

Supplementary information

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Fig. S1. Schematic illustration of Caco-2/RAW264.7 co-culture system. dEE was administered to Caco-2 cells grown for 21 days in transwell inserts, while LPS was administered to RAW264.7 cells to induce an inflammatory response.

Fig. S2. Total ion chromatograms (TIC) of dEE (A) negative ionization mode and (B) positive ionization mode, and (C) the chemical structures of tentatively identified compounds.

Fig. S3. Cytotoxic effect of dEE on RAW264.7 and Caco-2 cells measured by MTT ($*p < 0.05$).

Fig. S4. Effect of dEE on the morphology changes of RAW264.7 cells in the LPS-induced Caco-2/RAW264.7 co-culture system. The cellular morphology was observed under 40× magnification using an EVOS FL microscope (AMG, Bothell, WA). Red arrow points to cell differentiation, white arrow points to cell disruption, and black arrow points to cellular oedema.

Fig. S5. Effect of dEE on the secretion of LDH in the LPS-induced Caco-2/RAW264.7 co-culture system.

Table S1. Sequences of the primers used for qPCR.

Gene	Sequence (5' to 3')
IL-1 β	Forward: AGCACCTCACAAGCAGAGC
	Reverse: AAGGCATTAGAAACAGTCCAG
IL-6	Forward: CCCACCAAGAACGATAGTCAA
	Reverse: CAGTCCCAAGAAGGCAAC
TNF- α	Forward: CACCACCATCAAGGACTCAA
	Reverse: TCAGGGAAGAATCTGGAAAG
COX-2	Forward: CCCATTAGCAGCCAGTT
	Reverse: GGAAGAGCATCGCAGAGG
iNOS	Forward: CACGGACGAGACGGATAG
	Reverse: CCACTGACACTTCGCACA
ZO-1	Forward: GAAAGGCGGATGGTGCT
	Reverse: TACTGTCCGTGCTATACATTGAG
Claudin-1	Forward: CGATGCTTTCTGTGGCTAA
	Reverse: CAGTGGCTGACTTTCCTTGT
Occludin	Forward: TTCTGTTGGCGTTGGC
	Reverse: AGGGATGTCGGAAATCTAAT
β -actin	Forward: CTGTCCCTGTATGCCTCTG
	Reverse: TGTCACGCACGATTTCC

Table S2. Total phenolic and total flavonoid content of dEE.

	Total phenolic (mg GAE/g dw)	Total flavonoid (mg RE/g dw)
dEE	113.42±3.69	155.08±5.41

GAE: gallic acid equivalent; RE: rutin equivalent.

dEE: digested ethanol extracts; dw: dry weight.

Table S3. Correlation coefficients between the parameters^a.

	ROS	Cell viability	NO	PGE ₂	TNF- α	IL-1 β	IL-6	iNOS	COX-2	TNF- α mRNA	IL-1 β mRNA	IL-6 mRNA
TP	-0.857**	0.882**	-0.970**	-0.970**	-0.948**	-0.950**	-0.968**	-0.909**	-0.950**	-0.988**	-0.919**	-0.981**
ROS	1	-0.578*	0.873**	0.834**	0.778**	0.851**	0.779**	0.750**	0.889**	0.854**	0.912**	0.856**

	ZO-1 mRNA	Claudin- 1 mRNA	Occludin mRNA	TLR4	p-P65 /P65	p-I κ B α /I κ B α	p-P38 /P38	p-JNK /JNK	p-ERK /ERK	ZO-1	Claudin- 1	Occludin
TP	0.942**	0.893**	0.947**	-0.691*	-0.497	-0.332	-0.733**	-0.305	-0.642*	0.550	0.338	0.358
ROS	-0.679*	-0.784**	-0.683**	0.792**	0.488	0.054	0.811**	0.460	0.379	-0.205	-0.570	-0.004

^a Data represents Pearson Correlation Coefficient R. TP: total phenolics content; *p < 0.05, **p < 0.01.

