Supplementary information

Encapsulation efficiency (EE). One milliliter of astaxanthin nanoparticles were mixed with 1.0 mL of anhydrous ethanol, centrifuged at 10000 ×g for 10 min, and the supernatant was collected. The operation was repeated until the supernatant was colorless. The astaxanthin of the supernatant was regarded as the content of free astaxanthin, which was measured using a UV-visible spectrophotometer (SP-754, Shanghai Spectrum, Shanghai) at 476 nm. The EE was calculated according to equation (1).

$$EE\ (\%) = (1 - content\ of\ free\ astaxanthin/total\ amount\ of\ astaxanthin) \times 100 \quad (1)$$

The size and zeta potential of the particles with the highest EE were determined at 25 ℃ using a nanoparticle size and zeta potential analyzer (Malvern Zetasizer Nano ZSE, Malvern Panalytical, UK).

X-ray diffraction (XRD). The crystalline structures of astaxanthin, MFGM-GA, and astaxanthin nanoparticles were determined using an X-ray diffractometer (XRD, D-MAX 2500, Rigaku, Japan). We used Cu Ka radiation at 40 kV and 30 mA, and scans were made between 5 and 55 degrees at a scanning rate of 10 degrees/min.

Thermal analysis. The thermal weight loss behaviors of astaxanthin, carrier, and astaxanthin nanoparticles were determined using a Pyris 1 TGA thermogravimetric analyzer (TGA, PerkinElmer, Inc., UC). Appropriate amounts (about 3 mg) of samples were taken flatly into an aluminum tray and heated from 30 °C to 500 °C at a heating rate of 10 °C/min under a nitrogen flow of 100 mL/min.

Gastrointestinal stability. To study the digestive behavior of astaxanthin nanoparticles, a model of gastrointestinal digestion of astaxanthin was built. The astaxanthin nanoparticles and the aqueous solution containing a comparable amount of free astaxanthin (0.5 mL) were mixed with an equal amount of ultrapure water. Then, 1 mL of simulated gastric fluid (pH 7.0) was added. It was shaken for 1 h at 100 rpm in a water bath at 37 °C in the dark. Sampling and analysis were performed at 30 and 60 min. Subsequently, 2 mL of simulated intestinal fluid (pH 7.0) was added and shaken in a water bath (100 rpm) for 2 h at 37 °C in the dark. The digested samples were centrifuged at 10000 × g for 15 min, and the supernatant was collected to determine the bioaccessibility of astaxanthin. The digestibility of astaxanthin was calculated according to the equation (2).

$$Digestibility\ of\ astaxanthin\ (\%) = {}^{A_s}/_{A_0} \times 100 \qquad (2)$$

Where: A_0 denoted absorbance of the supernatant at 476 nm without digestion; A_s denoted absorbance of supernatant at 476 nm after digestion.

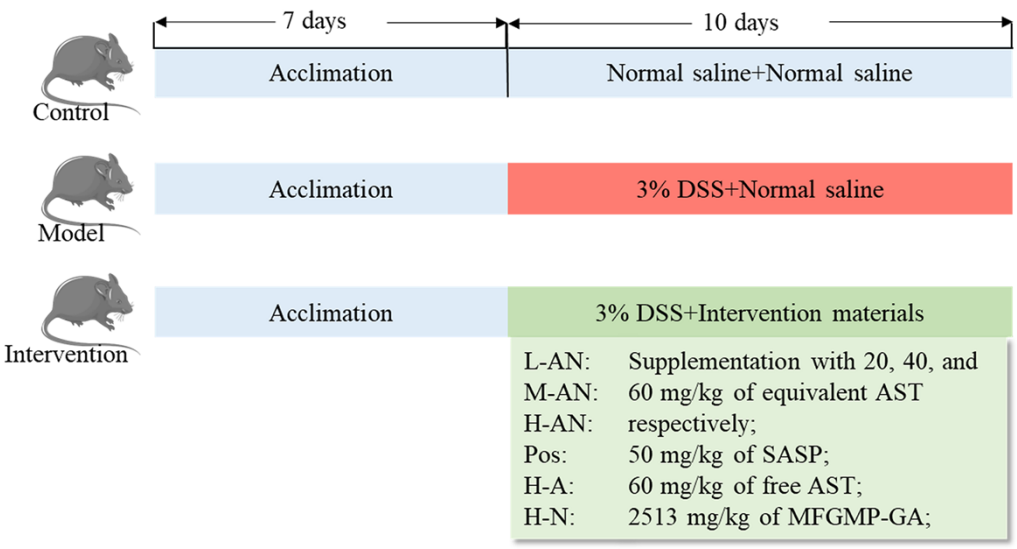

Figure S1. Schematic diagram of the animal experiment.

