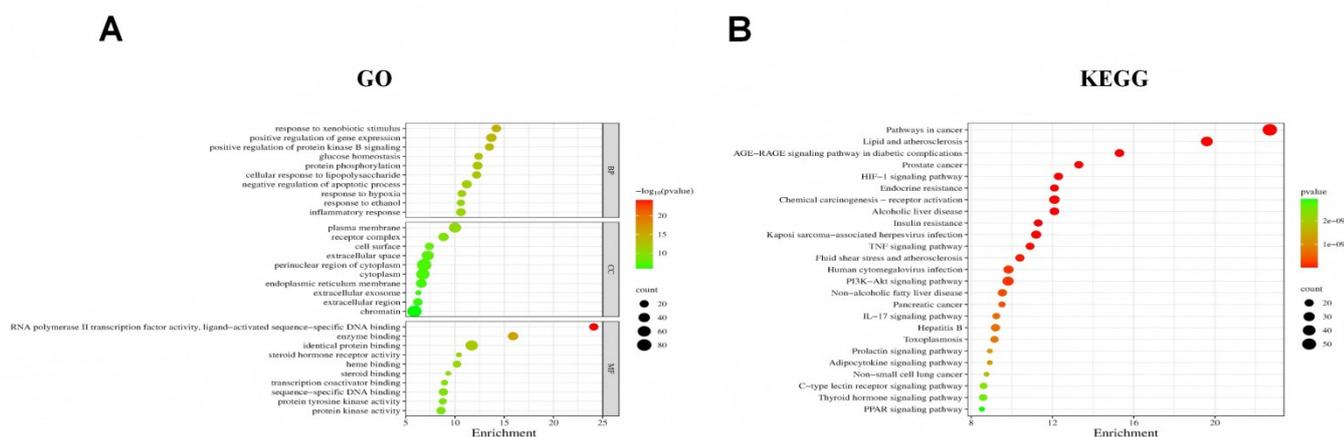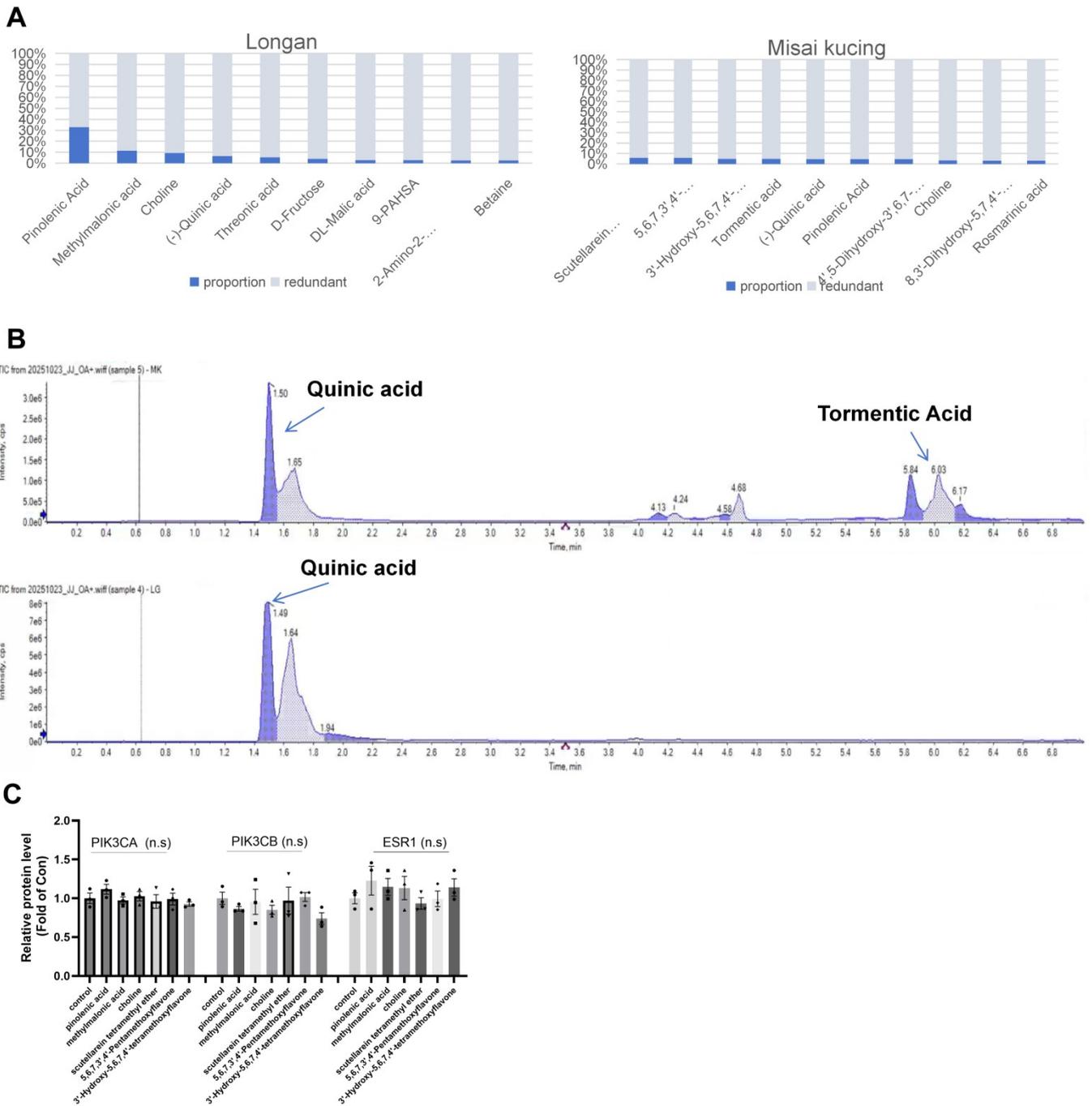1