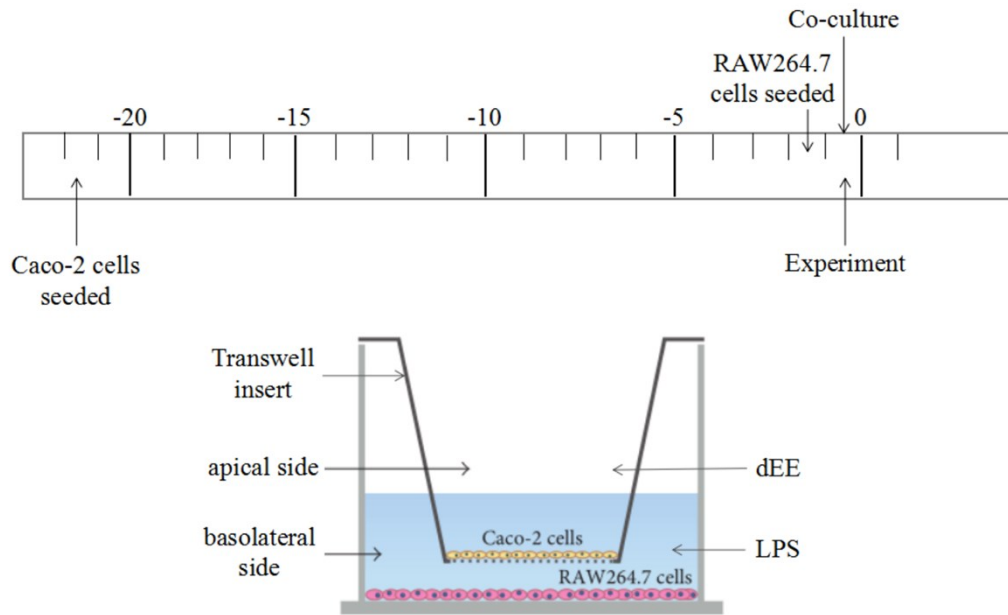


Fig. S1. Schematic illustration of Caco-2/RAW264.7 co-culture system. dEE was administered to Caco-2 cells grown for 21 days in transwell inserts, while LPS was administered to RAW264.7 cells to induce an inflammatory response.

