Electronic Supplementary Material (ESI) for RSC Advances.
This journal is © The Royal Society of Chemistry 2023

Supplementary Information
for
Enhanced inhibition of protein disulfide isomerase and anti-thrombotic activity of a rutin derivative: rutin:Zn complex

Xinyuan Liao[a], Panpan Ji[b], Kunxiang Chi[a], Xueying Chen[a], Yang Zhou[a], Shanli Chen[a], Yuan Cheng[a], Robert Flaumenhaft[c], Cai Yuan[b,*] and Mingdong Huang[a,*]

[a]College of Chemistry, Fuzhou University, Fujian 350108, China
[b]College of Biological Science and Engineering, Fuzhou University, Fuzhou, Fujian, 350108, China
[c]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215

Rutin

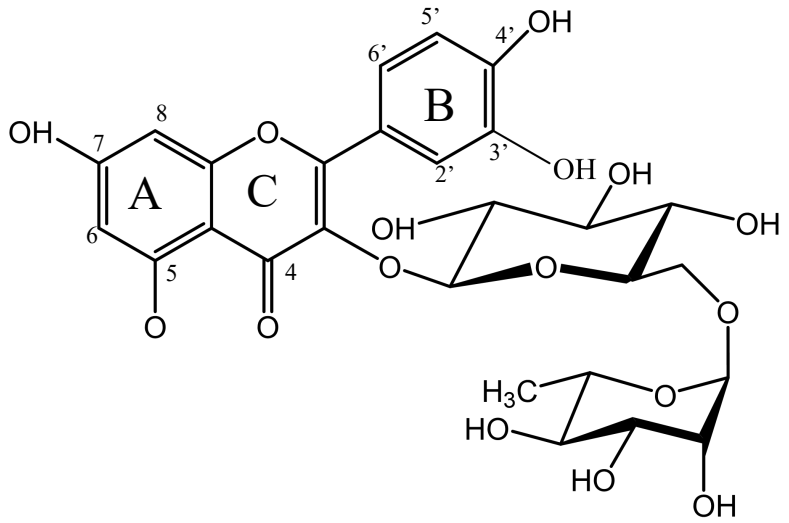

Fig.S1 The chemical structure of rutin.

