ePlantLIBRA introduction

Welcome and overview of PlantLIBRA project and database

Demonstration of ePlantLIBRA

Data included: Composition, Beneficial effects, Adverse effects

Users and Uses, Sustainability and plans
Aim: To develop, test and apply a sustainable integrated meta-database of biologically active compounds, residues and contaminants

**ePlantLIBRA:** A sustainable, reliable, flexible and fit-for-purpose internet-deployed database, providing a unique comprehensive resource on PFS for researchers, health professionals, health educators, the food industry and policy makers.

http://eplantlibra.eurofir.eu/
ePlantLIBRA functions

Data inputting:
Via 5 online systems
• Composition data
• Beneficial data
• Adverse effects
• PFS information
• Plant information:

Data reporting:
user led data retrieval software system, searchable by:
compound, food, biological effect:
• Composition
• Bio-effects
• PFS info
• Plant details
• Contaminants
Contaminant information

**MoniQA**

- Contaminant/residue
- Level
- Unit
- Analysis/Regulation

**385** plants within the database have been categorised and encoded against commodities in the MoniQA database.

**Plant**

**Plant Part**

**Linked to**

**ePlantLIBRA database**

**Table of Contaminant Information**

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>Regulatory plant classification</th>
<th>Level</th>
<th>Unit</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadmium</td>
<td>3.2.15. Vegetables and fruit, excluding leafy vegetables, fresh herbs, leafy brassicas, fungi, stem vegetables, root vegetables and potatoes</td>
<td>0.05</td>
<td>mg/kg wet weight</td>
<td>Regulation (EC) 333/2007 EFSA Opinion - cadmium</td>
</tr>
<tr>
<td>Lead</td>
<td>3.1.13. Berries and small fruit</td>
<td>0.2</td>
<td>mg/kg wet weight</td>
<td>Regulation (EC) 333/2007 EFSA Opinion - lead</td>
</tr>
<tr>
<td>Pesticides</td>
<td>015. Berries and small fruit - Other small fruit and berries</td>
<td>MRLs for elderberries (0154080) apply</td>
<td>mg/kg</td>
<td>Regulation (EC) No 396/2005 and its Annex amendments</td>
</tr>
</tbody>
</table>
## Horizon Scan: New features under development – an example

<table>
<thead>
<tr>
<th>Plant</th>
<th>Latin name</th>
<th>Exporter/source</th>
<th>Reported commodity</th>
<th>Issue (residue or contaminant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camomile</td>
<td><em>Chamaemelum nobile</em> (L.) All.</td>
<td>Germany</td>
<td>Chamomile flowers</td>
<td>Acetamiprid, Carbofuran, Chlorimequat, Dimethoate, Fonofos, Glyphosate, Heptachlor, Methamidophos, Methiocarb, Oxydemeton-methyl, Triazophos</td>
</tr>
<tr>
<td>Camomile</td>
<td><em>Chamaemelum nobile</em> (L.) All.</td>
<td>The Former Yugoslav Republic of Macedonia</td>
<td>Chamomile flowers</td>
<td>Acetamiprid, Chlorpyrifos, Dimethoate, Methomyl, Monocrotophos, Omethoate, Procymidone</td>
</tr>
<tr>
<td>Chanterelle</td>
<td><em>Cantharellus cibarius</em> Fr. var. <em>cibarius</em></td>
<td>France</td>
<td>Wild mushrooms</td>
<td>High radioactive concentration (220 Bq/kg) in Chanterelles</td>
</tr>
<tr>
<td>Onion</td>
<td><em>Allium cepa</em> L.</td>
<td>Morocco</td>
<td>from Onions</td>
<td>Cadmium in fresh wild onions</td>
</tr>
<tr>
<td>Onion</td>
<td><em>Allium cepa</em> L.</td>
<td>Ukraine</td>
<td>from Onions</td>
<td>Lead (0.15 mg/kg - ppm) in fresh onions from Ukraine</td>
</tr>
<tr>
<td>Onion</td>
<td><em>Allium cepa</em> L.</td>
<td>Ukraine</td>
<td>from Onions</td>
<td>Lead (0.33 mg/kg - ppm) in fresh onions from Ukraine</td>
</tr>
</tbody>
</table>
Plant/PFS Coverage

51 prioritised plants

Adverse Effects (41)
Beneficial Effects (33)
Composition (27)

