

The inhibition of interaction with serum albumin enhances the physiological activity of curcumin by increasing its cellular uptake.

Mayuko Itaya<sup>a</sup>, Taiki Miyazawa<sup>b</sup>, Saoussanne Kalifa<sup>a</sup>, Naoki Shimizu<sup>a</sup>, Kiyotaka Nakagawa<sup>a\*</sup>

<sup>a</sup> Food and Biodynamic Chemistry Laboratory, Graduate School of Agricultural Science, Tohoku University, 468-1 Aramaki Aza, Aoba-ku, Sendai, 980-8572, Japan.

<sup>b</sup> New Industry Creation Hatchery Center (NICHe), Tohoku University, 6-6-10 Aramaki Aza, Aoba, Aoba-ku, Sendai 980-8579, Japan

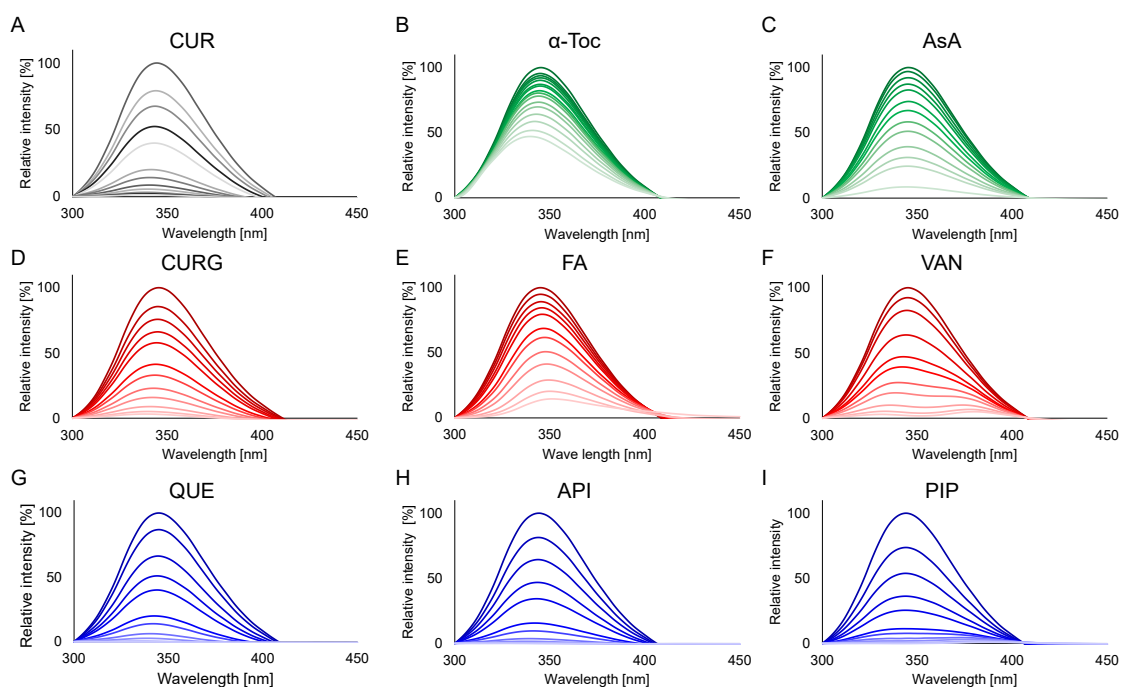
\*Kiyotaka Nakagawa: Food and Biodynamic Chemistry Laboratory, Graduate School of Agricultural Science, Tohoku University, Sendai, 980-8572, Japan

