

Toxicological risk assessment of *Aristolochia* species

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Aristolochia

Large plant genus of the family Aristolochiaceae

Common names: birthwort, pipevines, Duchtman's pipes

Occur on all continents



Aristolochia manshuriensis



Aristolochia maxima



Aristolochia clematitis



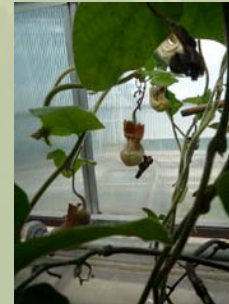
Aristolochia gigantea



Aristolochia tricaudata



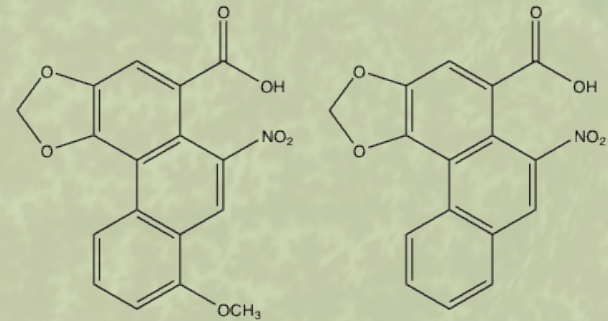
Aristolochia serpentaria



Aristolochia californica

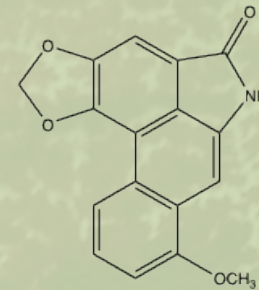
Aristolochic acid nephropathy

- Progressive form of renal fibrosis¹
- Initially reported in more than 100 Belgian patients after the intake of slimming pills
- Chinese herb *Stephania tetrandra* has been replaced with *Aristolochia fangchi*
- *Aristolochia* contains carcinogenic and mutagenic aristolochic acids¹ as well as aristolactams
- AAN cases observed all over the world (including the UK)²
- *Aristolochia clematitis* could be responsible for the so-called Balkan-endemic nephropathy³

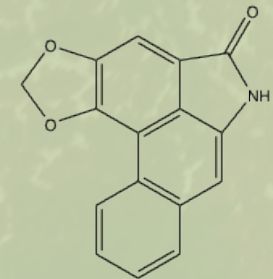


aristolochic acid I

aristolochic acid II



aristolactam I



aristolactam II

¹ Nortier et al. (2000) *NEJM*

² DeBelle et al. (2008) *Kidney Int*

³ Grollman et al. (2007) *PNAS*

Traditional Chinese Medicine

Pin Yin name	plant part	species	uses
guang fang ji	root	<i>Aristolochia fangchi</i>	anti-rheumatic and diuretic
han fang ji	root	<i>Stephania tetrandra</i>	anti-asthmatic, diuretic
mu fang ji	root	<i>Cocculus trilobus</i>	diuretic, gonorrhea
guan mu tong	stem	<i>Aristolochia manshuriensis</i>	diuretic, anti-inflammatory
chuan mu tong	root	<i>Clematis armandii</i> or <i>C. montana</i>	diuretic, anti-inflammatory
ma dou ling	fruit	<i>Aristolochia contorta</i> or <i>A. debilis</i>	anti-tussive, anti-asthmatic
tian xian teng	herb	<i>Aristolochia contorta</i> or <i>A. debilis</i>	diuretic, anti-rheumatic
qing mu xiang	root	<i>Aristolochia debilis</i>	pain relief

