

**P-055: INHIBITORS OF NF- $\kappa$ B ACTIVATION PATHWAY FROM *CHRYSOTHAMNUS NAUSEOSUS***

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Activation of the nuclear factor- $\kappa$ B (NF- $\kappa$ B) signaling pathway leads to induction of target genes that can interfere with apoptosis, cell cycle regulation, cell invasion and metastatic growth, as well as radio- and chemotherapy. This pathway is particularly important in the pathogenesis of diffuse large B-cell lymphoma (DLBCL). Thus, regulation of the signaling pathways involved in NF- $\kappa$ B activation constitutes a promising therapeutic target. We have developed a high throughput screen using DLBCL cell lines engineered to express a chimeric NF- $\kappa$ B-luciferase reporter protein.

The organic extract of *C. nauseosus* activated the reporter in OCI-LY3 cells, suggesting induction of IKK $\beta$ . Dereplication of the extract showed 3 groups of fractions with moderate activity and no toxicity. The active constituents were characterized as polyacetylenes from the UV and MS data. Scale up isolation led to identification of one new chlorinated polyacetylene and two known compounds, methyl 10-hydroxymatricariate and methyl-10-hydroxy-8,9-epoxydecen-4,6-dienoate. A Sharpless epoxidation was employed to determine the stereochemistry of the latter compound. The known metabolites were transformed to the corresponding acetylated compounds, also detected in the active fractions.

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