

Figure S1. Analysis of sea cucumber saponins EA, HA and their derivatives EA2, HA2 by liquid chromatogram. Purity analysis of EA (A) and HA (B) by HPLC. Total ion chromatography and mass spectrometry of sea cucumber saponins EA (C) and HA (D) as well as corresponding metabolites EA2 (E) and HA2 (F) by LC-MS.

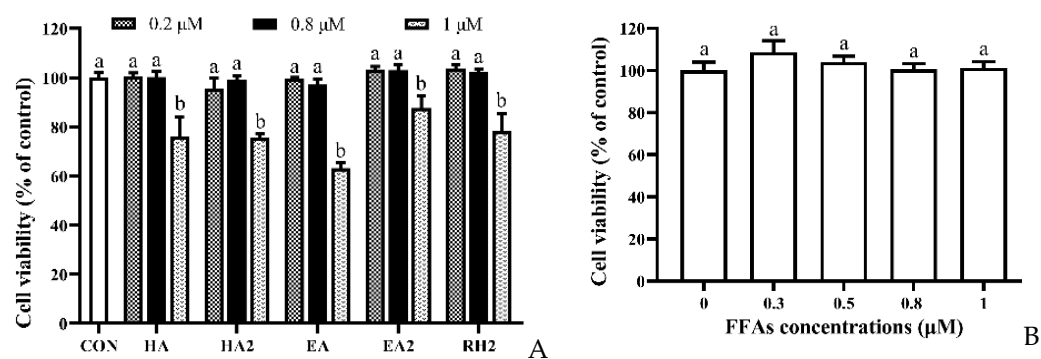


Figure S2. Cytotoxic effects on HepG2 cells after 24h incubation with gradient concentration of saponins (A) and free fatty acids (B). The free fatty acids (FFAs) were mixed with palmitic acid (PA) and oleic acid (OA) at a ratio of 1:2, and the concentration was calculated by total. Data were obtained from three independent experiments and were presented as Mean \pm SEM. Different letters represented significant differences at $P < 0.05$ among treated groups.

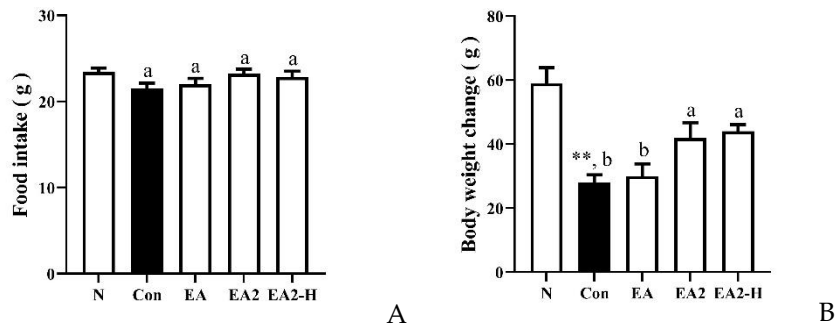


Figure S3. Effects of EA (0.05%), EA2 (0.05%), and high-dosage EA2 (0.15%) on food intake and body weight change in Wistar rats fed with experimental diets. A: Food intake; B: Body weight change. Data were presented as Mean \pm SEM. ** $P < 0.01$ indicates significant differences between normal and control group. Different letters represented significant differences at $P < 0.05$ among control and treated groups.

