Investigating and exploiting the metabolomic richness of plant germplasm

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The majority of the world's medicinal compounds have derived from compounds obtained from natural sources. In this project we are exploring the prospects for discovering new uses for plant germplasm, both native wild plants and non-native genebank material. The strategy being pursued is to identify key interesting compounds using high throughput screening for biological activity. Extracts of plant material are subjected to tests for useful biological activity which target, amongst others, Alzheimer's, tumour growth, inflammatory reactions and analgesia. It is already clear that bryophytes possess an unexpected richness at both the biochemical and screening levels, and progress towards understanding the diversity in bryophytes and other plants will be presented.

The Germplasm

Clockwise from bottom left, three mosses in the genera *Campylopus*, *Bryum* and *Drepanocladus* and a liverwort, *Aneura.*

Bryophytes

The Scottish and UK flora is particularly rich in bryophytes, both mosses and liverworts, and these form a significant component of the woodland and mountain vegetation. In comparison with flowering plants natural populations of bryophytes show little evidence of damage from fungal or insect attack, yet are under-explored for compounds of medicinal use. We are collecting and evaluating most of the genera available in the UK.

The range of Flora Celtica species include *Allium ursinum* (left) and *Phegopteris connectilis* (right)

Vascular plants

A range of vascular plants are also included in the study, focusing particularly on species represented in Flora Celtica, a database of plants with traditional uses held at the Royal Botanic Garden Edinburgh.

Solanum species

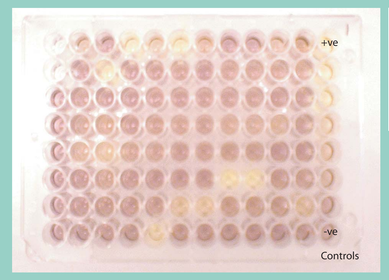
The Solanaceae is a family known to be rich in bioactive compounds, particularly steroidal compounds including alkaloids. Most of the diversity in the tuber-bearing part of the *Solanum* genus has been captured in germplasm collections and is available in living form. We are surveying around 80 taxa for activity in the screens described below, and propose to exploit any discoveries according to the aspirations of agreements such as the CBD and the IUPGRFA.

Clockwise from bottom left, *Solanum ochranthum*, *S. tarijense*, *S. oplocense* and *S. multidissectum*..

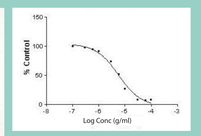
The Strategy

1. Collection and extraction

Dried tissues are milled, extracted in acidified methanol, and lyophilised prior to screening in high-throughput assays



2. First-level screening for bioactivity



Antioxidant activity of each extract is determined by its ability to reduce DPPH to a yellow form (left). A dose response curve for a *Rosa* leaf sample is shown above.

Assays include:

- general cytotoxicity
- anti-cancer
- anti-psoriasis
- anti-leukaemia
- anti-inflammatory
- anti-epilepsy
- analgesia
- anti-schizophrenia
- antibiotic
- diabetes

3. Fractionation

4. Repeat assays

5. Fine-scale fractionation

e.g LCQ-Deca LC-MS

6. Identification and validation

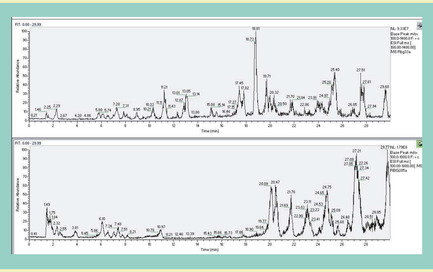
Findings

Bioactivity assay potential targets

	Cancer	Anti-inflammatory	Analgesia	Alzheimers	Anti-oxidant
Bryophytes	+	+	+		
Vascular plants	+	+	+	+	+
Solanum	+	+	+		

Identifying active compounds

These two LC-MS traces represent two geographically separate collections of the aquatic moss *Fontinalis antipyretica*. The upper sample displays bioactivity and the lower sample does not, indicating some candidate compounds. Further work on fractionated samples with LC-MS and GC-MS will identify candidate compounds for hits in key assays.



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