Fig. S1†. Food and water intake in single or combination treatment. (A-B) Food intake in 24 hours in four groups: Control, Longan, Misai Kucing, Longan+Misai Kucing. Quantitative results are shown in Figure B. (C-D) Water intake in 24 hours in four groups. Quantitative results are shown in Figure D. n=6. P values were determined by two-way ANOVA tests.

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Fig. S2†. Overlapping enriched pathways between gene changes triggered by Longan and Misai Kucing extracts and those associated with hyperlipidemia. (A-B) GO and KEGG enrichment analysis of potential active ingredients in Longan and Misai Kucing targeting hyperlipidemia.

A

Longan

Misai kucing

Pinolenic Acid, Methylmalonic acid, Choline, (-)-Quinic acid, Threonic acid, D-Fructose, DL-Malic acid, 9-PAHSA, 2-Amino-2-..., Betaine

■ proportion ■ redundant

Scutellarein..., 5,6,7,3',4'-..., 3'-Hydroxy-5,6,7,4'-..., Tormentic acid, (-)-Quinic acid, Pinolenic Acid, 4',5-Dihydroxy-3',6,7-..., Choline, 8,3-Dihydroxy-5,7,4'-..., Rosmarinic acid

■ proportion ■ redundant

B

TIC from 20251023_JJ_OA+.wiff (sample 5) - MK

Quinic acid

Tormentic Acid

TIC from 20251023_JJ_OA+.wiff (sample 4) - LG

Quinic acid

C

Relative protein level (Fold of Con)

PIK3CA (n.s)   PIK3CB (n.s)   ESR1 (n.s)

control, pinolenic acid, methylmalonic acid, choline, scutellarein tetramethyl ether, 5,6,7,3',4'-Pentamethoxyflavone, 3'-Hydroxy-5,6,7,4'-tetramethoxyflavone