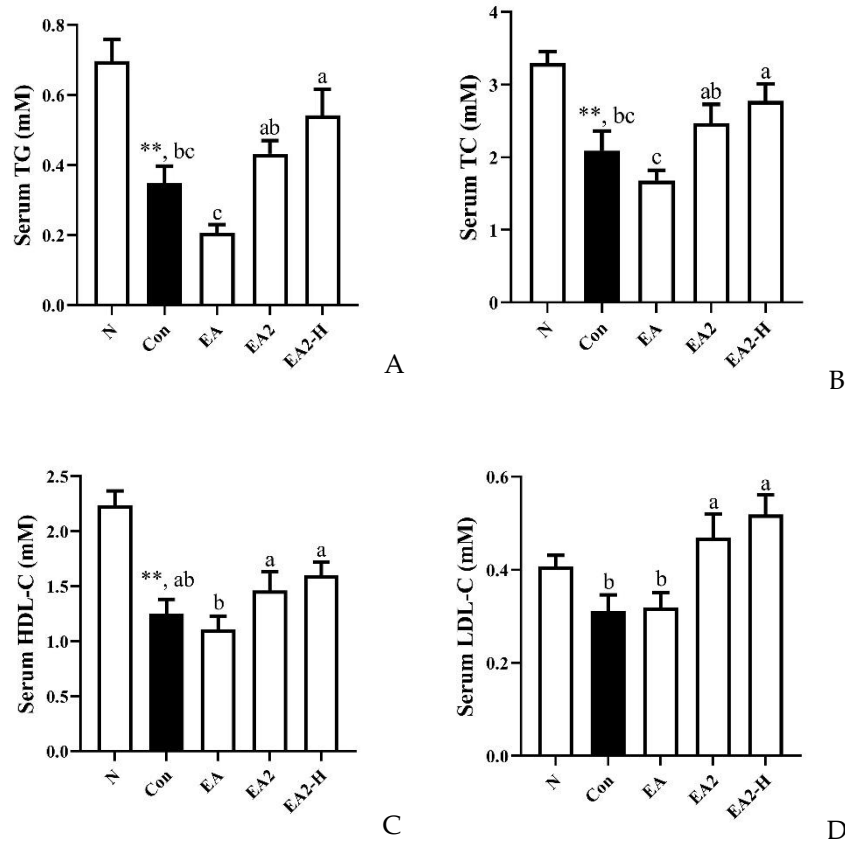


Figure S4. Effects of EA and EA2 on serum lipids. A: Serum TG; B: Serum TC; C: Serum HDL-C; D: Serum LDL-C. Data were presented as Mean \pm SEM. ** $P < 0.01$ indicates significant differences between normal and control group. Different letters represented significant differences at $P < 0.05$ among control and treated groups.

Table S1. Detection and identification of prepared saponins and their metabolites.

| Name | Molecular mass | Precursor ion | Formula | Retention time (min) |
|------|----------------|----------------------|--|----------------------|
| EA | 1183.522 | [M-2H] ²⁻ | C ₅₄ H ₈₆ O ₂₆ SH | 4.2 |
| HA | 1197.499 | [M-2H] ²⁻ | C ₅₄ H ₈₄ O ₂₇ S | 4.0 |
| EA2 | 845.400 | [M-H] ⁻ | C ₄₁ H ₆₅ O ₁₆ SH | 10.4 |
| HA2 | 859.38 | [M-H] ⁻ | C ₄₁ H ₆₂ O ₁₇ S | 6.8 |

Table S2. Compositions of experimental diets.

| Ingredients (g/kg) | Normal | Control | EA | EA2 | EA2-H |
|--------------------|--------|---------|-----|-----|-------|
| Casein | 200 | 200 | 200 | 200 | 200 |
| Cornstarch | 499.5 | 489.5 | 489 | 489 | 488 |
| Sucrose | 100 | 100 | 100 | 100 | 100 |
| Corn oil | 100 | 100 | 100 | 100 | 100 |
| Mineral mix | 35 | 35 | 35 | 35 | 35 |
| Vitamin mix | 10 | 10 | 10 | 10 | 10 |
| Choline bitartrate | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| Cellulose | 50 | 50 | 50 | 50 | 50 |
| DL-methionine | 3 | 3 | 3 | 3 | 3 |
| Orotic acid | - | 10 | 10 | 10 | 10 |
| EA | - | - | 0.5 | - | - |
| EA2 | - | - | - | 0.5 | 1.5 |