Wu et al. (2007) *Phytomedicine*



Aristolochia manshuriensis



Stephania tetrandra



Clematis vitalba

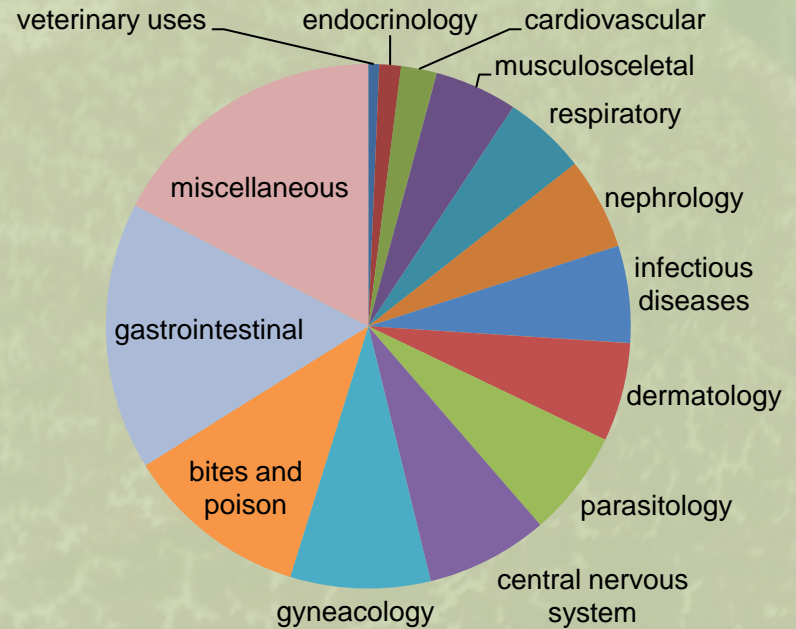
Medical uses



Aristolochia repens



Aristolochia pilosa



Heinrich et al. (2009) *J Ethnopharmacol*

Aristolochia species are used all over the world and for most species their chemistry is not known.

Aims

- Chemical characterization of medicinally used *Aristolochia* species
- Identification and quantification of all aristolochic acid and aristolactams present
- Toxicological screening of *Aristolochia* extracts
- Comparison of toxicological properties of aristolochic acid analogues
- Comparative risk assessment of *Aristolochia* species

Metabolomics

“The systematic study of the unique chemical fingerprints that specific cellular processes leave behind.”

Separation

- Liquid chromatography
- Capillary electrophoresis
- Gas chromatography

Structure elucidation

- NMR
- QTOF
- Orbitrap
- UV

Quantification

- relative
- absolute

Chemistry

Biology

Informatics

Plants

Microbes

Animal organs

unsupervised

PCA
ICA
SOM
HCA

supervised

PLS PLS-DA
OPLS SVM
AAN

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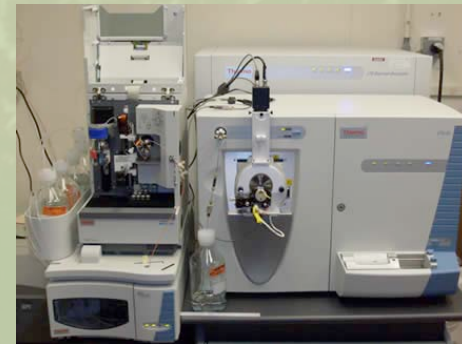
^1H -Nuclear magnetic resonance (NMR)

- Measures properties of all protons present in the samples
- Primary and secondary metabolites

