

**Title** SYNTHESIS OF NOVEL CAPSINOID ANALOGUES  
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### ABSTRACT

Capsinioids are promising natural substances using for energy boost, improvement oxygen consumption, blood circulation and immunity. However, one drawback is the highly unstable of capsinioids when exposed to temperature and light. Additionally, they are highly sensitive with polar solvent such as water or buffer making them less likely to be utilized. This study demonstrated how to enhance capsinioids stability *via* simple modification by inversion of ester linkage position while maintaining H-bonding interaction of hydroxy group of phenolic residue. The capsinoid analogues were easily prepared *via* esterification reaction of homovanillic acid (**14**) and lipophilic chain (*E/Z*-7-methyl-5-octenol (**12**, **13**), (*E*)-8-methyl-6-nonenol (**17**) and 8-methylnonanol (**18**), respectively) by using *N,N'*-dicyclohexylcarbodiimide (DCC), and 4-dimethyl aminopyridine (DMAP), and 1-hydroxybenzotriazole (HOBt) as a coupling reagent then followed by isomerization. The synthesis of capsinoid analogues (**4-7**) were achieved with yields in the range of 62-70%. The stability test in polar protic solvent (CH<sub>3</sub>OH:H<sub>2</sub>O/80:20 v/v with 0.025 M AcOH) were investigated by HPLC technique. It was clearly shown that capsinoid analogues (**4-7**) were stable over the periods of 24 hours and exhibited no sign of cytotoxicity in the range of concentration from 0.1-200 μM. In conclusion, this was the first series of capsinoid analogues with inversion of ester linkage position with very high stability.