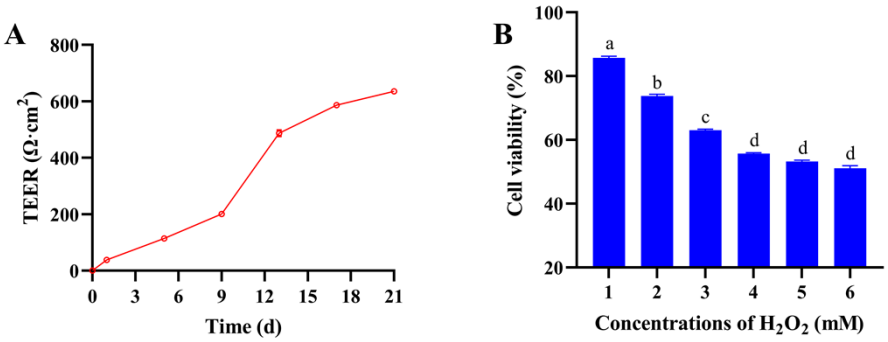

Figure S2. Effect of astaxanthin nanoparticles on Caco-2 cells. (A) Relationship between TEER of Caco-2 monolayers and incubation time; (B) Effect of H_2O_2 on cell viability. Different lowercase letters (a, b, c, and d) represent statistically significant differences at the level of $p < 0.05$.

Table S1 DAI scoring criteria of mice

Score	Weight loss (%)	Stool character	Fecal occult blood
0	0	Normal	Normal
1	1-5	Soft but still formed	Weak positive blood
2	6-10	Soft stool	Positive blood
3	11-15	Loose stools	Visible bleeding
4	>15	Watery stool	gross bleeding

The DAI was recorded as the equation:

$$DAI = (body\ weight\ score + stool\ consistency\ score + rectal$$

51 Table S2 The pathology scoring criteria of colon

Score	Intestinal epithelium	Inflammation severity
0	Normal	None
1	Goblet cells damage	Infiltration limited to the crypt
2	Extensive goblet cell damage	Infiltrate present in muscular mucosa
3	Ioss of goblet cells	Covering large areas of muscular mucosa, mucosal edema
4	Iarge areas without crypts	Infiltration in submucosa

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Table S3 The ratio of alkaline phosphatase activity on AP to BL

Time (d)	Activity (AP)	Activity (BL)	AP/BL
5	4.93±0.12	5.12±0.07	0.96[d]
10	6.22±0.23	5.22±0.13	1.19[c]
15	14.46±0.31	8.96±0.44	1.61[b]
20	18.87±0.12	10.01±0.02	1.89[a]

[a-d] Different letters in each column indicate significant differences ($p < 0.05$).

57 Table S4 The visceral index of mice in each group

	Cardiac Index (%)	Liver index (%)	Kidney index (%)	Spleen index (%)	Thymus index (%)
Con	0.56±0.01^{a}	4.14±0.12^{a}	1.11±0.11^{b}	0.26±0.08^{b}	0.16±0.01^{a}
Mod	0.51±0.03^{a}	3.66±0.14^{bc}	1.32±0.09^{a}	0.36±0.11^{a}	0.18±0.01^{a}
L-AN	0.52±0.12^{a}	3.77±0.15^{b}	1.02±0.01^{b}	0.28±0.01^{ab}	0.16±0.02^{a}
M-AN	0.50±0.06^{a}	3.96±0.08^{ab}	1.05±0.03^{b}	0.29±0.03^{ab}	0.16±0.01^{a}
H-AN	0.51±0.11^{a}	4.04±0.34^{a}	1.09±0.09^{b}	0.25±0.01^{b}	0.16±0.03^{a}
Pos	0.44±0.05^{b}	3.56±0.21^{c}	1.15±0.11^{b}	0.18±0.02^{c}	0.17±0.05^{a}
H-A	0.52±0.13^{a}	3.76±0.18^{b}	1.20±0.08^{ab}	0.22±0.07^{c}	0.16±0.04^{a}
H-N	0.53±0.11^{a}	3.81±0.15^{b}	1.24±0.06^{ab}	0.20±0.06^{c}	0.16±0.03^{a}

58 $^{a\text{-}c}$ Different letters in each column indicate significant differences ($p < 0.05$).

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