IRIDOIDS – A PHARMACIST’S PROSPECTIVE
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Lecturis salutem!

My name is dr. ZSOLT PETENDI
I’m a pharmacist from Budapest, Hungary
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoids… are the „materials of life”
IRIDOIDS – A PHARMACISTS PROSPECTIVE

The knowledge of pharmacists are fused together from three parts: botany, chemistry, physiology.

So when I talk different audiences – even to healthcare professionals’ – and I see the uncertain expression over their faces when I say I will speak about the iridoids… about the [yet] not-so-widely recognized new merits of them I know first I need to brush up all what they learned at the university. So I always follow this sequence: BCP (botany, chemistry, physiology)
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoids can be found in a lot of plants, which have mostly well-known and time-proven beneficial effects; they are real medicinal – ethno-, and folk medicinal plants.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoids are secondary metabolites of different plants* – they are not basically necessary for the plant. Sometimes they are strong insect-deterrents and they are often intermediers in the process of alkaloid synthesis.

*and they can be found also in some animals
IRIDOIDS – A PHARMACIST’S PROSPECTIVE

We find iridoids mostly in the following plant families (I will speak only about some of them)

Ericaceae
Gentianaceae
Lamiaceae
Loganiaceae
Menyanthaceae
IRIDOIDS – A PHARMACISTS PROSPECTIVE

(contd)

Oleaceae
Plantaginaceae
Rubiaceae
Scrophulariaceae
Valerianaceae
Verbenaceae
IRIDOIDS – A PHARMACISTS PROSPECTIVE

This plants have some common properties:

• they are well-known by the local inhabitans and have been used since many hundred / thousand years

• usually they can tolerate harsh conditions (mechanical impacts, droughts etc.)

• they have few side effects (if any)

• they are widespread and cheap
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Ericaceae (Heat/heather family)

Vaccinium myrtillus (Huckleberry)

(German: Heidelbeere, Heubeere, Schwarzbeere, Wildbeere, Waldbeere, Bickbeere, Zeckbeere, Moosbeere)

Just to begin with: there are very few fruits which contain iridoids. Vaccinium species are one of them.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

A book which is considered as a modern and the best guide in pharmabotanics is Hungary...

Prof Dr. Bela Danos: 
Farmakobotanics – medicinal plants

…doesn’t mention any iridoid-containing fruits except Vaccinium sp.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Ericaceae: Two iridoids were detected in 2002 with MS and NMR in different Vaccinium berries (cranberry, lingonberry, blueberry):

monotropein and 6,7-dihydromonotropein

Jensen HD et al:
**Ericaceae: Jensen HD et al: Iridoids in Vaccinium berries:**

<table>
<thead>
<tr>
<th>Cranberry</th>
<th>Lingonberry</th>
<th>Blueberry</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Vaccinium macrocarpon</em></td>
<td><em>Vaccinium vitis-idaea</em></td>
<td><em>Vaccinium corymbosum</em></td>
</tr>
<tr>
<td>amerikai tőzegáfonya (HU)</td>
<td>vörös áfonya (HU)</td>
<td>fürtös áfonya (HU)</td>
</tr>
<tr>
<td>red</td>
<td>red</td>
<td>dark blue</td>
</tr>
<tr>
<td><strong>monotropein</strong></td>
<td><strong>monotropein</strong></td>
<td></td>
</tr>
<tr>
<td><strong>6,7-dihydromonotropein</strong></td>
<td><strong>6,7-dihydromonotropein</strong></td>
<td></td>
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</tbody>
</table>
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Ericaceae:
Vaccinium corymbosum
(wikipedia)
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Ericaceae:
Vaccinium macrocarpon
(wikipedia)
Ericaceae: *Vaccinium macrocarpon*

A newer article:

Turner A *et al*:
Coumaroyl iridoids and a depside from cranberry (*Vaccinium macrocarpon*).

Depsides are two or more monocyclic aromatic units linked by an ester bond; they have antibiotic\(^1\), anti-HIV\(^2\), antioxidant\(^1\), and anti-proliferative\(^3\) activity, they are good NSAID’s\(^4\).

IRIDOIDS – A PHARMACISTS PROSPECTIVE

Ericaceae:
Vaccinium vitis-idea
(wikipedia)
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Ericaceae: Vaccinium berries in folk medicine:

Cranberry juice is a traditional folk remedy as a cure for urinary infections, but also against diarrhea and bowel problems.

Sometimes the juice and also its jam was and are consumed for a – purported – better night vision.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Gentianaceae (Gentian) (GER: Enzian) (HU: tárnics)

The *Gentianaceae* family is a real treasury of iridoids: their members are known for millenia (their name comes from the Illyrian – Dalmatian – king Gentius, who recommended it 2200 years ago against diarrhea and severe fatigue).
When I decided to study articles about iridoid research I collected cca 1.200 articles; almost 10% of them are dealing with some Gentianaceae, thus making them to the most represented plant family in my survey.
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Gentianaceae

This plant family contains about 1,500 species\(^1\), the most known are *Gentiana lutea*, *G. kurroo*, *G. algida*, *G. macrophylla*, *G. pedicellata*, *G. mansurica*, *G. rhodantha*, *G. scabra* etc. Many of them are used as a medicinal plant.

