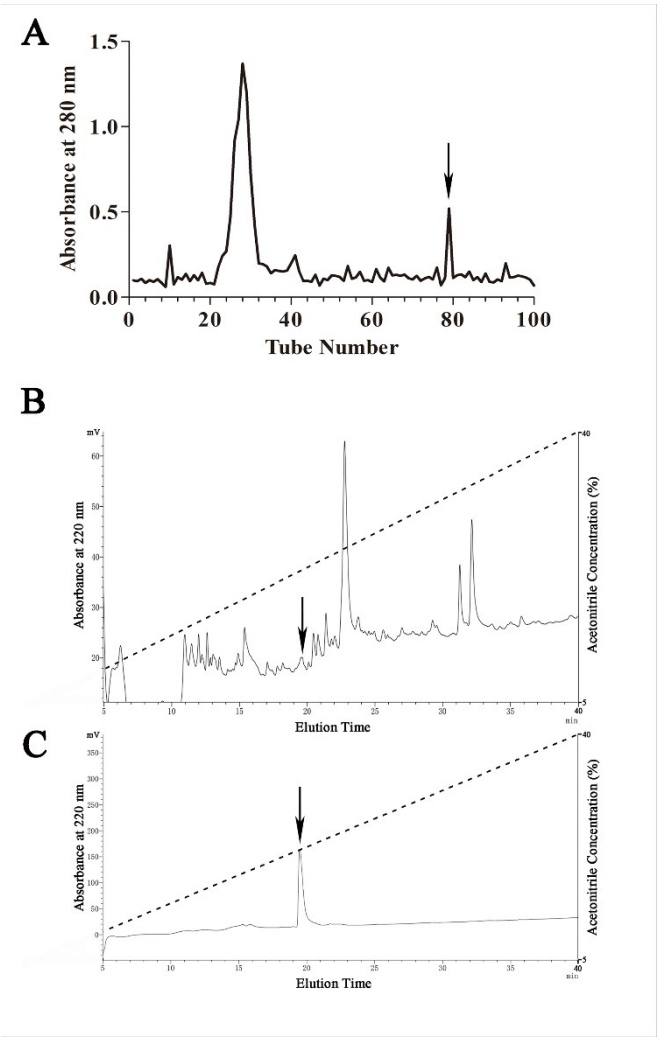
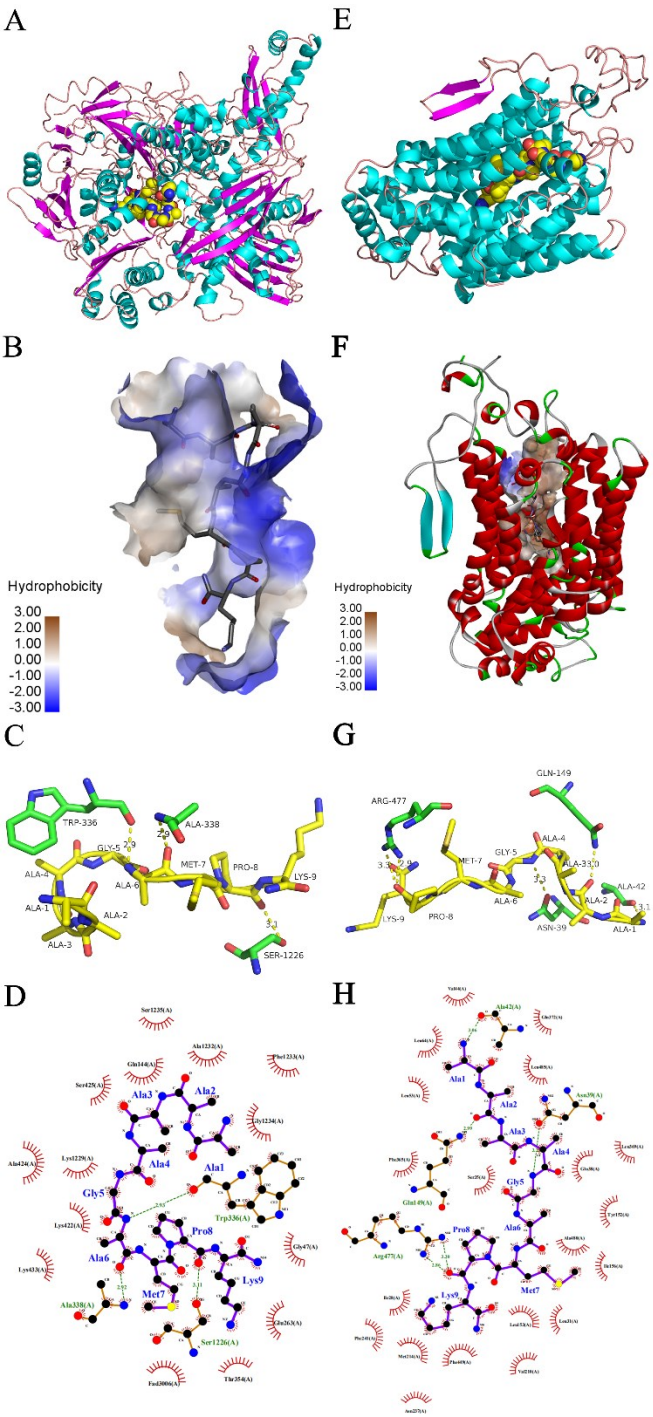
Supplemental Data



