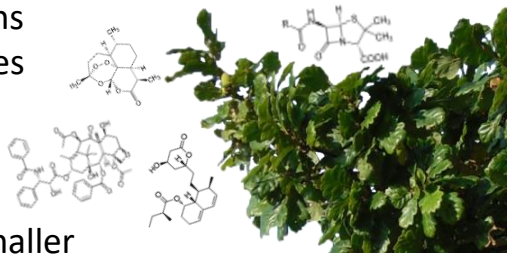
Phytotitre

Caithness BIOTECHNOLOGIES

Natural product extract library

Drug discovery is evolving….

Natural products have historically been the most successful source of new drugs. [1] Indeed, although the 1990s and early 2000s saw a refocus towards greater interest in the screening of large libraries of synthetic compounds, experience has shown that the success rate of natural product library screens remains superior.[2] As a result, natural product libraries are once again returning to the forefront of drug discovery.



But the landscape of early-stage drug discovery is also undergoing another major transformation, as smaller research groups in academia and spinouts are now expected to develop the next generation of therapeutic targets and drug leads. *Phytotitre*, a uniquely focused and optimised high quality plant extract library, has been developed to meet the specific challenges of this new paradigm.

Key features of the *Phytotitre* library

- Unique focus on plants with a history of medicinal use or association with health in man maximises potential for drug discovery
- 800 extracts of plants and fungi are supplied in 96-well format suitable for manual or robotic screening
- Excellent diversity: 367 unique species and 304 unique genera
- Published library with proven activity [3]
- You keep all the IP you generate, no licensing or MTAs required

Potential uses

• *Drug discovery* - particularly where low toxicity over the longer term is desirable

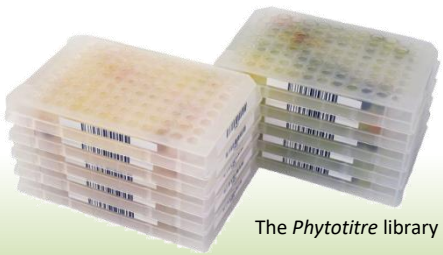
• *Nutraceuticals* - an essential resource for the discovery of novel functional food additives

• *Agrochemicals* - potential for new plant hormones, herbicides and insecticides

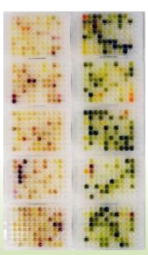
• *Cosmetic industry* - to help meet consumer demand for natural product-derived cosmetics

What are the advantages of a plant extract library over a synthetic compound library?

Phytochemicals occupy a chemical space with a far greater structural diversity than synthetic compound libraries, and tend to be more 'drug-like', with superior ADME/T (absorption, distribution, metabolism, excretion and toxicity) properties. The typical 'hit-rate' of natural product library screens also tends to be far higher,[1] largely due to their inherent enrichment in molecules that interact with conserved protein domains, and the millennia of intense selective pressure faced by plants to develop secondary metabolites that target specific pathways in microbes or herbivores, including mammals. Accordingly, more than half of new drugs approved between 1981 and 2010 were derived or inspired from nature.[4]



The *Phytotitre* library



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Won't I just discover known compounds?

The *Phytotitre* library contains many plants which have been very little studied, and therefore has potential for discovery of new compounds. However, although those hits which turn out to be established compounds are not directly patentable, derivatives of these compounds or their scaffolds offer excellent opportunities for IP generation, especially if a means of synthesis can be described. This model has yielded some of the most profitable drugs of all time (e.g. the statins, with global sales of >$130 Bn), and continues to be a fruitful source of IP (>50% of new drugs from 1981-2010 were nature-inspired).[4]

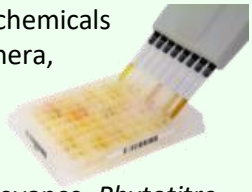
It must be remembered, however, that in terms of novelty, the true value of the screen is in the new target and the assay based upon it.

Key advantages of *Phytotitre*

High-throughput screening of natural product libraries, especially by smaller research groups, has traditionally faced a number of challenges. *Phytotitre* addresses these in the following ways:

1) Balancing diversity with library size

Most natural product libraries are very large (hundreds of plates), thus requiring very costly reagent and labour inputs for preliminary screens. However, because many phytochemicals are expressed widely across genera, optimum structural diversity can be obtained without a very large library size.[5] By focussing only on plants of biomedical relevance, *Phytotitre* balances excellent molecular diversity with manageable workflow for independent labs.



2) Recollection and the Nagoya protocol

All plants in the library are commercially available, so negating any potential issues with recollection, sustainability or national genetic resources.

3) Viscosity and precipitation

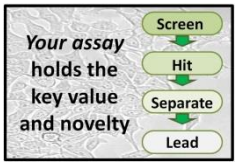
Insoluble or viscous residues have been removed from all extracts after resuspension in DMSO, leaving samples easily pipetted.

4) Accessibility to smaller research groups

Most libraries are sized and priced beyond the means and throughput of smaller laboratories.

Will I be able to generate IP?

To date, only about 400 targets are targeted by drugs. By contrast, tens of thousands of potential protein targets have never been screened before. These targets, and the bioassays of their function, offer vast potential for new drug discovery. In other words, your assay holds the key value and novelty. *Phytotitre* aims to bring accessible high-quality screening to these new targets and assays.

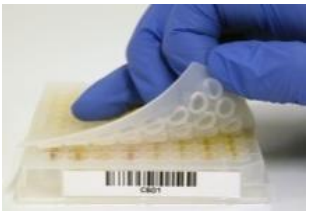


Progressing from hit to lead

Establishing the structure of compounds identified as hits from your screens will require activity-guided separation. Please see our website for details of how we may help you with this. Rapid resupply of freeze-dried extract powder or dried unextracted plant material is offered.

Library format

- 800 plant extracts are supplied in DMSO at 10 mg/ml in SBS compliant 96-well round bottom polypropylene microplates
- Both polar (aqueous) and non-polar (dichloromethane) solvent extracts of each plant product are provided with plate maps
- Each plate contains 80 extracts with two empty columns for positive and negative controls
- Bar codes (code 128) and human readable plate numbers are printed on all plates
- DMSO-resistant re-sealable cap mats maximise sample integrity and ease of use



References:

[1] Li JW, et al. Science 325:161-5 (2009)
[2] Scannell JW, et al. Nat Rev Drug Discov 11:191-200 (2012)
[3] Fischer W, *et al*. Redox Biol 21:101089 (2019)
[4] Newman DJ, et al. J Nat Prod 75:311-35 (2012)
[5] Tulp M, et al. Trends Pharmacol Sci 5:225-31 (2002)

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