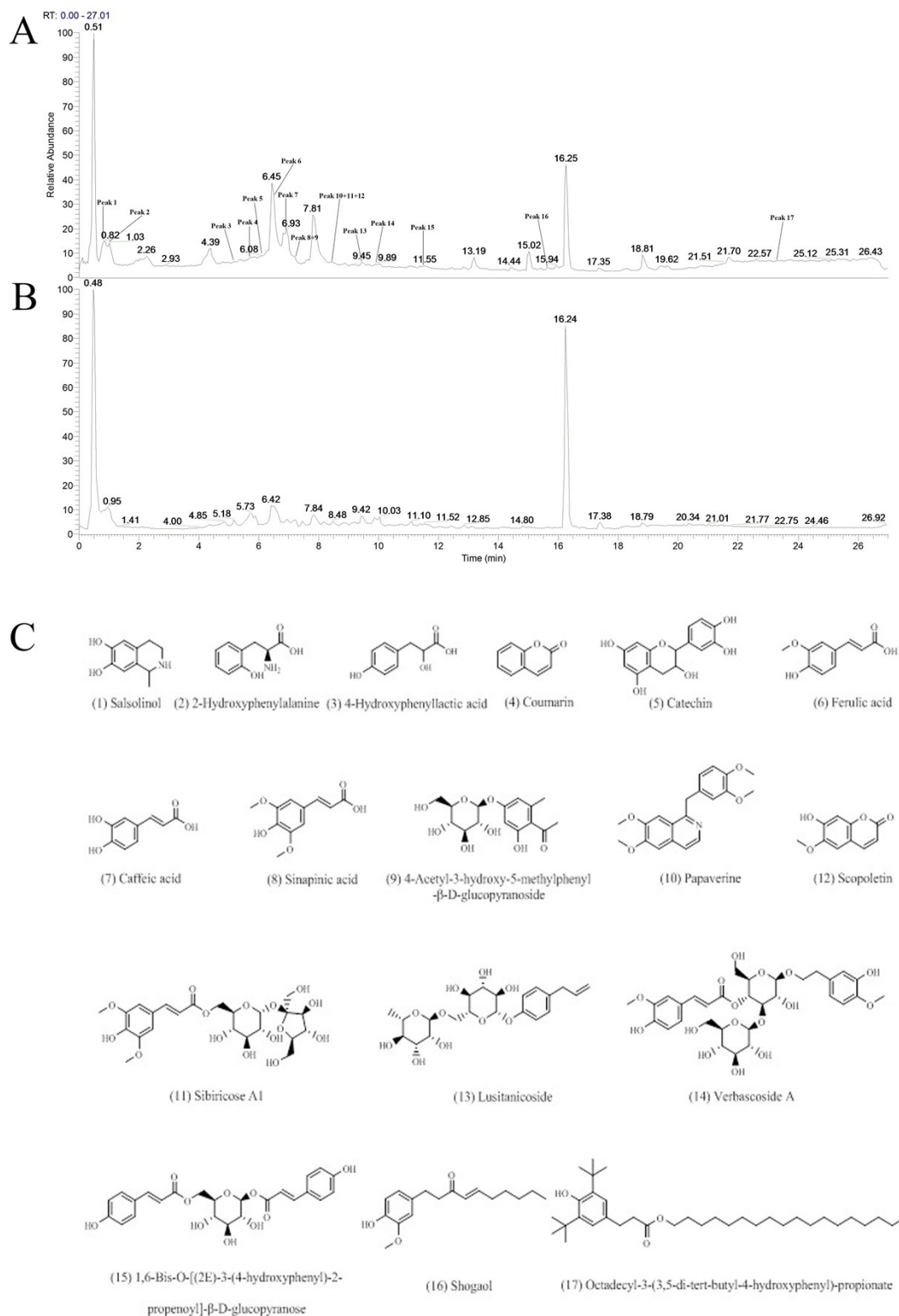


Fig. S2. Total ion chromatograms (TIC) of dEE (A) negative ionization mode and (B) positive ionization mode, and (C) the chemical structures of tentatively identified compounds.

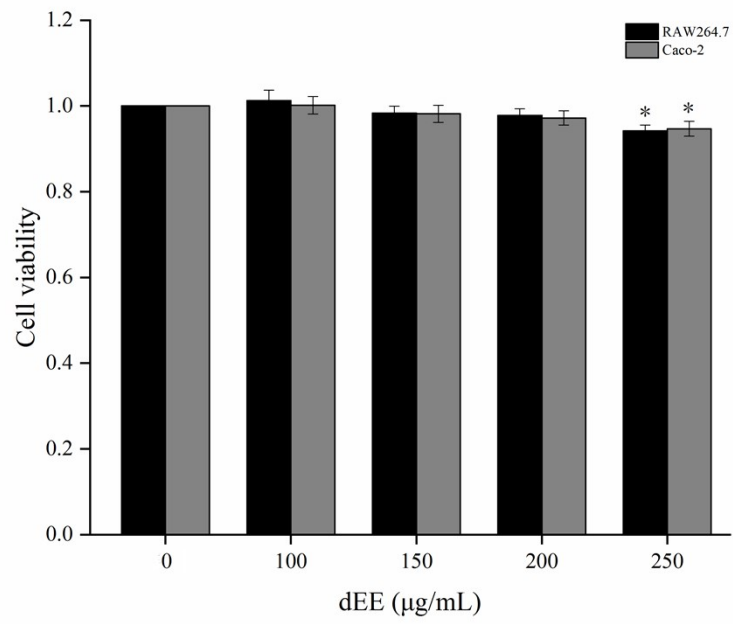
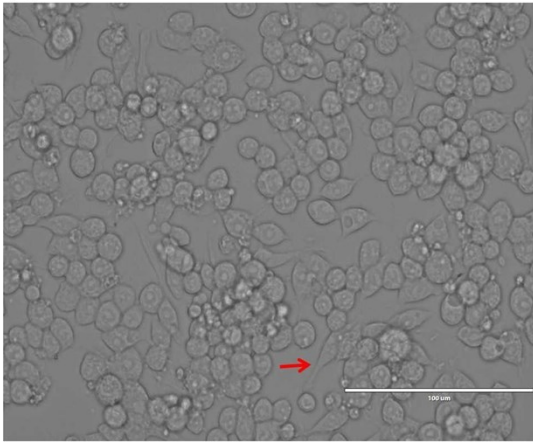


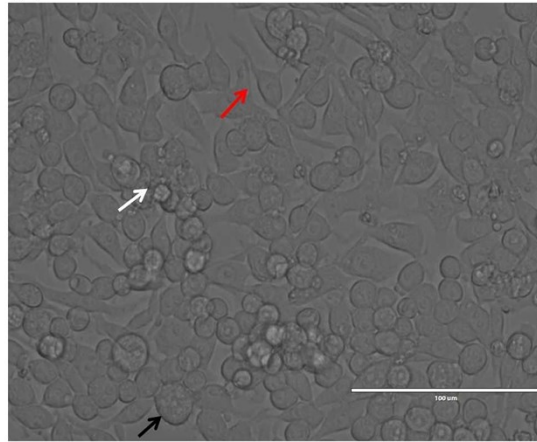
Fig. S3. Cytotoxic effect of dEE on RAW264.7 and Caco-2 cells measured by MTT

(* $p < 0.05$).