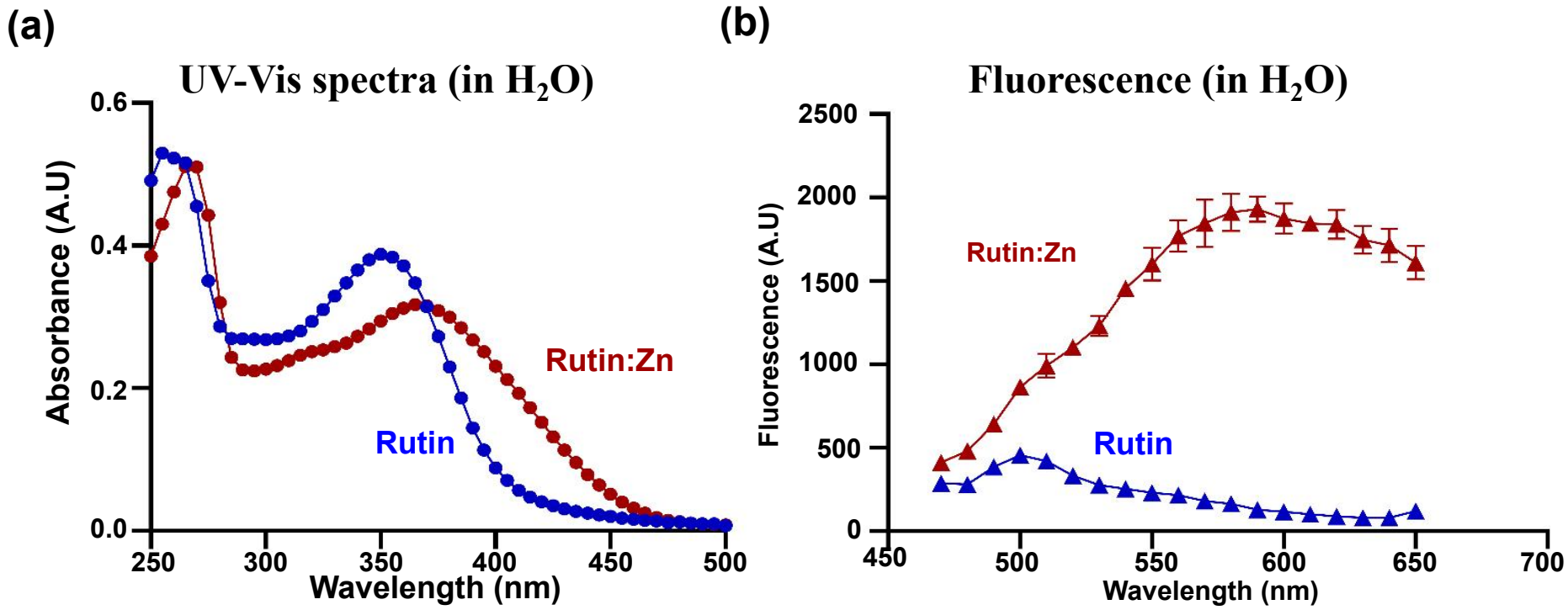

Fig. S2 Rutin:Zn complex was not dissociated after rutin:Zn complex dissolved in the H_2O (a) UV-VIS spectra of Rutin (blue) and Rutin:Zn (red) in H_2O. (b) Fluorescence spectra of Rutin (blue) and Rutin:Zn (red) in H_2O, rutin:Zn showed higher fluorescence than rutin.

Rutin:Zn

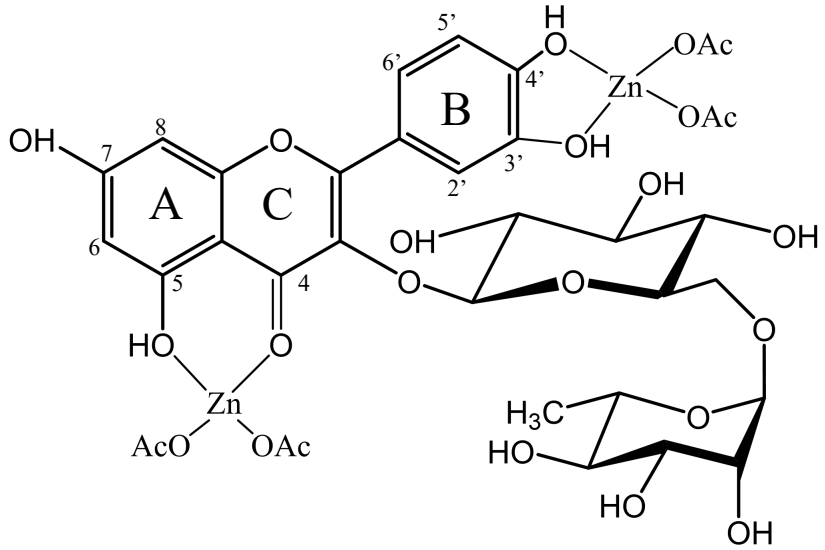

Fig.S3 The chemical structure of rutin:Zn complex. Zinc ion chelates at the 4-keto,5-phenoxy position and 3'-4'-catechol moiety of rutin.

