# Supplementary materials and methods

## HPLC analysis

Hot-water extracts from the leaves of *H. serrata* (Thunb.) Ser (WHS) and hydrangenol were prepared according to our procedure previously reported. HPLC was performed on Waters 1500 series HPLC system (Waters) equipped with a 1525 binary pump, Empower 3 software, column oven, and photodiode array detector (model 2996) using a Luna C18 column (5 μm, 250 × 4.6 mm, Phenomenex, Torrance, CA, USA). The temperature of the column was maintained at 30°C during the chromatographic separation. The gradient mobile phases consisted of solvent A (100% acetonitrile) and solvent B (water) with a gradient elution as follows: 0 to 15 min, 20% to 25%; 15 to 30 min, 25% to 50%; 30 to 40 min, 50% to 100%; 40 to 50 min, 100% to 20% as percent of solvent A at a flow rate of 1.0 mL/min. The flow rate was set at 1.0 mL/min for 50 minutes in a gradient mode. The identification of the chromatographic peaks was performed by comparing the retention times of the samples by recording the UV spectra of the peaks in the range of 210 - 400 nm.

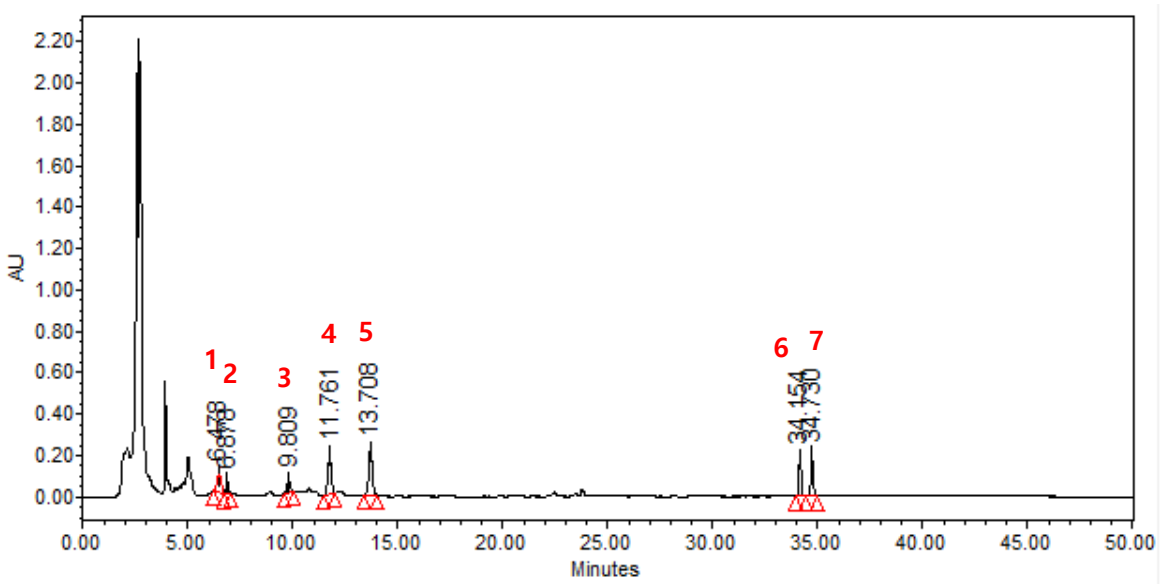
## Construction of colitis animal model

During experiments, the Control group was given drinking water and administered the vehicle orally, and the DSS group was given 4% DSS and administered the vehicle orally. The ASA group was given 4% DSS and daily administered 5-ASA (75 mg/kg/day, p.o., a reference drug). WHS groups were given 4% DSS and administered WHS (25 or 100 mg/kg/day, p.o.; WHS 25 or WHS 100 group) daily.