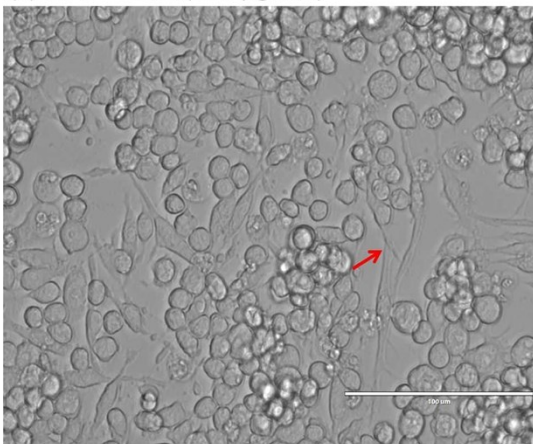
(1) Control



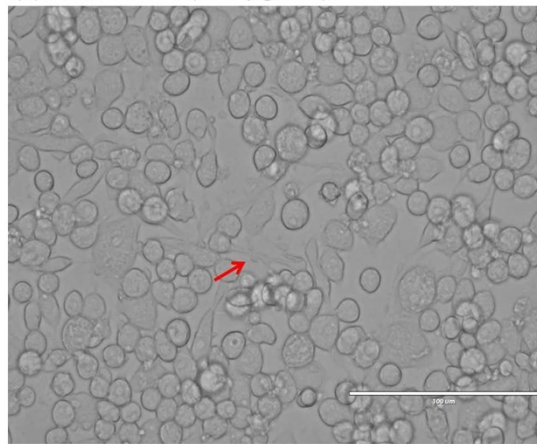
(2) LPS



(3) LPS + dEE (100 µg/mL)



(4) LPS + dEE (150 µg/mL)



(5) LPS + dEE (200 µg/mL)

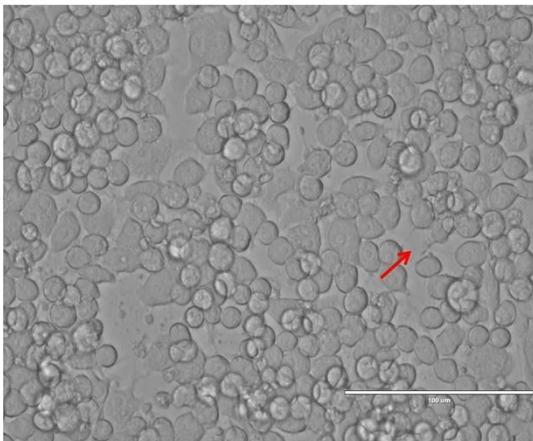


Fig. S4. Effect of dEE on the morphology changes of RAW264.7 cells in the LPS-induced Caco-2/RAW264.7 co-culture system. The cellular morphology was observed under 40× magnification using an EVOS FL microscope (AMG, Bothell, WA). Red arrow points to cell differentiation, white arrow points to cell disruption, and black arrow points to cellular oedema.

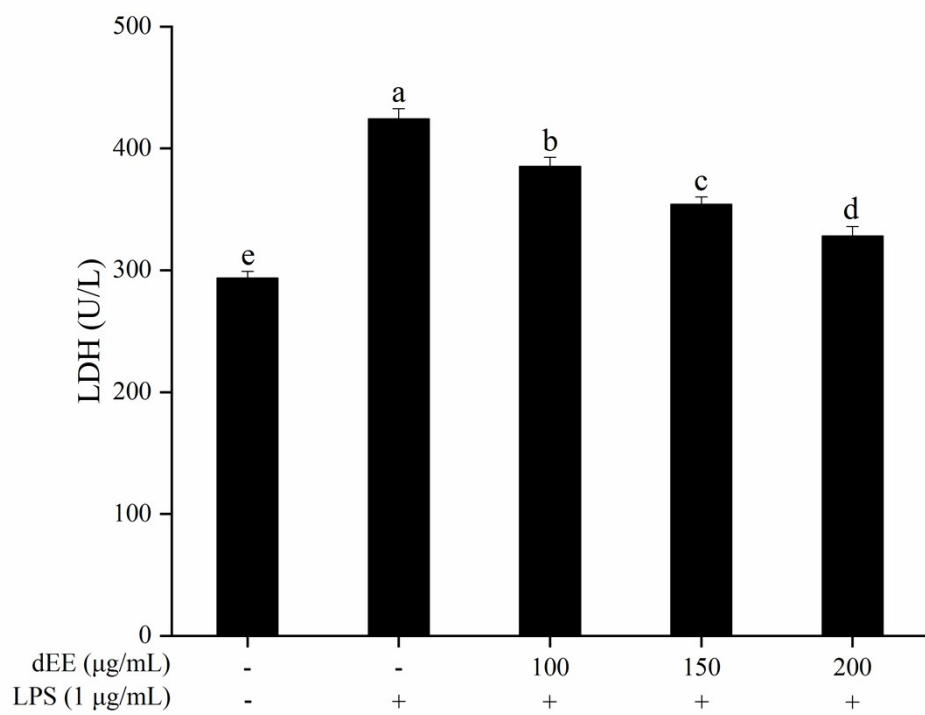


Fig. S5. Effect of dEE on the secretion of LDH in the LPS-induced Caco-2/RAW264.7 co-culture system.