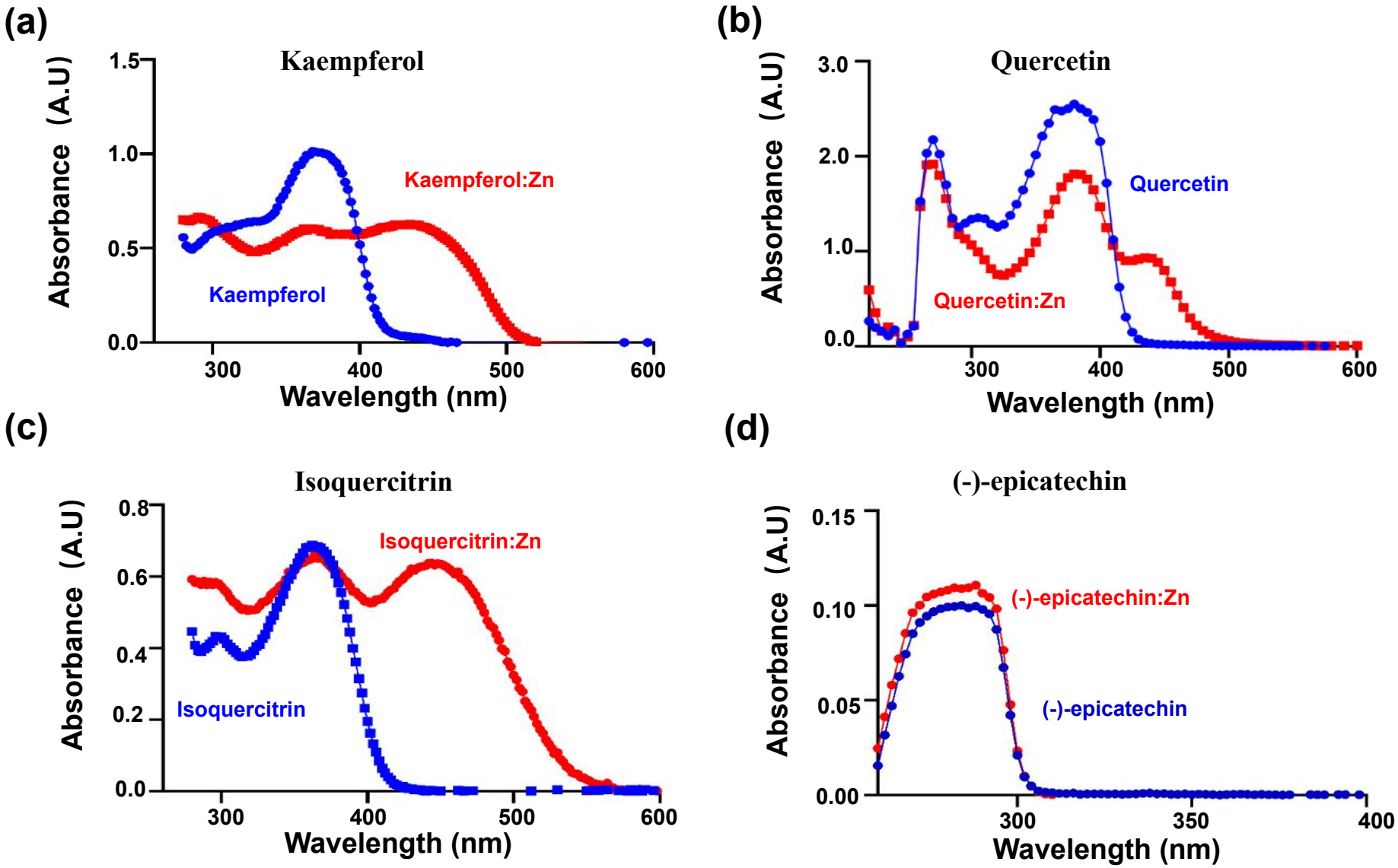

Fig. S4 The addition of zinc acetate significantly changed the UV-VIS of flavonoids containing adjacent 4-keto,5-phenoxy. The zinc ion chelation changed the UV-VIS spectra of the molecules' containing the The adjacent keto and phenoxy (red): kaempferol (a), quercetin (b), Isoquercitrin (c), in DMSO at 10mM (ratio 1:1), showed additional new peaks compared to the native compounds (blue), demonstrating the direct coordination of zinc ion. In contrast, the UV-VIS spectra of the molecules without adjacent keto and phenoxy group ((-)-epicatechin (d) didn't shift after adding the zinc ion.