**Fig. S3†. Quantification of major active components and effects on ERα-PI3K signaling.** (A) Identification of the top 10 compounds by peak area in Longan and Misai Kucing extracts. (B) Targeted quantification of quinic acid and tormentic acid. (C) Effects of the remaining top compounds on the transcription of PIK3CA, PIK3CB, and ESR1. n=3. P values were determined by unpaired t-test. n.s, statistically insignificant.
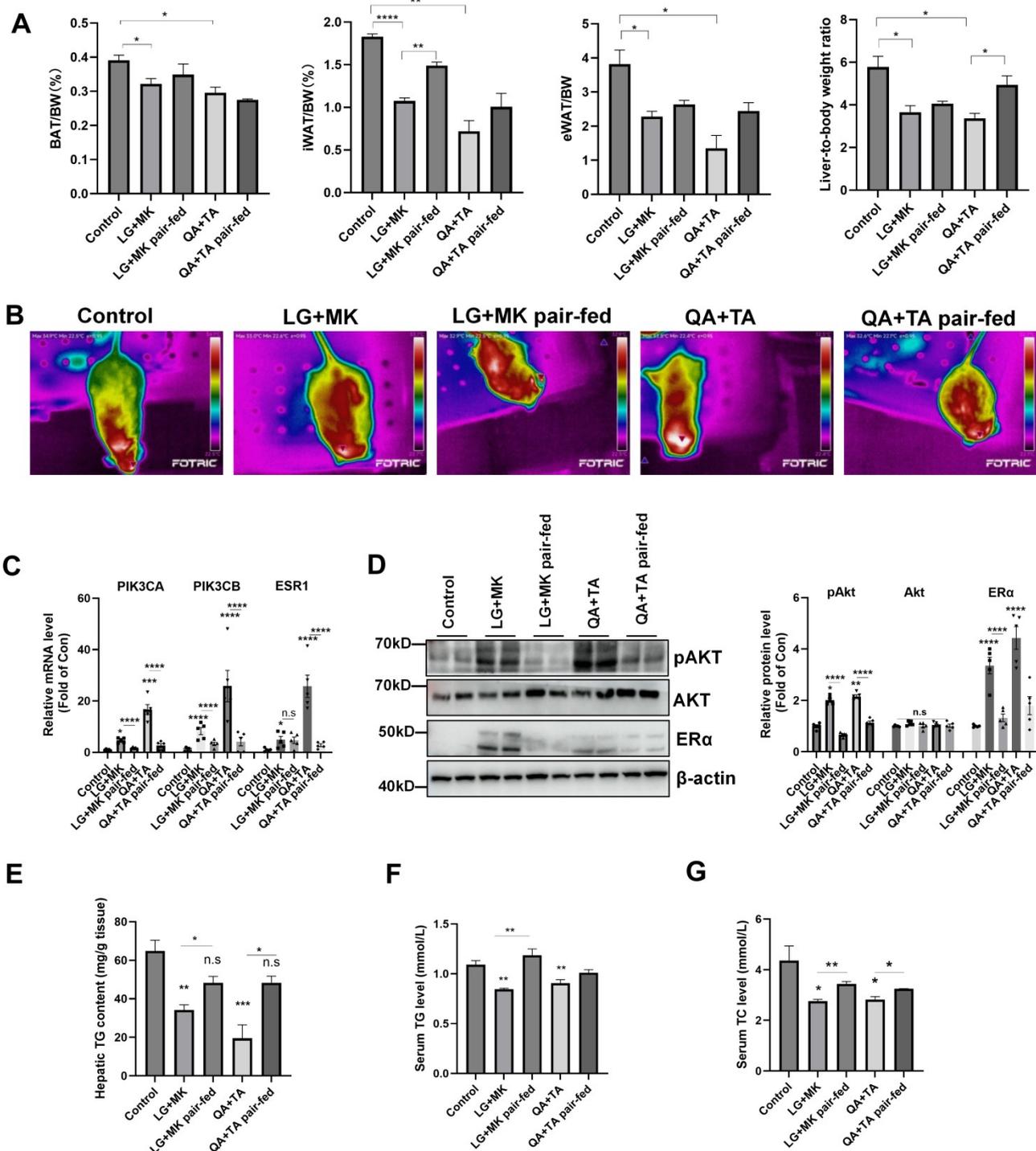
Fig. S4†. Metabolic phenotypes in mice treated with Longan and Misai Kucing crude extracts or active compounds versus pair-fed controls. (A) Relative organ weights (BAT, iWAT, eWAT, and liver). (B) Representative thermal images following cold exposure. (C-D) Hepatic mRNA transcription and protein expression across the five experimental groups. (E) Hepatic triglyceride (TG) content, and (F-G) serum levels of TG and total cholesterol (TC). BAT, brown adipose tissue. iWAT, inguinal white adipose tissue. eWAT, epididymal white adipose tissue. n=5. P values were determined

24 by two-way ANOVA tests. *P < 0.05, ** p < 0.01, *** p < 0.001,**** p < 0.001. n.s, statistically

25 insignificant.

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