6
10
20
5
8

1

EuroFIR
European Food Information Resource
### Detailed breakdown of content

<table>
<thead>
<tr>
<th>Category</th>
<th>Plants covered</th>
<th>PFS covered</th>
<th>Compounds</th>
<th>References</th>
<th>Datapoints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composition</strong></td>
<td>240*</td>
<td>27</td>
<td>511</td>
<td>400*</td>
<td>25,500*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>220**</td>
<td>4400**</td>
</tr>
<tr>
<td><strong>Beneficial Bioeffects</strong></td>
<td>71*</td>
<td>33</td>
<td>161</td>
<td>563*</td>
<td>894*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>82**</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse Bioeffects</strong></td>
<td>41</td>
<td>41</td>
<td>-</td>
<td>210</td>
<td>243</td>
</tr>
<tr>
<td><strong>Contaminants</strong></td>
<td>374</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Includes data inherited from eBASIS database
**New references evaluated and entered specifically for ePlantLIBRA

[http://eplantlibra.eurofir.eu](http://eplantlibra.eurofir.eu)
ePlantLIBRA Database:

Demonstration (Jenny Plumb, IFR)
Composition data (Jenny Plumb, IFR)
Beneficial Bioeffects (Jackie Lyons UCC)
Adverse Effects (Patricia Restani UMIL)
ePlantLIBRA: Composition

- Composition data entry
- Composition data included
- Example of use
Compilation process

Selection of
• Evaluators
• Compound classes
• Food plants/PFS

Reference selection
Identification of data sources, relevant plants/PFS relevant compound classes

Useful data in reference?
Yes
Continue evaluation

No - STOP evaluation

Storage of quality evaluated data

Document
YES
SOP
Correct?

NO

Check on evaluator data entry

Submission to 'holding database'

Data entry by evaluator
Attribution of quality score to all original data

DBM requests revision

http://eplantlibra.eurofir.eu
### Composition literature search

**Plant/food terms** combined using ‘OR’

**Compound terms** combined using ‘OR’

**Composition terms** combined using ‘OR’

---

<table>
<thead>
<tr>
<th>Field</th>
<th>Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOPIC</td>
<td>(Camellia sinensis OR Tea*)</td>
</tr>
<tr>
<td></td>
<td>AND</td>
</tr>
<tr>
<td>TOPIC</td>
<td>(polyphenol* OR flavan* OR flavon* OR catechin* OR quercetin* OR <em>quinic</em> OR <em>cyanidin</em> OR phenol* OR kaempferol* OR theaflavin* OR theobromin*)</td>
</tr>
<tr>
<td></td>
<td>AND</td>
</tr>
<tr>
<td>TOPIC</td>
<td>(composit* OR analy* OR content* OR evaluat* OR quantif* OR concentrat*)</td>
</tr>
</tbody>
</table>
Composition: Data Entry

Online form: **35 fields, 14 picklists:**

- Bibliographic Reference Information
- Plant/PFS information
- Processing
- Sampling information
- Compositional information
- Quality assessment:
  - Food description
  - Processing defined
  - Sampling plan
  - Sample handling
  - Compound identification
  - Analytical method
  - Analytical performance

![Quality Assessment: 89/100 points](image)
Breakdown of Composition content

- **345 papers** sourced on composition PFS/botanical ingredients
- **237 papers completed**
- **4700 inputs** (26800 including inherited data)
- **315 compounds**
- **78 Botanicals** (353 including inherited data)
- **30 Generic PFS products e.g:**
  - Artichoke, liquorice, boswellia, ginkgo, ginseng, st Johns Wort, camellia sinensis (tea)
Example of use:
Consumption Survey, Intake calculation

http://eplantlibra.eurofir.eu
Example of composition data use:

Intake of selected bioactive compounds from plant food supplements containing fennel (*Foeniculum vulgare*) among Finnish consumers

- 12-month retrospective PFS consumption survey conducted in Finland
- Estimated average intake
  - estragole was 0.20 mg/d,
  - trans-anethole 1.15 mg/d,
  - rosmarinic acid 0.09, etc...
- The intakes of kaempferol, quercetin, luteolin, matairesinol and lignans from fennel-containing PFS were low in comparison with their dietary supply.
- The intake of estragole was usually moderate, but a heavy consumption of fennel-containing PFS may lead to a comparably high intake of estragole.
- To our knowledge, this study presents the first intake estimates of trans-anethole, p-coumaric acid and rosmarinic acid in human populations.
ePlantLIBRA: beneficial effects data

Dr Jacqueline Lyons
University College Cork, Ireland

Jenny Plumb | Karin Nørby | Erik Nørby | Paul Finglas | Máiréad Kiely

Brussels, March 2014
Why study beneficial effects?

