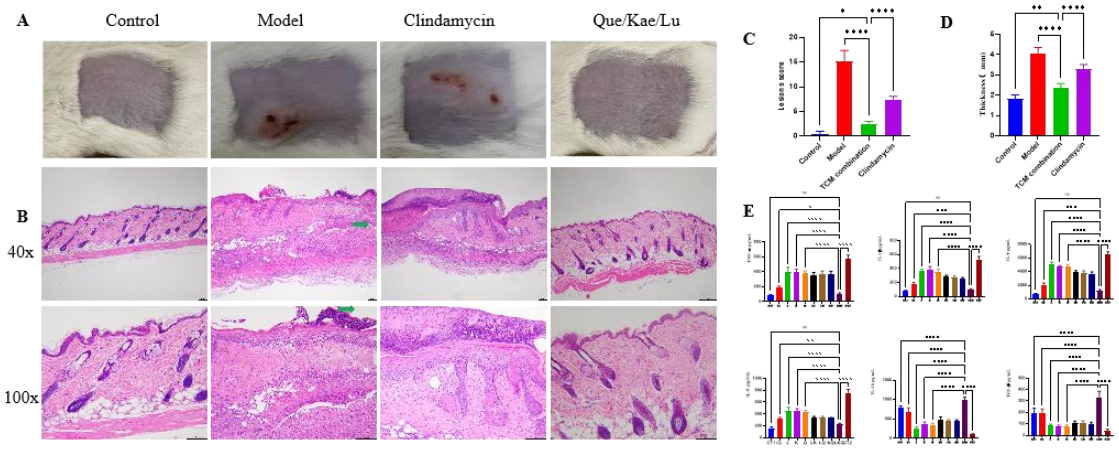

Figure 4. In vivo anti-inflammatory activity of flavonoid against P acnes. P acnes was intradermally injected into the dorsal skin. (A) Effect of flavonoid combination therapy on P acnes-induced skin inflammation. (B)

Paraffin sections of the back skin were stained with hematoxylin and eosin, observed by microscope (40× and 100×magnified); (C) Lesions score and (D) Auricle thickness. (E) Effect of flavonoid against P acnes-induced cytokines in dorsal skin models. Data were analyzed by one-way ANOVA test (* $p < 0.05$ versus control and ** $p < 0.05$ versus P acnes alone, n=5 each group). Abbreviation: ns, no statistically significant.