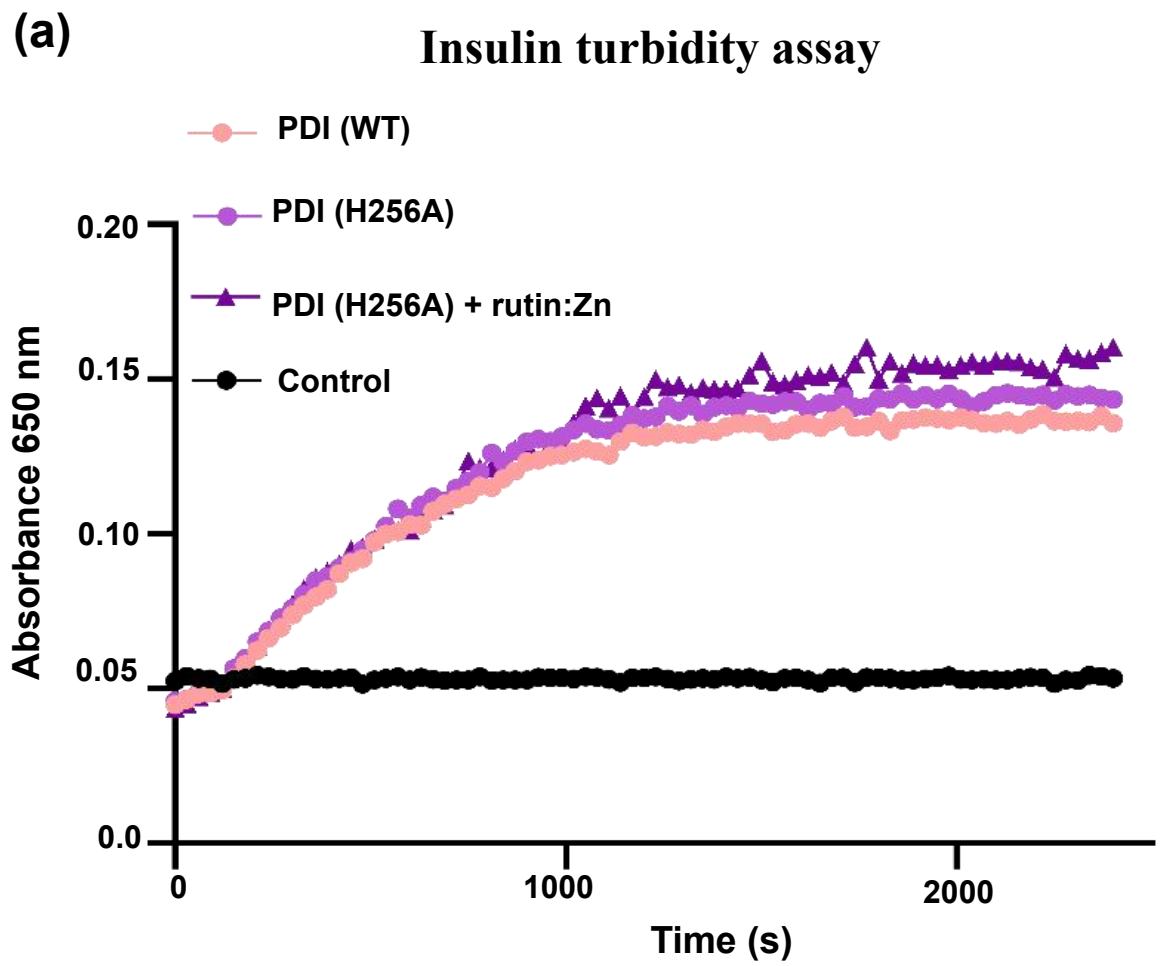

Fig.S5 H256 is important for rutin:Zn binding to PDI. (a) Mutant 256 abolished rutin:Zn inhibition efficacy to PDI.

