

Screening for antiparasitic leads from a library of natural products from temperate zone plants

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There is an urgent need to identify and evaluate novel chemical scaffolds to seed the drug discovery pipeline for parasitic diseases. Complementing international efforts to explore the potential of huge commercial chemical libraries, the search for new leads also encompasses the evaluation of natural products. PhytoQuest, a UK-based Industrial Biotechnology small to medium-sized enterprise, has produced a library of approximately 1000 molecules, isolated predominantly from temperate zone plants. As such, this library represents a unique resource for lead discovery of high value chemicals from temperate zone plants against parasitic diseases, with previous studies focusing largely on plants from tropical and subtropical zones. The library comprises a wide range of chemical classes, two thirds of which are novel, and the remaining third not commercially available. Critically, the compounds are pure, overcoming common issues with screening fractions of complex mixes, and have been selected to reflect potential development, with a high degree of functionality and physiochemical properties that match Lipinski's Rule of Five. A subset of approximately 650 compounds have been screened against the intraerythrocytic stages of *Plasmodium falciparum* and axenic amastigotes of *Leishmania mexicana*, with a further screen against *Trypanosoma brucei* now underway. Here we report a characterization of our hits against *P. falciparum* and *L. mexicana*. This research is supported by a BBSRC-funded High Value Chemicals from Plants (HVCfP) Proof of Concept award to PhytoQuest and Keele University.