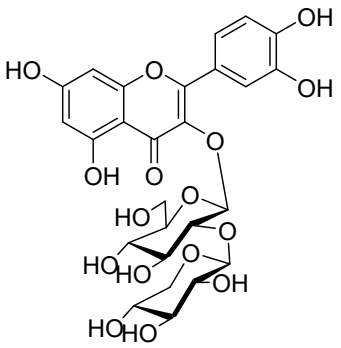
# Supplementary results

## HPLC-based chemoprofile for WHS

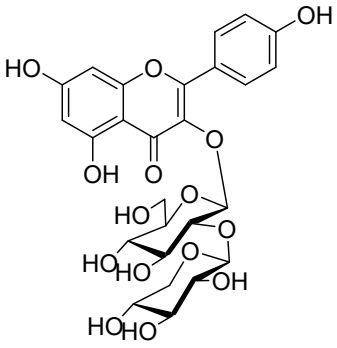
To analyze the chemoprofile of WHS, HPLC analyses were performed on the extract. As shown in supplementary Figure 1 and 2, seven major phenolic compounds: quercetin 3-*O*-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside (**1**), kaempferol 3-*O*-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside (**2**), 4-hydroxybenzaldehyde (**3**), 3*S*-phyllodulcin 8-glucopyranoside (**4**), 3*R*-phyllodulcin 8-glucopyranoside (**5**), hydrangenol (**6**) and phyllodulcin (**7**) were isolated and identified from WHS.



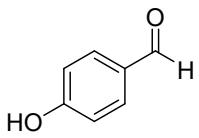

**Supplementary Figure 1.** Representative high-performance liquid chromatography profile of hot-water extract from the leaves of *H. serratea* at 210 nm. 1: quercetin 3-*O*-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside ($R_t$ 6.478 min), 2: kaempferol 3-*O*-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside ($R_t$ 6.878 min), 3: 4-hydroxybenzaldehyde ($R_t$ 9.809 min), 4: 3*S*-phyllodulcin 8-glucopyranoside ($R_t$ 11.761 min), 5: 3*R*-phyllodulcin 8-glucopyranoside ($R_t$ 13.708 min), 6: hydrangenol ($R_t$ 34.154 min), and 7: phyllodulcin ($R_t$ 34.730 min).



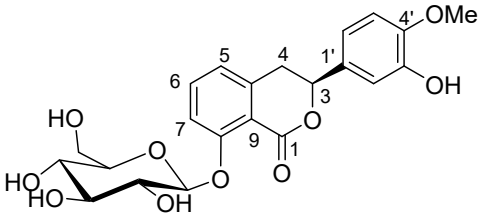
Quercetin 3-O-β-D-xylopyranosyl (1➔2)-β-D-glucopyranoside (**1**)



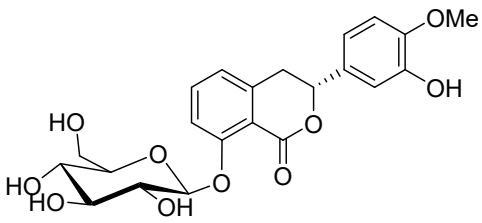
Kaempferol 3-O-β-D-xylopyranosyl (1➔2)-β-D-glucopyranoside (**2**)



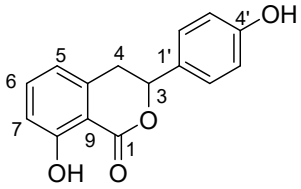
4-hydroxybenzaldehyde (**3**)



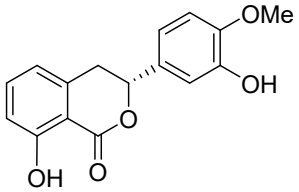
3*S*-Phyllodulcin 8-glucopyranoside (**4**)



3*R*-Phyllodulcin 8-glucopyranoside (**5**)