Supplementary Figure 1. Purification procedure of RDP2.

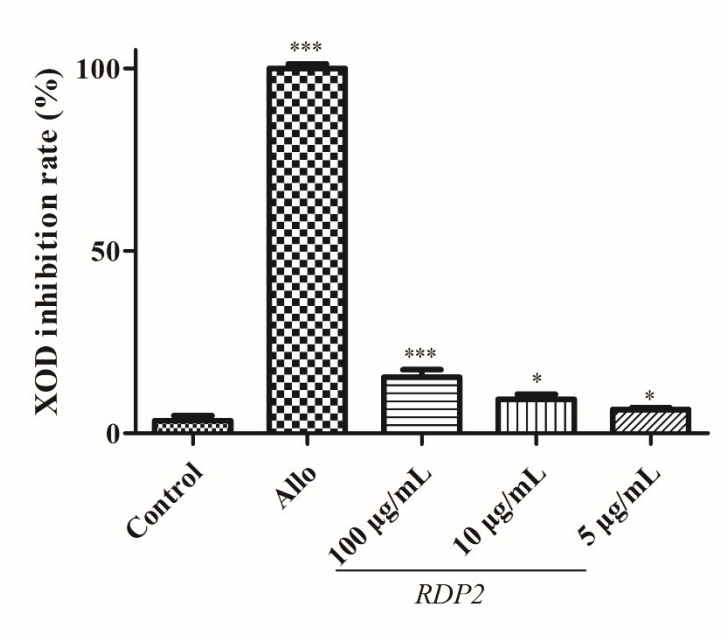
First separation procedure was performed using a Sephadex G50 column, with arrow in Fig. S1A indicating sample separated by RP-HPLC. Sample indicated by arrow in Fig. S1B was further purified by RP-HPLC. Final purified peptide was obtained, as shown by arrow in Fig. S1C (Fig. S1A and Fig. S1B were reported in our previous research[1], with a different elution time shown in C).

(Reference: 1. Liu, N, Wang, Y, Yang, M, Bian, W, Zeng, L, Yin, S, et al. (2019). New Rice-Derived Short Peptide Potently Alleviated Hyperuricemia Induced by Potassium Oxonate in Rats. J Agric Food Chem ***67****: 220-228.)*