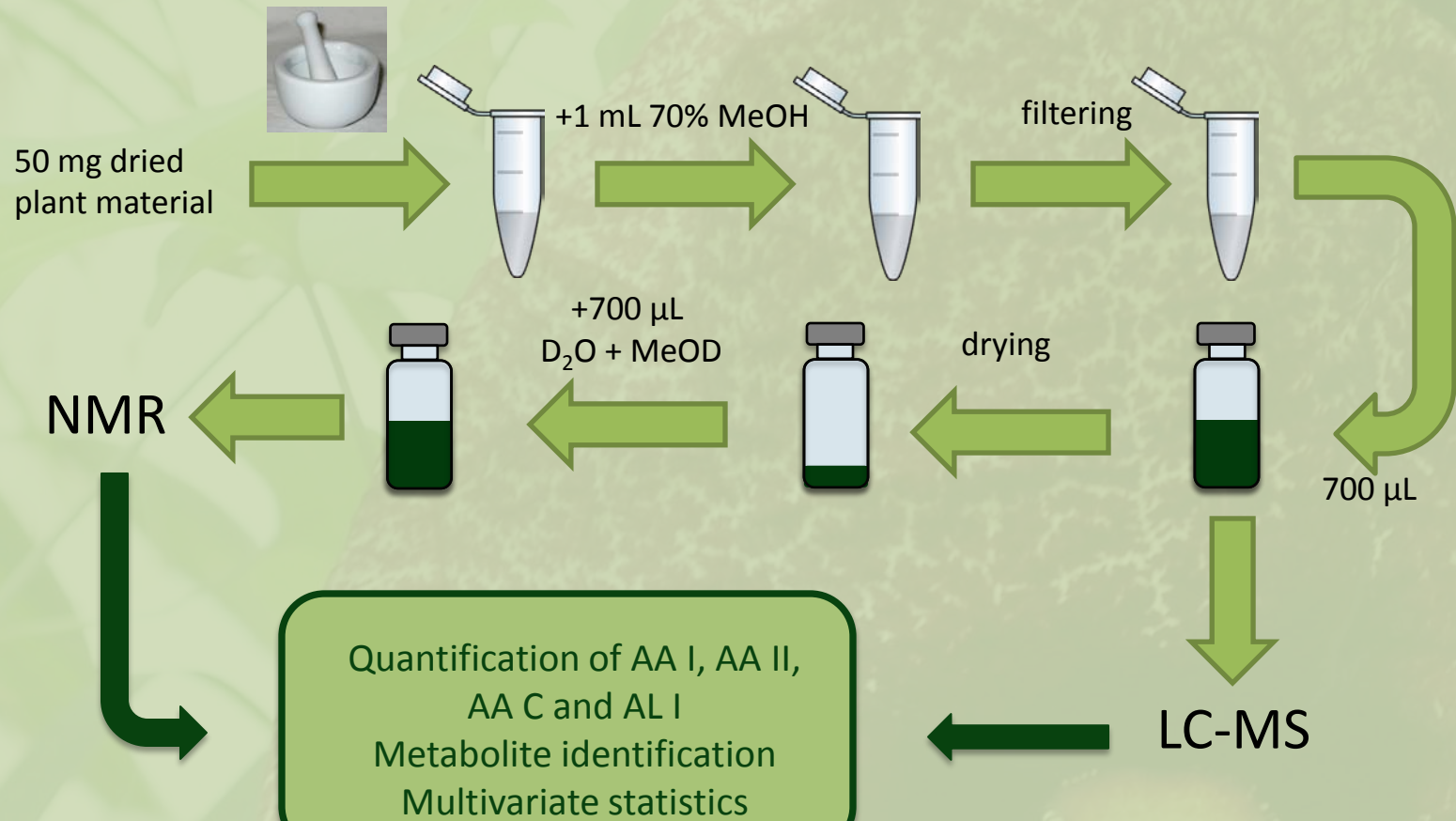


Liquid chromatography – mass spectrometry (LC-MS)

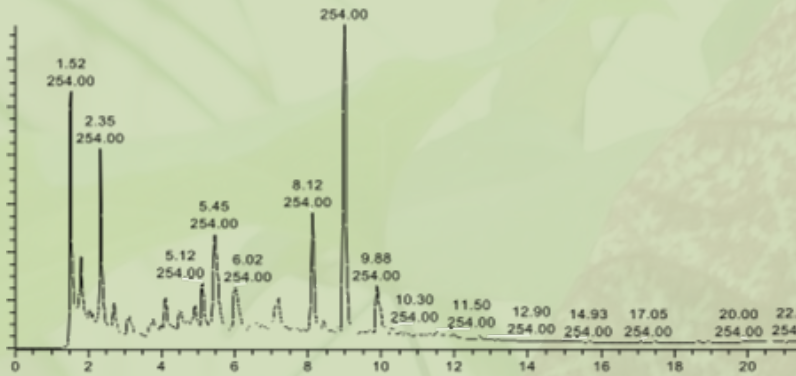
- Separates compounds and measures their mass spectra
- Mainly secondary metabolites
- Great for identification of compounds