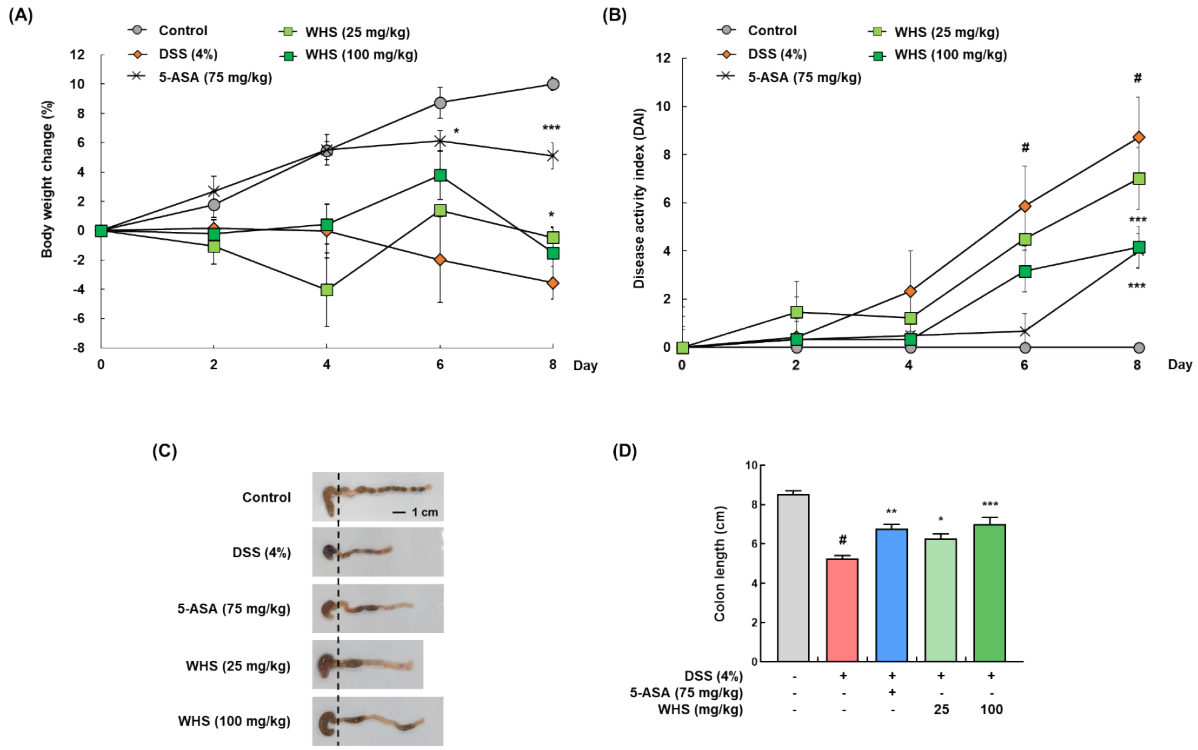
Hydrangenol (**6**)



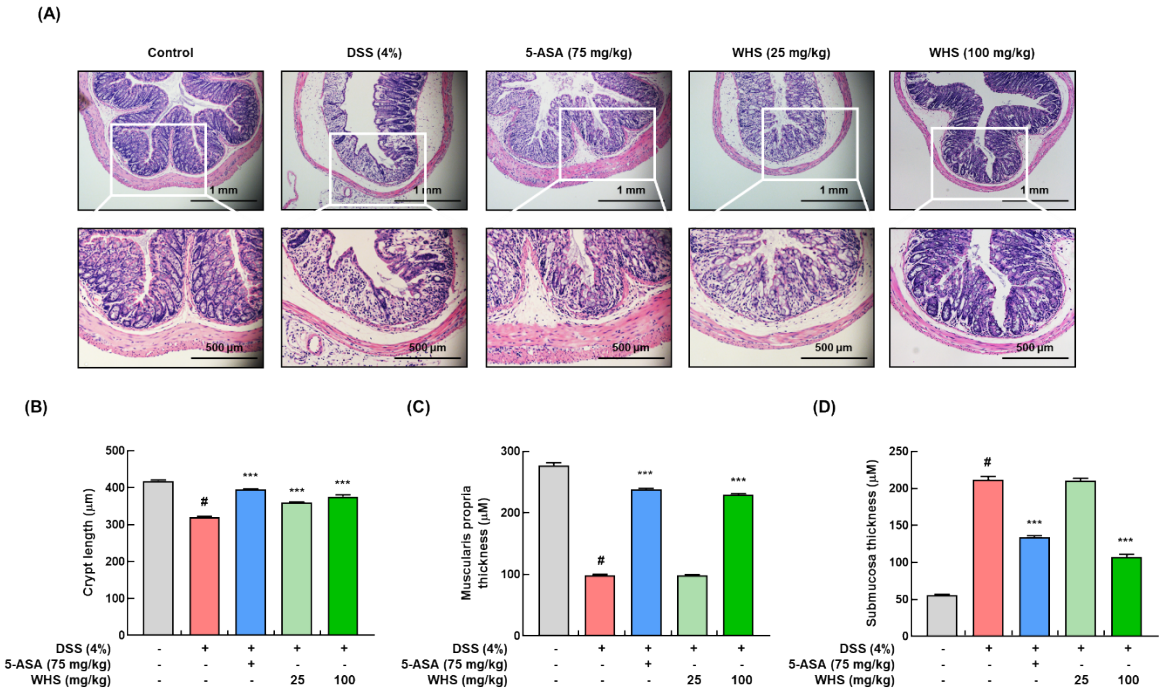
Phyllodulcin (**7**)

