

**Synergistic enhancement of *in-vitro* cell migration by ethuliacoumarin and stigmasterol from *Jeffreyia zeylanica*:
A preliminary investigation using the response additive approach**

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Scratch wound assay (SWA) directed fractionation of the hexane extract of aerial parts of *J. zeylanica* led to the isolation of ethuliacoumarin (1) and stigmasterol (2). These two compounds exhibited enhanced *in-vitro* cell migration activity each at 12.5 μ M (1-67.0% and 2-73.5%) compared to the negative control (20.1%) in SWA performed on Madin-Darby Canine Kidney (MDCK) cells. The interaction between 1 and 2 was studied by employing the response additive approach. In this method, the SWA was performed for compounds 1 and 2 separately at the doses lower than ED_{50} and the dose pair combinations of compounds 1 and 2 in which the concentration of each is less than its ED_{50} value. The mean percent wound closures (E_{Observed}) were determined for each dose pair combination. For each dose pair, the expected additive effect (E_{Expected}) was determined by summing the mean percent wound closures observed for each compound when they were individually subjected to SWA at the corresponding doses in the combinations. The combination index (CI)

for each dose pair combination was calculated. It was found that the tested dose pair combinations showed significantly higher cell migration effect (E_{Observed}) than the expected additive effect (E_{Expected}) in which $CI > 1$. Therefore, the presence of ethuliacoumarin (1) and stigmasterol (2) in the hexane extract of aerial parts of *J. zeylanica* may contribute synergistically to its effective cell migration activity. Further studies with different pharmacological approaches/models are necessary to draw firm conclusions on the interaction between compounds 1 and 2.

Keywords:

Synergistic interaction, cell migration, ethuliacoumarin, stigmasterol, *Jeffreyia zeylanica*

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