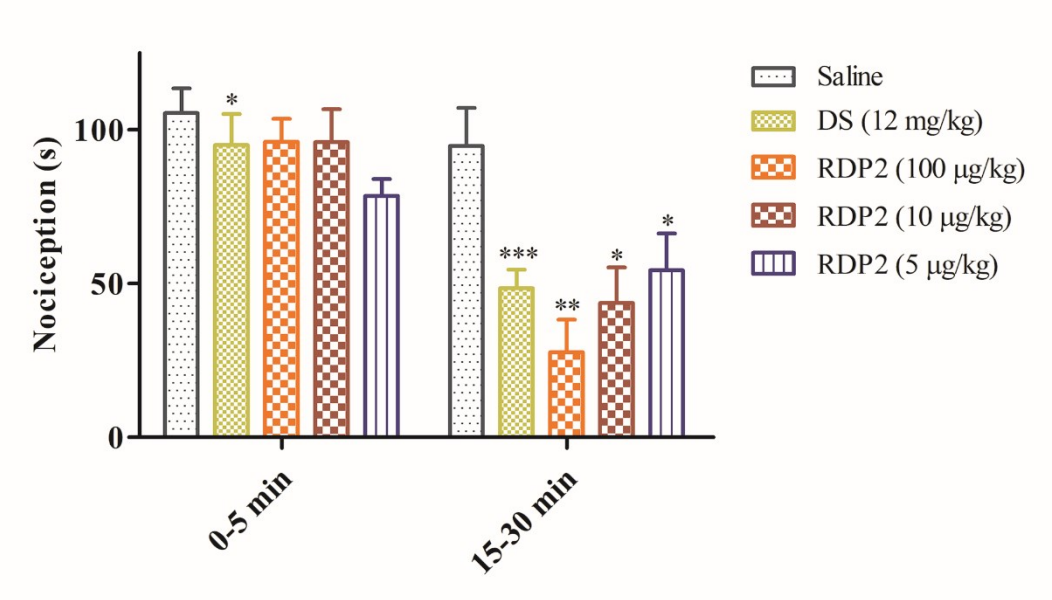
Supplementary Figure 2. Molecular docking of RDP2-XOD and RDP2-URAT1.

Binding of RDP2 with xanthine oxidase (XOD, A-D) and urate transporter 1 (URAT1, E-H). Whole RDP2 integrated with XOD (A, B) and URAT1 (E, F); hydrogen bond between RDP2 and XOD (C)/URAT1 (G); pocket residue of combination of RDP2 and XOD (D) / URAT1 (H).



Supplementary Figure 3. XOD inhibition assay of RDP2 *in vitro*.