- Bioactive compounds defined as “inherent non-nutrient constituents of food plants with anticipated health-promoting (beneficial) and/or toxic effects when ingested”

- May help to promote optimal health and to reduce the risk of chronic disease

- Epidemiological evidence for the health benefits derived from a diet rich in fruit and vegetables thought to be largely explained by bioactive compounds
How can ePlantLIBRA help?

• Unique on-line database containing quality assessed data from peer-reviewed literature

• Contain composition and biological effects data (both beneficial and adverse) for plants, plant food supplements, compounds

• Contain additional information (e.g. notes on plants, links to contaminant data, etc)
How can ePlantLIBRA help?

• Specific data can be easily extracted and manipulated

• Useful to those with an interest in beneficial effects of bioactive compounds, e.g.
  • Researchers
  • Epidemiologists
  • Food regulatory authorities
  • Product developers in plant food supplement (PFS) industry
<table>
<thead>
<tr>
<th>Ref no</th>
<th>Plant</th>
<th>Compound</th>
<th>Experimental design</th>
<th>Adverse effects, text</th>
<th>Quality comments</th>
<th>Gender specific</th>
<th>Study subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>L0054</td>
<td>Tea</td>
<td>Catechin</td>
<td>Study examined green tea consumption in 20 young healthy chronic smokers. FMD was measured before green tea consumption, and changes in vascular endothelial function and EPC were assessed. Subjects consumed powdered green tea (8g/day) dissolved in 1L water for 2 weeks. Researchers were blinded. Fasting bloods were obtained before and at the</td>
<td>None described</td>
<td>Relatively small sample size (n=20), and short duration (2 weeks). Adverse effects not described. Treatment dose chosen 'at random'. No control group included.</td>
<td>Not applicable</td>
<td>20 healthy chronic smokers; mean age 27.6y; subjects who consumed herbs or vitamins were excluded; subjects with underlying hypertension, diabetes or other diseases were excluded; mean BMI at baseline 23.6 (S.D. 3.0).</td>
</tr>
<tr>
<td>B0501</td>
<td>Tea</td>
<td>Catechins</td>
<td>This Teas Effect on Atherosclerosis (TEA) pilot study was a randomized, parallel design, assessor-blinded clinical trial of black tea consumption among men and women with cardiovascular risk factors. The participants assigned to consume 3 glasses black tea daily (318 mg total catechins) or 3 glasses water for 6 months. They followed their typical diet and visited the hospital for screening at 2 weeks, 3 and 6 months. Blood samples were collected at baseline and 6 months.</td>
<td>The major adverse effects, recorded in 2 participants, were chest pain and tooth staining.</td>
<td>This is a well-organized study with sufficient discussion of the results and sufficient description of subjects and test material.</td>
<td>not studied</td>
<td>31 men and women, aged 55 years and older, were recruited to the study. All participants had either diabetes or 2 other cardiovascular risk factors (hypertension, current smoking, LDL cholesterol&gt;130 mg/dl, HDL cholesterol180/110 mgHg, serum creatinine&gt;2,5 mg/dl or dialysis, history of hyponatremia, use of vitamin supplements greater than the recommended daily allowance, inability to speak English and lack of working telephone.</td>
</tr>
<tr>
<td>B0367</td>
<td>Tea</td>
<td>Catechins</td>
<td>20 healthy male smokers,</td>
<td>No adverse</td>
<td>-There is not</td>
<td>Not specified</td>
<td></td>
</tr>
</tbody>
</table>
Which plants are included, and why?

- PlantLIBRA Task 2.1 (2010): “Review of evidence for PFS benefit from epidemiological, clinical and intervention studies”

- Health areas chosen as important were:
  - Cardiovascular health
  - Post-menopausal bone health
  - Menopausal symptoms
  - Gastrointestinal health
  - Inflammation
Which plants are included, and why?

• Choice of PFS to be included was based on an initial search of the prioritised health benefit areas

• Key PFS in each health area were selected, in order to limit the number of studies to be reviewed to a manageable level

• Systematic literature search covered the period 1970 – 2010

• The Cochrane Library | Embase | PubMed | SciFinder Scholar
• Inflammation

**Outcomes investigated (test and measurements)**
Several tests were used to evaluate the anti-inflammatory effect of the 10 PSF under study. The following tests have been extensively used: 1) test ELISA for measuring cytokines production, C reactive protein (CRP) and metalloproteases; 2) immunoturbidimetric tests (for pRC and cytokines); 3) Joint score, swollen joint, disability score and osteoarthritis index for osteoarthritis of knee; 4) WOMAC test, VAS, Arhus index and Lequesne functional index for pain; 5) Clinical activity index (CAI) and endoscopic index (EI) for ulcerative colitis. Tests will be more deeply discussed in task 2.2.