**Supplementary Figure 2.** Chemical structures of seven major compounds from the water extract of leaves of *H. serrata*.

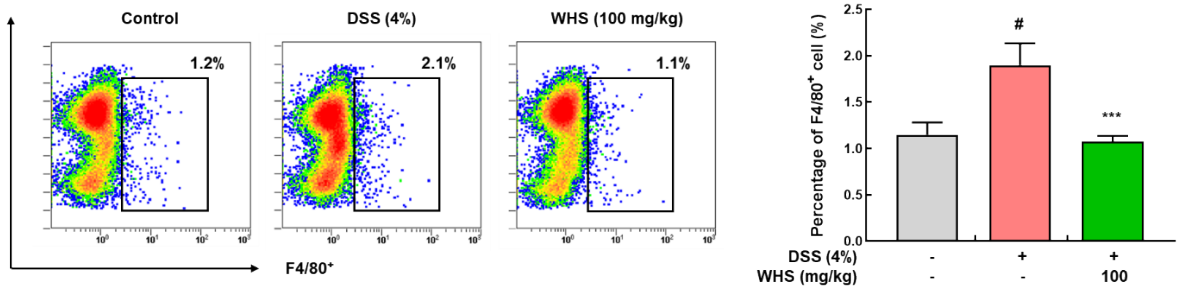
**WHS suppressed colitis with the improvement of colonic structural damage and macrophages accumulation in DSS-treated mice**




**Supplementary Figure 3.** WHS administration mitigated clinical symptoms of dextran sodium sulfate (DSS)-induced colitis in mice. (A) During the experimental period, the body weight change of each group was determined. (B) The DAI score of each group was assessed on the 8th day of the experimental period. (C) Representative macroscopic images of the colon from each group and (D) the colon length was measured. Data are presented as mean ± SEM ($n$ = 6 mice per group). $^{\#}P < 0.05$ compared with the vehicle-treated control group, and $^{**}P < 0.01$, $^{***}P < 0.001$ compared with the DSS-treated group.




**Supplementary Figure 4.** WHS improved colonic structure in dextran sodium sulfate (DSS)-induced colitis. (A) Representative microscopic pictures of H&E-stained colon tissues from each group. (B) Villus height, (C) muscularis propria thickness, and (D) submucosa thickness were measured using OLYMPUS cellSens Standard 1.9. Data are presented as mean ± SEM. $^{\#}P < 0.05$ compared with the vehicle-treated control group, and $^{***}P < 0.001$ compared with the DSS-treated group.




**Supplementary Figure 5.** WHS administration inhibited macrophage infiltration in DSS-induced colitis mice. Representative scatterplots of flow cytometry analysis of macrophages based on surface markers F4/80 in the MLNs (left) and summarized data (right). Data are presented as mean ± SEM. $^{\#}P < 0.05$ compared with the vehicle-treated control group, and $^{***}P < 0.001$ compared with the DSS-treated group.