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Biflavonoids from Torreya nucifera displaying SARS-CoV 3CL(pro) inhibition.

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Abstract

As part of our search for botanical sources of SARS-CoV 3CL(pro) inhibitors, we selected Torreya nucifera, which is traditionally used as a medicinal plant in Asia. The ethanol extract of T. nucifera leaves exhibited good SARS-CoV 3CL(pro) inhibitory activity (62% at 100μg/mL). Following bioactivity-guided fractionation, eight diterpenoids (1-8) and four biflavonoids (9-12) were isolated and evaluated for SARS-CoV 3CL(pro) inhibition using fluorescence resonance energy transfer analysis. Of these compounds, the biflavone amentoflavone (9) (IC(50)=8.3μM) showed most potent 3CL(pro) inhibitory effect. Three additional authentic flavones (apigenin, luteolin and quercetin) were tested to establish the basic structure-activity relationship of biflavones. Apigenin, luteolin, and quercetin inhibited 3CL(pro) activity with IC(50) values of 280.8, 20.2, and 23.8μM, respectively. Values of binding energy obtained in a molecular docking study supported the results of enzymatic assays. More potent activity appeared to be associated with the presence of an apigenin moiety at position C-3' of flavones, as biflavone had an effect on 3CL(pro) inhibitory activity.

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