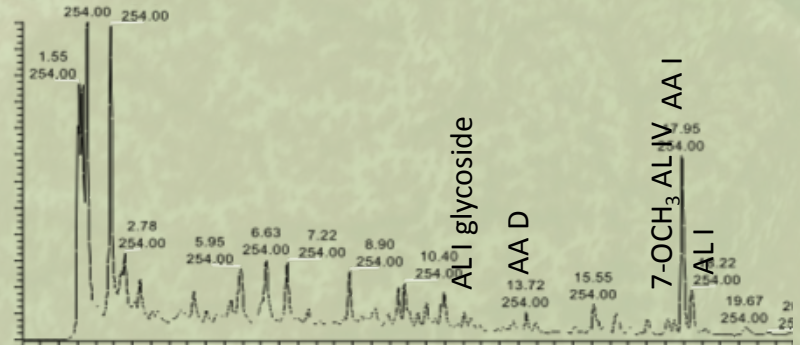
Workflow



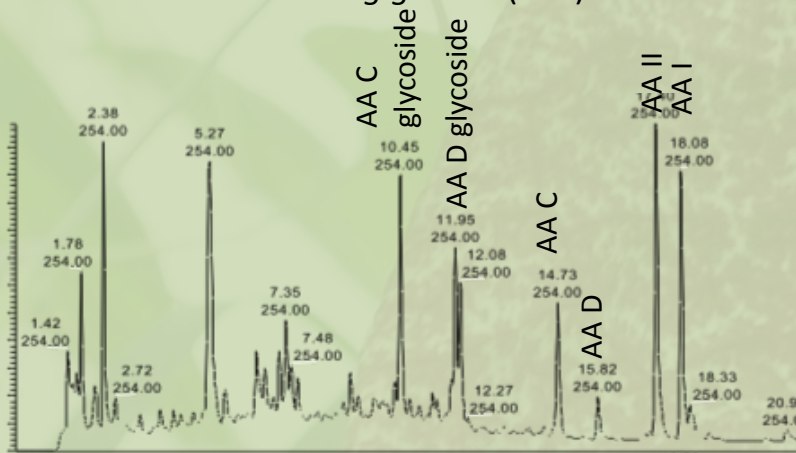
Results



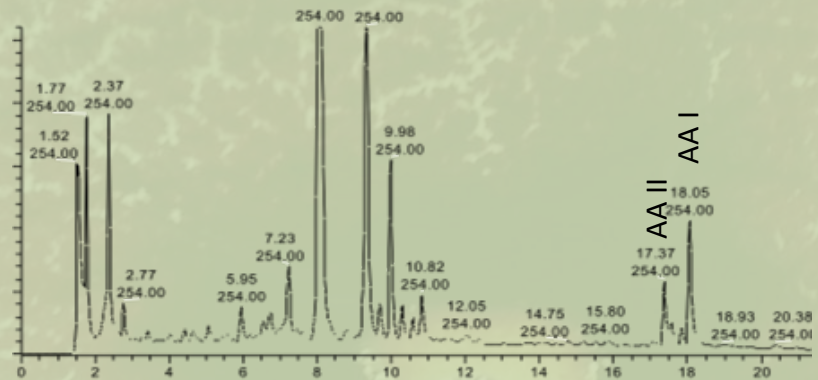
Aristolochia gigantea (leaf)



Asarum heterotropoides (flower)



Aristolochia manshuriensis (stem)



Aristolochia clematitidis (leaf)

Future work

- LC-MS and NMR analysis of *Aristolochia* species
- Data processing
- Metabolite identification
- Toxicological screening of all extracts
- Further pharmacological tests on selected extracts and pure compounds
- Botanical fieldwork in India/Bangladesh

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