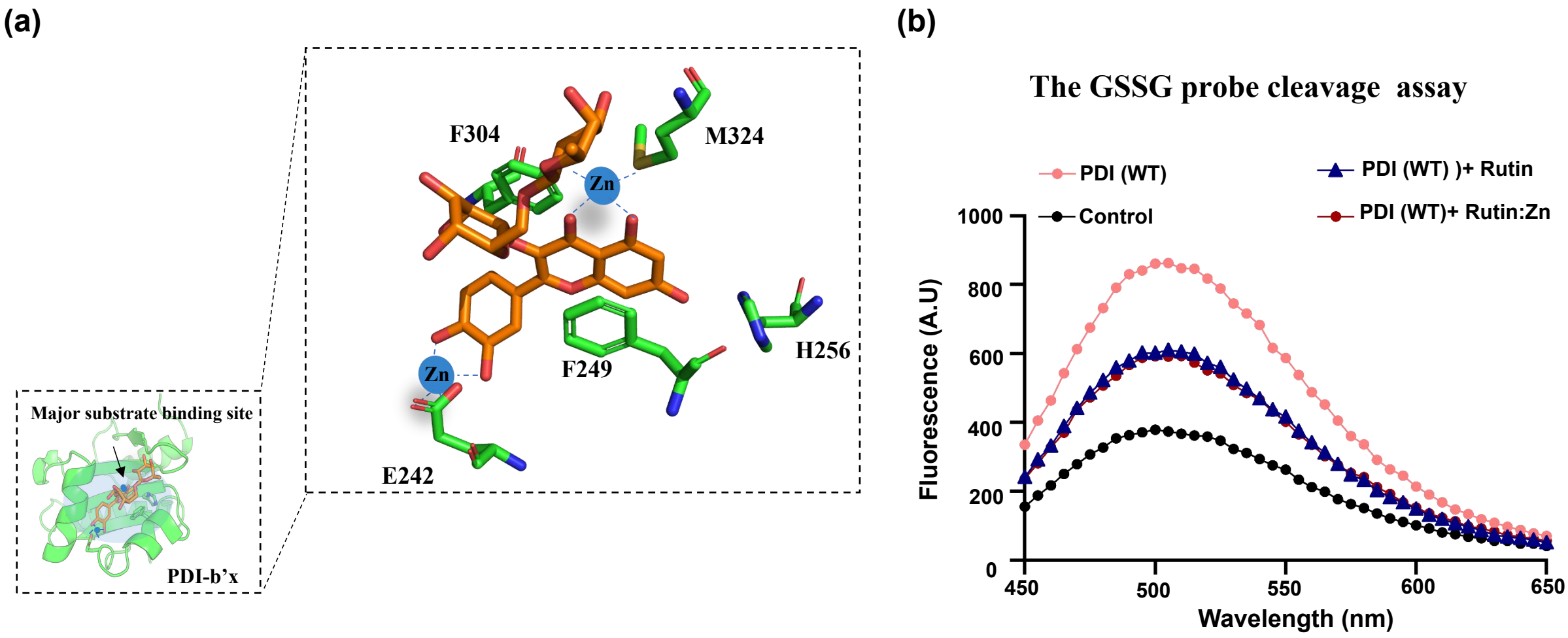

Fig. S6 Rutin:Zn inhibition to PDI is comparable to rutin in the GSSG probe cleavage assay. (a) The molecular dynamic model showed rutin:Zn interaction with PDI in the major substrates binding site of PDI. The rutin was colored orange, the zinc ion was colored blue and the interaction amino acids of PDI were colored in green sticks. (b) Rutin:Zn and Rutin (each at 35 μM) had the comparable inhibition to PDI-mediated cleavage of the probe (Dabcyl)-GSSG-(EDANS), leading to lower fluorescence emission.