• Digestive health

**Outcomes investigated (test and measurements)**
The most frequent bowel function outcomes found in the review were: symptoms of irritable bowel syndrome, stool weight in irritable bowel syndrome, gut transit time, bowel habits, abdominal pain and bloating, preparation for colonic cleansing, bowel movement, defecation events and stool consistency. Also, outcomes related to digestive dysfunctions such as alleviation of infant colic symptoms, crying time in breastfed colicky infants and gastrointestinal symptom score of dyspepsia were also evaluated. Finally, some outcomes addressed liver disorders: symptoms related to biliary retention and hepatitis C (such as indicators of quality of life), as well hepatic biomarkers: lipid profile (LDL, cholesterol, HDL-cholesterol, triglycerides), SGOT, SGPT, liver alkaline phosphatise, indirect bilirrubin, direct bilirrubin.
Three categories of terms combined with ‘AND’ to give relevant papers

<table>
<thead>
<tr>
<th>Field</th>
<th>Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOPIC</td>
<td>(Camellia sinensis OR Tea*)</td>
</tr>
<tr>
<td>AND</td>
<td></td>
</tr>
<tr>
<td>TOPIC</td>
<td>(cardiovascular disease* OR cardiovascular* OR hypertens* OR oxidative stress* OR metabolic syndrome)</td>
</tr>
<tr>
<td>AND</td>
<td></td>
</tr>
<tr>
<td>TOPIC</td>
<td>(control* OR stud* OR random* OR control* OR trial* OR random* OR clinical* OR control* OR stud* OR RCT OR Human Intervention Stud*)</td>
</tr>
</tbody>
</table>
The stats...

- Following the systematic search (Task 2.1), 219 papers were identified for evaluation

- Of these, 8 were later deemed unsuitable for evaluation
  - Non-English language
  - Duplicates
  - Abstract only
  - Systematic reviews