Phone: +81-22-757-4416,

Email: kiyotaka.nakagawa.c1@tohoku.ac.jp

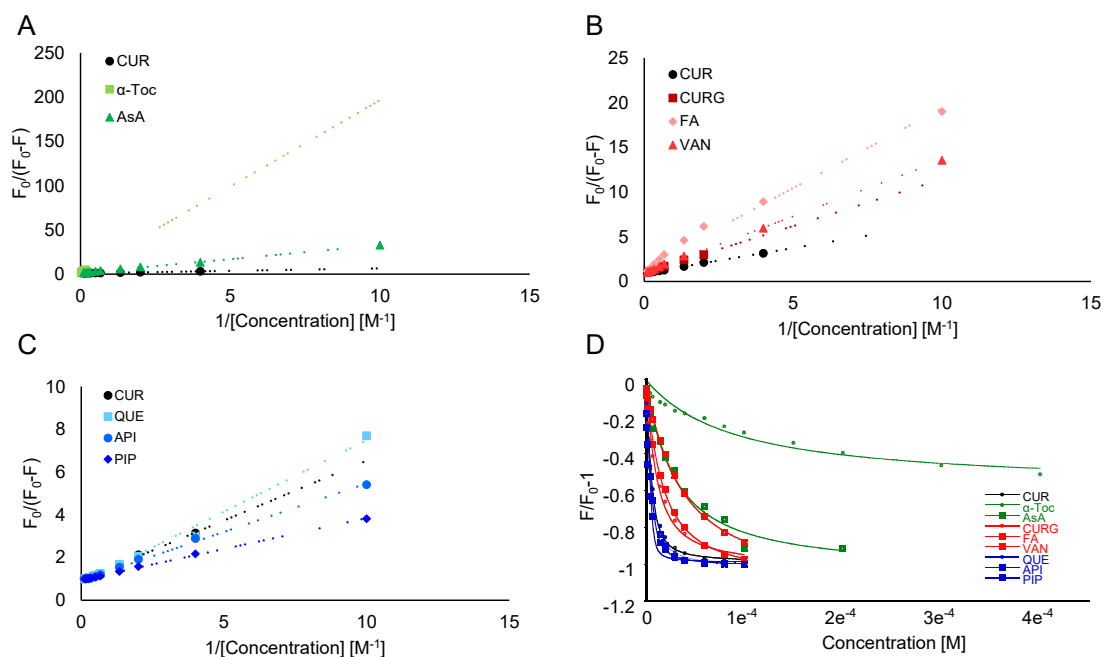
Supplementary Information

## S1. Screening compounds that bind to BSA strongly than CUR with fluorescence quenching technique



Supplemental Figure S1. Fluorescence emission spectra of (A) curcumin (CUR)-bovine serum albumin (BSA), (B)  $\alpha$ -tocopherol ( $\alpha$ -Toc)-BSA, (C) ascorbic acid (AsA)-BSA (D) curcumin glucuronide (CURG)-BSA, (E) ferulic acid (FA)-BSA, (F) vanillin (VAN)-BSA, (G) quercetin (QUE)-BSA, (H) apigenin (API)-BSA, (I) piperine (PIP)-BSA. Each group was measured with adjusted concentration of compounds at 0–100  $\mu$ M in 1 $\times$ phosphate buffered saline buffer under 1% dimethyl sulfoxide and 7.5  $\mu$ M BSA (pH 7.4).

## S2. Plot of the data obtained from the fluorescence quenching technique



Supplemental Figure S2. (A) The plot of  $F_0 / (F_0 - F)$  as a function of  $1 / [\text{compounds concentration}]$  with Stern-Volmer constant ( $K_{sv}$ ) of curcumin (CUR)-BSA,  $\alpha$ -tocopherol ( $\alpha$ -Toc)-BSA and ascorbic acid (AsA)-BSA, (B) CUR-BSA, curcumin glucuronide (CURG)-BSA, ferulic acid (FA)-BSA and vanillin (VAN)-BSA (C) CUR-BSA, quercetin (QUE)-BSA, apigenin (API)-BSA and piperine (PIP)-BSA, (D) The plot of  $F / F_0 - 1$  as a function of concentration with each compounds.

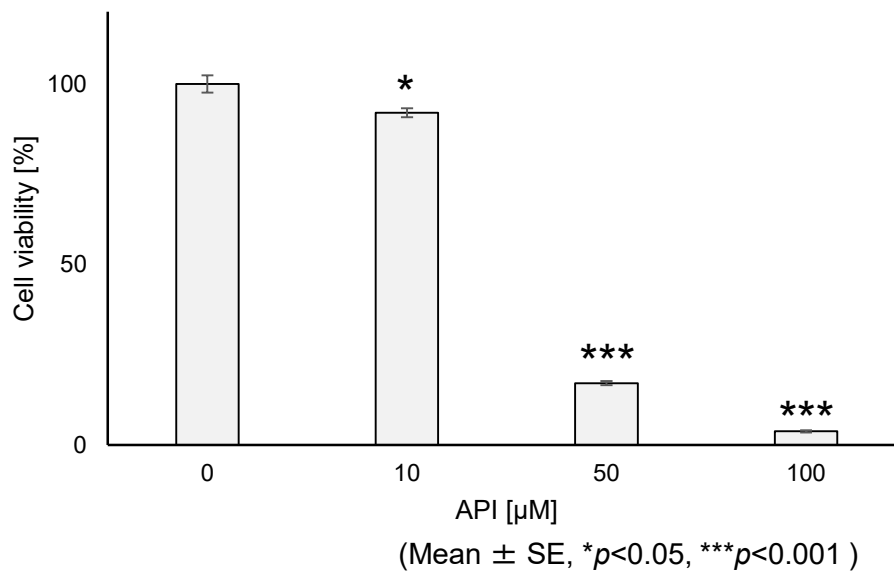
### S3. Cell viability THP-1 monocytes treated with API

#### S 3-1. Method

Cellular viability of THP-1 monocytes treated with API were evaluated using MTT assay described in section 2.4 of the main article.

#### S 3-2. Result

Compared to PIP (Figure 5A), 50  $\mu$ M API was highly cytotoxic to THP-1 monocytes. The cell viability of THP-1 monocytes significantly decreased when the cells were treated with each concentration of API (10, 50, 100  $\mu$ M).



Supplemental Figure S3. Cell viability of THP-1 monocytes treated with API.

Table S1. The Stern-Volmer constant (K<sub>sv</sub>) and apparent binding constant (K<sub>a</sub>) of curcumin (CUR), alpha-tocopherol (α-Toc), ascorbic acid (AsA), curcumin glucuronide (CURG), ferulic acid (FA), vanillin (VAN), quercetin (QUE), apigenin (API) and piperine (PIP). Data for QUE and PIP were cited with reference to supplemental data from our previous reports. The values of PIP and QUR were referred to our previous report<sup>1</sup>.

	K <sub>sv</sub> × 10 <sup>5</sup> [M <sup>-1</sup> ]	K <sub>a</sub> × 10 <sup>5</sup> [M <sup>-1</sup> ]
CUR	1.6	5.4
α-Toc	0.077	0.12
AsA	0.42	0.23
CURG	1.3	1.4
FA	0.84	0.33
VAN	0.78	0.80
QUE	1.2 [1]	4.9 [1]
API	2.1	7.9
PIP	3.3 [1]	25 [1]

(n=1)

[1] M. Itaya, T. Miyazawa, J. M. Zingg, T. Eitsuka, A. Azzi, M. Meydani, T. Miyazawa and K. Nakagawa, The differential cellular uptake of curcuminoids in vitro depends dominantly on albumin interaction, *Phytomedicine*, 2019, **59**, 152902-152913.