**Supporting Information**

# Quercetin Remodels the Tumor Microenvironment to Improve the Permeation, Retention and Antitumor Effects of Nanoparticles

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**Synthesis and characterization of quercetin phosphate (QP).** The synthetic scheme illustrated in Figure S1 was followed. The molecular weight of the ethyl protected QP intermediate was confirmed by MS spectrum (m/z=982.99). The presence of five phosphate groups of the final QP was confirmed by the appearance of fivesinglets in the

$^{31}$P-NMR spectrum (See Figure S2). The five phosphate groups on QP were further confirmed by $^{1}$H-NMR, $^{13}$C-NMR (Figure S2) and LC-MS (m/z=702.88). The QP has improved hydrophilicity compared to parent quercetin.

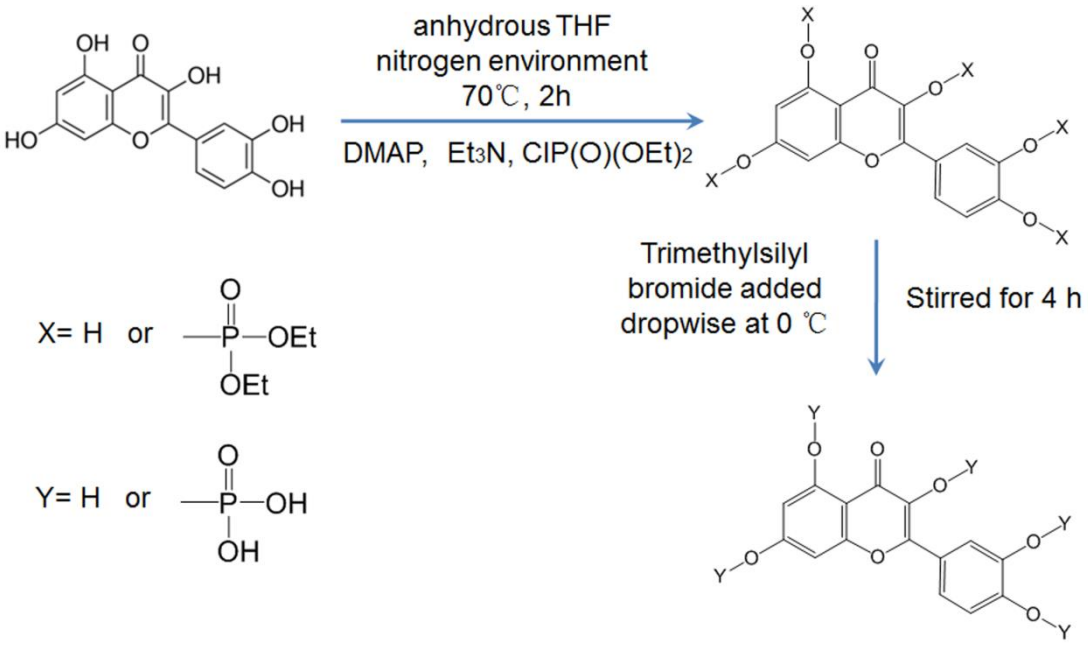
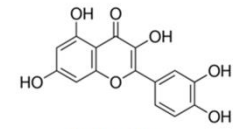
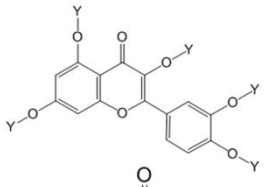



**Figure S1.** Scheme for synthesis of phosphorylated quercetin

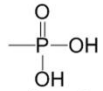
NMR-$^{31}$P



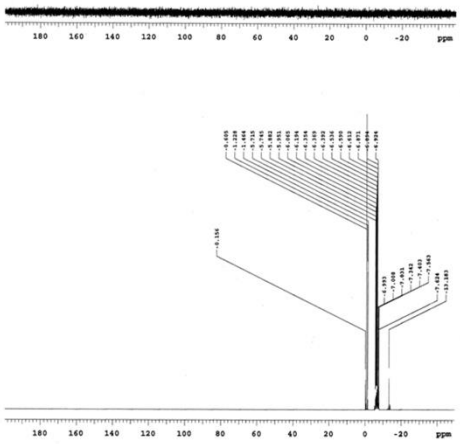
Quercetin



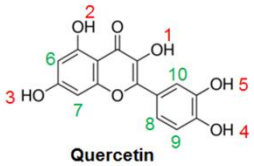
Y= H or



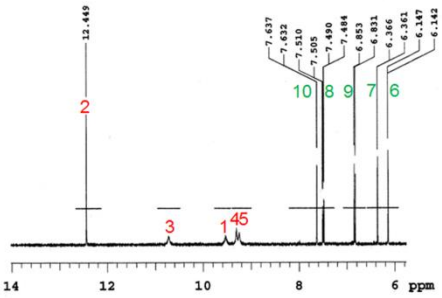
Quercetin phosphate

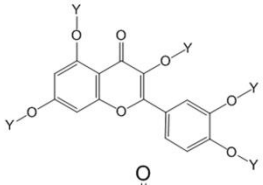


NMR-$^{1}$H



Quercetin





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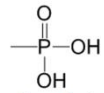
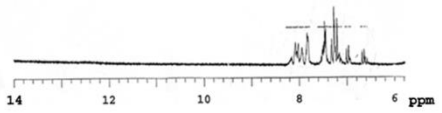
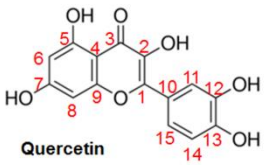


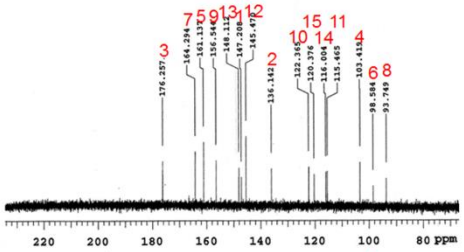
Quercetin phosphate

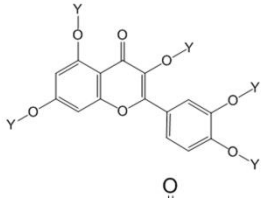


NMR-$^{13}$C



Quercetin





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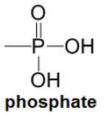

Quercetin phosphate

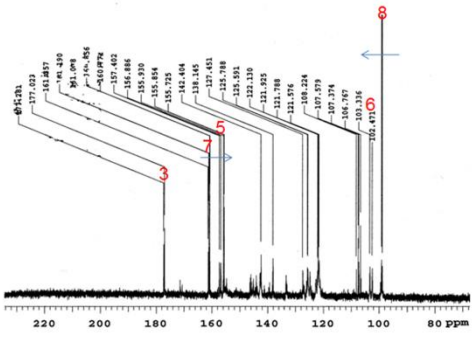

**Figure S2.** Structure and $^{31}$P-NMR, $^{1}$H-NMR, $^{13}$C-NMR spectrum of quercetin and phosphorylated quercetin.