- As of January 2014, all 211 papers have been evaluated
<table>
<thead>
<tr>
<th>Ref.</th>
<th>Plants/PFS studied</th>
<th>Biomarkers examined</th>
<th>Beneficial effects?</th>
</tr>
</thead>
<tbody>
<tr>
<td>L0001</td>
<td><strong>Green tea (beverage/extract)</strong></td>
<td><strong>Inflammation</strong> biomarkers; features of metabolic syndrome</td>
<td>Minimal effect on inflammation biomarkers</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L0002</td>
<td><strong>Boswellia product</strong></td>
<td><strong>Pulmonary function</strong> and asthmatic symptoms; plasma biomarkers</td>
<td>↓ in plasma levels of leukotriene, nitric oxide and malondialdehyde ✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L0003</td>
<td><strong>Green tea</strong></td>
<td><strong>Endothelial dysfunction</strong> in smokers</td>
<td>High-dose acute and chronic supplementation associated with improved endothelial function in smokers (↑ nitric oxide production, ↓ ADMA levels, ↓ oxidative stress) ✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L0004</td>
<td><strong>Boswellia product (5-Loxin and Aflapin)</strong></td>
<td>Pain scores and <strong>physical ability in osteoarthritic patients</strong></td>
<td>Significant improvements in pain and physical function scores; better efficacy observed with Aflapin ✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L0006</td>
<td><strong>Milk thistle</strong></td>
<td><strong>Hepatotoxicity</strong> in children with leukaemia (changes in levels of bilirubin, AST and ALT enzymes)</td>
<td>No effects observed after 28 days; a trend towards reduced toxicity observed after 56 days</td>
</tr>
<tr>
<td>Ref.</td>
<td>Plants/PFS studied</td>
<td>Biomarkers examined</td>
<td>Beneficial effects?</td>
</tr>
<tr>
<td>------</td>
<td>----------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>L0007</td>
<td><strong>Senna</strong> with docusate</td>
<td><em>Time to first bowel movement</em> following pelvic floor reconstructive surgery in women</td>
<td>Significant ↓ in time to first bowel movement and constipation compared with placebo group ✓</td>
</tr>
<tr>
<td>L0008</td>
<td><strong>Soy</strong> isoflavones</td>
<td>Effects on lumbar spine, total proximal femur, femoral neck and whole body <strong>bone mineral density</strong> (BMD) in non-osteoporotic women</td>
<td>Overall, very limited evidence for bone-sparing effects; modest protective effect on decline in femoral neck BMD observed only</td>
</tr>
<tr>
<td>L0009</td>
<td><strong>Soy</strong> isoflavones</td>
<td>Psychological, somatic and urogenital <strong>symptoms in symptomatic postmenopausal women</strong> (using Menopause Rating Scale)</td>
<td>Significant improvements observed in somatic and urogenital symptoms ✓</td>
</tr>
<tr>
<td>L0010</td>
<td><strong>Red clover</strong>-derived isoflavones</td>
<td>Anxiety and depressive <strong>symptoms in post-menopausal woman</strong></td>
<td>Significant decrease in depression scale scores (both Hospital and Self-rating) following 180-day treatment ✓</td>
</tr>
<tr>
<td>L0011</td>
<td><strong>Bilberry</strong> juice</td>
<td><strong>Markers of inflammation</strong> associated with cardiovascular disease (CVD)</td>
<td>Bilberry juice modulates inflammatory mediators in men and women at ↑ risk of CVD, and ↑ plasma polyphenol levels ✓</td>
</tr>
<tr>
<td>Ref.</td>
<td>Plants/PFS studied</td>
<td>Biomarkers examined</td>
<td>Beneficial effects?</td>
</tr>
<tr>
<td>-------</td>
<td>-------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>L0012</td>
<td><strong>Green tea</strong> polyphenols (GTP)</td>
<td>Clinical and histologic attributes of photo-aging skin</td>
<td>No significant improvements in GTP group compared with placebo group</td>
</tr>
<tr>
<td>L0013</td>
<td><strong>Grape</strong> seed extract</td>
<td>Markers of inflammation, glycaemia and oxidative stress (cardiovascular risk factors) in diabetic patients</td>
<td>Significant improvement in most markers of cardiovascular risk examined; improved markers of inflammation, glycaemia &amp; oxidative stress ✔</td>
</tr>
<tr>
<td>L0014</td>
<td><strong>Green tea</strong> extract (containing theanine, catechins and other polyphenols)</td>
<td>Blood pressure, blood lipid profile, serum amyloid alpha (SAA) and serum malondialdehyde (MDA)</td>
<td>The product lowered blood pressure, SAA and MDA levels; total cholesterol (CL) lowered in men; LDL-CL lowered in all subjects with baseline levels &gt;99 mg/dL ✔</td>
</tr>
<tr>
<td>L0015</td>
<td><strong>Milk thistle</strong> extract (silymarin)</td>
<td>Symptoms and biomarkers of acute hepatitis in symptomatic patients</td>
<td>Faster resolution of symptoms of impaired biliary excretion compared with placebo group ✔</td>
</tr>
<tr>
<td>L0023</td>
<td><strong>Black cohosh; red clover</strong></td>
<td>Cognitive function and frequency of hot flashes in menopausal women</td>
<td>No effect on cognitive function; no effect on ‘objective’ hot flashes (improvement in ‘subjective’ hot flashes reported)</td>
</tr>
</tbody>
</table>
2.4) Cardiovascular Health (UBA)

Selected botanicals for cardiovascular health were as follows:

<table>
<thead>
<tr>
<th>Latin name</th>
<th>Common name</th>
<th>Used portion</th>
<th>Active compounds</th>
<th>Main reported benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aloe ferox</em> Mill.</td>
<td>Bitter aloe/tap aloe</td>
<td>Leaves/Leaves Juice</td>
<td>Anthroquinones</td>
<td>Helps to promote intestinal regularity. Ease intestinal transit</td>
</tr>
<tr>
<td><em>Vaccinium myrtillus</em> L.</td>
<td>Bilberry</td>
<td>Leaves, fruits</td>
<td>Tannins and anthocyanosides</td>
<td>Astringent, enhance vascular tone, antioxidant, Antiphlogistic</td>
</tr>
<tr>
<td><em>Salvia hispanica L.</em> <em>Salvia columbariae</em></td>
<td>Chia seed</td>
<td>Seed</td>
<td>soluble and insoluble fibre and antioxidant activity of phenolic compounds</td>
<td>Dietary fibre; Phenolic compounds; Antioxidant activity; Lipid oxidation</td>
</tr>
<tr>
<td><em>Ginkgo biloba</em> L.</td>
<td>Maidenhair tree</td>
<td>Leaves</td>
<td>Ginkgolides</td>
<td>Memory and concentration enhancer Antiphlogistic, emollient, mildly ease intestinal</td>
</tr>
<tr>
<td><em>Panax ginseng</em></td>
<td>Ginseng</td>
<td>Roots</td>
<td>Ginsenosides</td>
<td>Adaptogen, tonic, immunomodulant, cardiotonic, enhance mental faculties</td>
</tr>
<tr>
<td><em>Vitis vinifera</em></td>
<td>Grapes and grapeseed</td>
<td>Grapes and grapeseed</td>
<td>Flavonoid-rich active compound in grape seed</td>
<td>Anti-inflammatory, antioxidant, laxative.</td>
</tr>
<tr>
<td><em>Camellia sinensis</em></td>
<td>Green Tea</td>
<td>leaves and leaf buds</td>
<td>Cathechins/hepatotoxicity</td>
<td>Angina pectoris, peripheral vascular disease, and coronary artery disease</td>
</tr>
<tr>
<td><em>Glycine max</em> (L.)Merr.</td>
<td>Soy/Lecithin</td>
<td>Soybean</td>
<td>Isoflavones / Phytosterols</td>
<td>antioxidant and phytoestrogenic properties. Isoflavones may reduce the risk of hormone-dependent cancers.</td>
</tr>
<tr>
<td><em>Valeriana officinalis</em> L.</td>
<td>Valerian</td>
<td>Roots</td>
<td>Monoterpenes, Sesquiterpene, etc</td>
<td>Mild ansiolitic, spasmodiotic</td>
</tr>
</tbody>
</table>
“Applications of an online database on plant food supplements: the ePlantLIBRA database” (in preparation)

- Papers to highlight practical uses of the database for special users

- Focus on applications in:
  
  (i) **safety assessment of botanicals** for use in PFS
  
  (ii) **estimating exposure to bioactive compounds** from PFS in population groups
Safety assessment of botanicals for use in PFS

- ePlantLIBRA combines literature on beneficial and adverse biological effects of PFS in a single platform, making it useful for assessing safety of botanicals for use in PFS using methods described by EFSA (2009)

- (i) Technical data
- (ii) Exposure data
- (iii) Toxicological data
Applications in exposure assessments (epidemiology)

• ePlantLIBRA composition data (i.e. data on content of bioactive compounds in PFS) is combined with PFS consumption data from a specific population group to address exposure to a particular bioactive in a more targeted way.

• Estimates are more meaningful where all of the available composition data for a particular plant are incorporated into the calculation (rather than using a single average value only).
Adverse effects data in ePlantLIBRA

Patrizia Restani
Dip. Scienze Farmacologiche e Biomolecolari
Università degli Studi di Milano
Adverse effects: why?

- A relative low number of case reports and clinical studies are at disposal on adverse effects in humans
- Necessity to collect these data using quality criteria
- Causality assessment according to the WHO guidelines
  - Certain
  - Probable
  - Possible
  - Unlikely/unclassifiable
The list of plant was based on information collected by researchers and stakeholders having a long experience in the field of food supplements containing botanicals. Finally a further addition was done during the first year of the project.

67 plants were searched and ranked for frequency of adverse effect.

Only papers with the highest causality classes are presently considered.
### Plants/PFS ingredient responsible for adverse effects in human: data from scientific papers (>10 cases)

<table>
<thead>
<tr>
<th>Plant ingredient</th>
<th>N</th>
<th>Plant ingredient</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine max (L.) Merr</td>
<td>89</td>
<td><em>Echinacea purpurea</em> (L.) Moench</td>
<td>24</td>
</tr>
<tr>
<td>Glycyrrhiza glabra L.</td>
<td>59</td>
<td><em>Cimicifuga racemosa</em> (L.) Nutt</td>
<td>23</td>
</tr>
<tr>
<td>Ginkgo biloba L.</td>
<td>42</td>
<td><em>Cinnamomum verum J Presl</em> (zeylanicium)</td>
<td>23</td>
</tr>
<tr>
<td>Camellia sinensis (L.) Kuntze</td>
<td>40</td>
<td><em>Vitex agnus castus</em> L.</td>
<td>22</td>
</tr>
<tr>
<td>Citrus aurantium L.</td>
<td>25</td>
<td><em>Harpagophytum procumbens</em> DC</td>
<td>12</td>
</tr>
</tbody>
</table>
Toxicological Input Form - TOX

Bibliographic Reference

Reference no: K0075
Author: Dara,L., Hewett,J. and Kartaik,J.
Title: Hydroxycut hepatotoxicity: A case series and review of liver toxicity from herbal weight loss supplements
Journal: World J Gastroenterol
Volume: 14(45)
Year: 2008
Pages: 6999,7004
Publisher:

Reference information: The authors describe two cases of acute hepatitis in the setting of Hydroxycut exposure, a popular weight loss supplement and describe possible mechanisms of liver injury.
## Plant Food Supplement

<table>
<thead>
<tr>
<th>Plant Food Supplement:</th>
<th>Green tea dietary supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Remarks:</strong></td>
<td>Camellia sinensis (green tea) EGCG 91 mg; Camellia sinensis (white tea) 15% EGCG; Camellia sinensis (oolong tea) 15% EGCG</td>
</tr>
<tr>
<td><strong>Additional information:</strong></td>
<td>The list of ingredients per serving (2 capsules): Calcium 156 mg, Chromium 133 mg, Potassium 118 mg, Garcinia cambogia (66% hydroxycitric acid); Gymnema sylvestre (25% gymnemic acid); Soy phospholipids, Rhodiola rosea extract (5% rosavin), Green tea as Camelia Sinensis (91 mg ECGC), White tea as Camellia sinensis (15% ECGC),</td>
</tr>
<tr>
<td><strong>Other bioactive compounds:</strong></td>
<td>Other plants contained in the Hydroxucut product and levo-tyroxine used for hypothyroidism. No other PFS or drug used</td>
</tr>
</tbody>
</table>
Event history

**Administration:** Oral

**Gender:** Female

**Subject characterization:** The subject was a 40-year-old female with a prior medical history notable only for hypothyroidism and diet-controlled hyperlipidemia. She did not smoke or drink.

**Description of the event:** One week prior to presentation at the Emergency Department, the patient began using Hydroxycut, 6 pills daily in preparation for a bodybuilding competition. Just prior to presentation she attended an office holiday party, although no other persons in attendance became ill.
# Adverse effects

## Main clinical effects:
- Acute hepatitis

## Clinical aspects:
- The subject arrived to the Emergency Department with 3 d of new-onset crampy, mid-epigastric abdominal pain and non-bloody diarrhea. She noted subjective fevers and chills, and two isolated episodes of nausea and vomiting, anorexia and profound fatigue. She did not experience jaundice, icterus, pruritus, arthralgias, acholic stools or dark urine. She otherwise does not take regular medications except for levothyroxine. She denied taking

## Dose ingested:
- 6 capsules of PFS/day

## Intake duration:
- One week

## Treatment of AE:
- Hospitalization, withdrawal of the supplement and diagnostic evaluations

## De-challenge / Re-challenge:
- None
Gender specific effect: None

Outcome: Upon outpatient follow-up, she had returned to her usual state of health with normalization of transaminases with AST 46 U/L and ALT 48 U/L. She has not experienced any further recurrence of symptoms or liver abnormalities within 10 mo of follow-up.

Causality assessment: According to the authors judgment, the temporal relationship to acute liver injury and the rapid resolution upon withdrawal of Hydroxycut make the drug associated hepatotoxicity probable/likely.

Conclusion: Authors consider the relationship probable

Effective dose: 273 mg of EGCG/day from green tea (no quantity reported)

Reviewer comments: According to WHO scale, the causality of suspected adverse reaction is probable. The role of other plants contained in the PFS is well considered and discussed.
Quality Assessment

PFS information:  ◦ 1  ○ 2  ○ 3  ○ 4  ○ 5  ○ 6

Are the following details reported?

• PFS name (i.e. International Nonproprietary Name INN or generic name)
• Brand name and/or manufacturer
• PFS composition

Intake:  ◦ 1  ○ 2  ○ 3  ○ 4

Are the following details reported?

• Daily dose and dosing regimen
• Length of intake (dates and duration of intake)
Quality code: ❖ A: Acceptable

Quality comments: According to WHO scale, the causality of suspected adverse reaction is probable. There is a temporal relationship between drug administration and the onset of the symptoms, dechallenge was positive and patient had no other factors that could be involved in the adverse effect. No biomarker of exposure was measured.