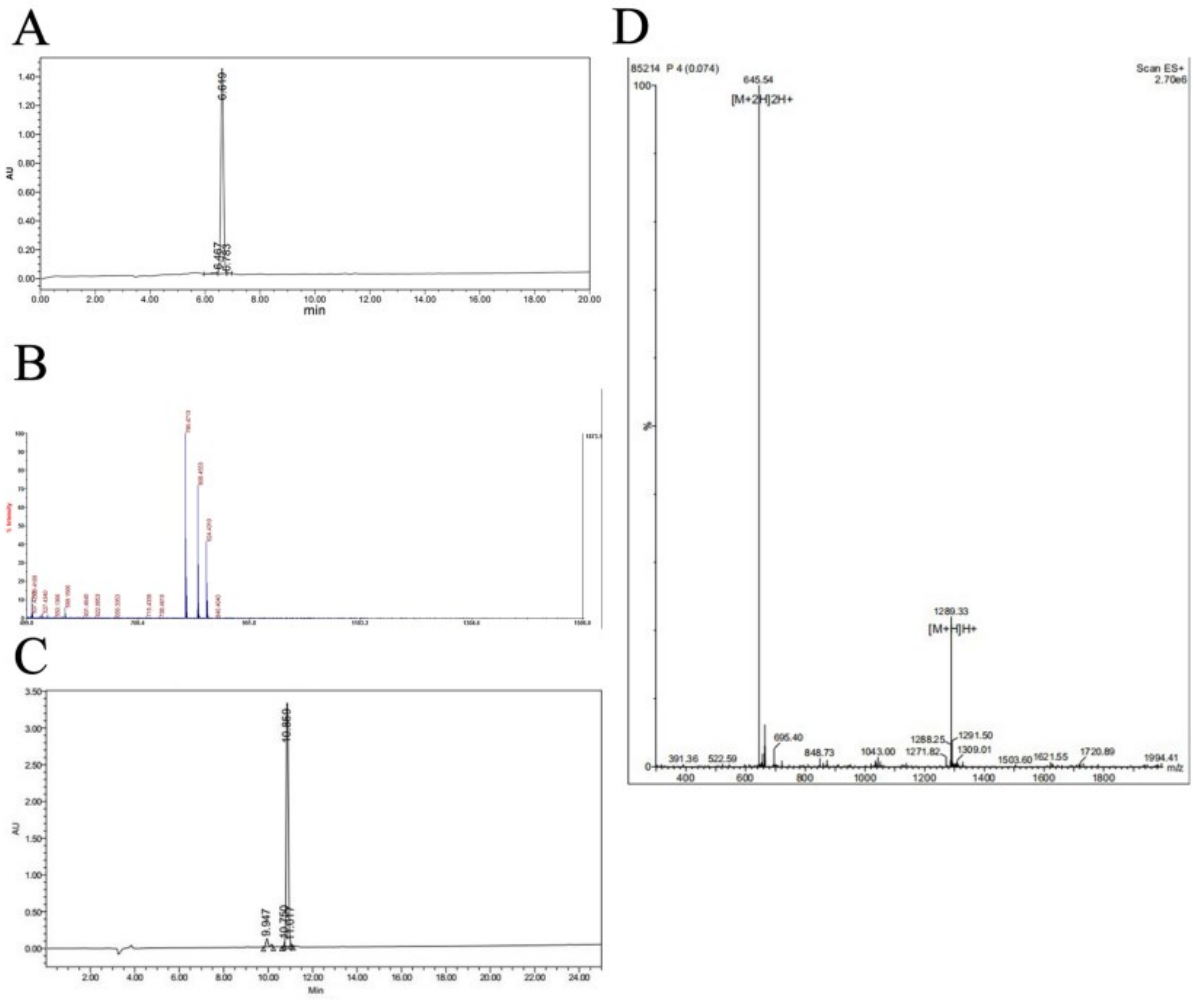
RDP2 showed XOD inhibition activity *in vitro* with a concentration dependent manner. RDP2s (100 μg/mL) inhibiting activity against XOD were 1/6 that of Allo (10 mg/mL) (n = 5). *P < 0.05 and ***P< 0.001 (Student's t tests).



Supplementary Figure 4. RDP2 alleviated formalin-induced paw licking in mice.

Within 0–5 min of formalin injection, no significant differences in licking time were found among groups, except for DS group (diclofenac sodium, 12 mg/kg)(n = 6, $*P < 0.05$ DS vs. Saline). Within 15–30 min of injection, licking time in DS and RDP2 groups was significantly lower than that in the Saline group, and RDP2 decreased licking time in mice in a concentration dependent manner.

$*P < 0.05$, $**P < 0.01$, and $***P < 0.001$ (Student's *t*-tests).



Supplementary Figure 5. The mass spectrum and chromatogram of RDP2 and FITC-RDP2.

A. Mass spectrometry of RDP2.

B. Chromatogram of RDP2 (AAAAGAPMK-NH2).

C. Mass spectrometry of FITC-RDP2.

D. Chromatogram of FITC-RDP2.

Supplementary Table 1. Hemolytic activity of RDP2.

RDP2 showed no hemolytic activity in human red cells (n = 5).

Group	Hemolytic ratio
Triton (0.1%)	100%
Saline	4.0% ± 0.13%
5 μg/mL RDP2	4.5% ± 0.70%
10 μg/mL RDP2	5.0% ± 0.14%
100 μg/mL RDP2	4.8% ± 0.11%

Supplementary Table 2. Acute toxicity of RDP2.

RDP2 showed no acute toxicity in mice.

	Number of mice		
Group	Male	Female	Mortality rate (%)
Negative control (saline, 1 mL/kg)	3	3	0
Experimental group			
100 μg/kg RDP2	3	3	0
10 μg/kg RDP2	3	3	0
5 μg/kg RDP2	3	3	0

Supplementary Table 3. Stability of RDP2 in plasma.

Time (h)	0	1	2	3	4	5	6	7

Intact RDP2 (%)	100.82±0.28	63.15±1.22	37.35±1.03	17.85±0.77	14.48±1.72	5.39±0.41	0.67±0.10	0