Department of Chemistry

Departmental Seminar:
Biodiscovery Month

You are cordially invited to a virtual lecture presented by

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Date: 10 December 2021
Time: 10:30 – 11:20
Venue: Google Meet
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HPLC-based purification and isolation of anti-HIV and latency reversal compounds from a *Gnidia species* (Thymelaeaceae)

The HIV/AIDS epidemic continues to be a global public health threat with 37.7 million people living with the virus as of 2020. This is mainly due to the presence of latently infected CD4+ T cells that avoid clearance by cART and detection by the immune system. One experimental method to identify and eliminate latently-infected CD4+ T-cells, frequently termed the "shock and kill" strategy aims to reactivate provirus expression in the presence of antiretroviral therapy and target virus-expressing cells for elimination. To achieve this, a particularly attractive therapeutic prototype would be a small molecule that can both inhibit viral replication and induce latency reversal simultaneously. In the realm of natural product-based chemical compounds a South African plant *species* (*Gnidia*) used as part of a mixture in the treatment of HIV has been proven to be a source of compounds that can both activate the latently infected CD4+ T-cells and inhibit viral replication. By means of HPLC-based activity profiling a total of four daphnane-type with a 9,13,14 ortho-ester motif and a 6α-epoxy were identified as the active compounds in the DCM extract and further isolated using repeated chromatographic techniques.

Of the four compounds screened, yuanhuacine and yuanhuacine A both inhibited the viral replication by greater than 80% when screened at (0.08 µg/ml) *in-vitro* against HIV (NL4-3) isolate. The anti-HIV activity of yuanhuacine A was re-assessed in PBMC using a subtype C viral strain and demonstrated exquisite activity with an IC_{50} and IC_{90} of 0.03 and 0.09 µM, respectively. It further showed excellent selectivity over cytotoxicity with a selectivity index of > 500. In addition to inhibiting HIV replication, yuanhuacine A and yuanhuacine exhibited similar levels of latency reversal (65.5 ± 6.3% and 58.2 ± 4.7%, respectively) at 0.15 µM, indicating 16.7-fold enhanced activity over prostratin (a known PKC activator). As a medicinal plant with LRAs through the PKC pathway, *G. sericocephala* could be a useful addition to HIV eradication. Moreover, the anti-HIV and latency reversal activity shown by these compounds justifies further investigation on the mechanisms of this plant in cell and animal models.