Comments to Database Manager

Comments to DBM:
Sustainability Task Force

Members:

Paul Finglas & Jenny Plumb (IFR)
Patrizia Restani (UMIL)
Carlos Ramos (EUROFIR)
Simon Pettman (EAS)
Miles R Thomas (FERA)
Roland Poms (ICC)
Hugo Kupferschmidt (STIC)
Joris Geelan (PAB-FPS)
Anne-Christine Goudar (SIAG -NAREDI)

Sustainability plan:

- Meeting users’ needs and requirements
- Involvement of experts and continuous updates on new data
- Appropriate dissemination and promotion including launch
- Develop membership model, pay-per-access & income
- Agree on continual access to include MoniQA data
Users and Uses of eplantlibra

- Regulatory issues,
- Science based decision making,
- Preparation of health claim dossiers
- Benefit/risk assessments

- Estimating exposure levels,
- Epidemiological studies,
- Supporting submissions to research

- New product development
- User friendly info on botanicals
- Easily accessible info on adverse effects
Examples of use:

**Benefit/Risk assessment**

Integration of databases:

OPASNET: an internet based interface where users can access, combine, by plant and compound, and discuss information for risk benefit assessment.

http://en.opasnet.org

**European Poisons Centres by STIC**

Establish a Network with Poison Centers
Example of use: Consumption Survey, Intake calculation

http://eplantlibra.eurofir.eu
The key services to users and stakeholders:

**Improve delivery of PFS data and expertise** for research and policy describing bioactive compounds in botanicals and herbal extracts with putative health benefits and adverse effects in PFS in Europe and globally;

**Support cooperation and exchange, and increased awareness of PFS** with other information providers, laboratories, regulators and industry to provide a forum for discussion and cooperation in Europe and globally (this could be in cooperation with other PlantLibra partners/ePlantLibra Board);

**Initiate new coordinated training and support** in conjunction with other research projects for users from the research community, health professionals, food and biotech industries, government agencies and departments.
Membership types and services

**Organisational:**
- Existing PlantLibra partners
- PAB (food authorities/policy/regulators)
- SIAG
- Laboratories
- New researchers/health professionals
- New food/PFS industry

*Typical annual fee 500€*

**Individual:**
- Poisons centres
- Students
- Pay-for-view (all types)

*Typical fee 50-100€*

**Additional services:**
- Quarterly update on new papers published with summary for 1 or more specific plants
- Reviews or dossier on some specific plants/topics (toxicological or beneficial for different industrial uses)
- Training and/or bespoke consultancies related to PFS
- New EU/EFSA grants
- Training/bespoke consultancies included in Hylobates/EuroFIR initiative
## Proposed requirements

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>EuroFIR AISBL (Polytec)</td>
<td>Promotion/ membership/ secretariat / hosting/ Maintenance &amp; bug-fixing</td>
</tr>
<tr>
<td>FERA</td>
<td>Maintaining MoniQA/ HorizonScan + monitoring emerging contaminants for PFS</td>
</tr>
<tr>
<td>DTU</td>
<td>Database Manager (DBM) adverse effects</td>
</tr>
<tr>
<td>UCC</td>
<td>DBM beneficial effects</td>
</tr>
<tr>
<td>IFR</td>
<td>DBM Composition</td>
</tr>
<tr>
<td>Data evaluations</td>
<td>Data Entry</td>
</tr>
<tr>
<td>SISTE</td>
<td>Sustaining PlantLIBRA Website</td>
</tr>
</tbody>
</table>
## ePlantLibra contents and plans for future updating

<table>
<thead>
<tr>
<th>Topic</th>
<th>Completed plant coverage (remaining)</th>
<th>Required additional papers for evaluations (post-PlantLibra)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composition</td>
<td>28 (33)</td>
<td>200 (4.5 pms total; evaluators: 3.0 &amp; DBM: 1.5)</td>
</tr>
<tr>
<td>Beneficial effects</td>
<td>33 (28)</td>
<td>175 (1 pm total; evaluators: 0.5 &amp; DBM: 0.5)</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>41 (20)</td>
<td>250-300 (4.5 pms total; evaluators: 3.0 &amp; DBM: 1.5)</td>
</tr>
<tr>
<td>Contaminants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[http://eplantlibra.eurofir.eu](http://eplantlibra.eurofir.eu)
Plans to project end

Introduction to the ePlantLIBRA database
26th March, 2014 Le Chatelain Hotel, Brussels
Demo and talks to: Stakeholders, PlantLIBRA members approx 50

International Plantlibra Conference, Vienna, May 2011
Plenary session 4, ePlantLIBRA database
Live Demonstration, detail coverage on database, user perspectives (SIAG, PAB, Poisons centres), sustainability plans.

Final version of sustainability plan after feed back from above meetings, May 2014

Delivery of database May 2014
Acknowledgements

PlantLIBRA WP 6 members and 3rd Parties

The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 245199. It has been carried out within the PlantLIBRA project (website: www.plantlibra.eu). This report does not necessarily reflect the Commission views or its future policy on this areas.