\(^1\)Struwe L et al (editors)  
*Gentianaceae*  
Cambridge University Press 2002
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Gentianaceae

*Gentianaceae* have a horribly strong bitter taste: *amarogentin* is bitter even at 1:50,000,000 dilution. But this bitter taste works sometimes wonders: all the world is producing different alcoholic and non-alcoholic extracts.

Bitters have a tremendous popularity: little old ladies, who never consider *drinking* rub their aching joints and use the ‘Bitter’ to every thinkable complaints and ailments.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Gentianaceae There are about 5,000 major bitters produced worldwide – some of them:

Angostura, Becherovka, Boonekamp's, Campari, Cynar, Demänovka, Fernet Branca, Jägermeister, Luxardo, Pelinkovac, Pimm's, Ramazotti, Suze, Swedish bitters, Underberg, Unicum…
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Gentianaceae

Purported medicinal properties of bitters

Bitters are alleged to have restorative properties. They were reported to be a remedy for hiccups, an upset stomach -- but manufacturers were not very faint-hearted…
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Gentiana ssp.
(wikipedia)
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Gentiana ssp. (wikipedia)
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Gentiana lutea (wikipedia)
The basic structure of the iridoids are simple: an oxygen-containing heterocyclic ring and a cyclopentane ring fused together.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoids are monoterpenes; they are synthethised in the plants and animals from isoprene and they are often the intermediers in the synthesis of alkaloids.

(Human body synthetises cholesterol and Q10 from isoprene, and natural rubber is made also from isoprene).
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Isoprene, C\textsubscript{5}H\textsubscript{8}, (2-metil-1,3-butadiene)
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The name „iridoids” originates from the name of an ant species (*Iridomyrmex*). It was discovered it that insects.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridomyrmex humilis
These ants, *Iridomyrmex humilis* – (argentin ant) – are producing iridoids. There was earlier a hypothesis that they have it as deterrent against their enemies.

It was discovered only two years ago (in 2009) that iridoids are playing a greater role: maybe they are one of the real “material of life”!
IRIDOIDS – A PHARMACISTS PROSPECTIVE

„Don’t bury me, I’m alive” that is the message of iridoids in the ants.

So iridoids are linked to a healthy life in a way that maybe we don’t even realise the extent and importance of it.

Ants can smell things very well. They detect the difference between their family and others. It is hardly to believe that they couldn’t smell the smell of decomposing tissues of a dead ant… But iridoids are so important that without it there is no life. At least no ant-life.
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Two entomologists, Rust and Jocelyn Millar worked together with a researcher in the field of analytical chemistry named Choe isolating the „life signals” at the ants. They are dolichodial and iridomyrmecin.
“These materials or their slightly modified forms are common at many ant species. And these ants all perform necroforesis” – says Choe.

“But at these ants necroforesis is triggered through the absence of life signals, and not the deteriorating effects of death itself.”
The researchers told that this two chief materials – *dolichodial és iridomyrmecin* – or their slightly modified versions are found at very many other insects, too.

IRIDOIDS – A PHARMACISTS PROSPECTIVE

This is **dolichodial** – the ‘material of life’ – the ants are proving with this (and with iridomyrmecin) to their fellow comrades that they are still alive.

*Structure of dolichodial*
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Iridomyrmecin, $C_{10}H_{16}O_2$

- molar weigh: 168.24
- CAS: 485-43-8
- can be found in *Actinidia polygama*
- and has antibiotic properties – like so many other iridoids.
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Google: ne temessetek el, még élek
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Plant of *Morinda citrifolia* is used by ants (*Oecophylla smaragdina*)…
There are insects which are synthetising iridoids *de novo* but mostly they consume ready iridoids; they are caterpillars. And at some species iridoids are ‘inherited’ to their butterflies, too.
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This is the „chequered Baltimore butterfly”
(Euphydryas phaeton)
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*Euphydryas phaeton*
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And this is the caterpillar of *Euphydryas phaeton*
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Its host plant is *Aureolaria flava*
Iridoids – A Pharmacists Prospective

...which can be easily recognised as the member of the family Scrophulariaceae.

This family has many well-known and widespread medicinal plants, (e.g *Linaria officinalis*).
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There is much research matter about the iridoid-consuming habits of butterflies but the real goal of this phenomenon is still unclear. Surely the deterrent effect (bitter taste!) is of one of them, but antibiotic effect also can play an important role.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

<table>
<thead>
<tr>
<th>Butterfly</th>
<th>Host plant</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Euphydryas phaeton</em></td>
<td><em>Aureolaria flava</em></td>
</tr>
<tr>
<td><em>Euphydryas phaeton</em></td>
<td><em>Plantago lanceolata</em></td>
</tr>
<tr>
<td><em>E. chalcedona</em></td>
<td><em>Scrophularia californica</em></td>
</tr>
<tr>
<td><em>E. anicia</em></td>
<td><em>Besseya plantaginea</em></td>
</tr>
<tr>
<td><em>Poladryas arachne</em></td>
<td><em>Penstemon virgatus</em></td>
</tr>
<tr>
<td><em>Junonia coenia</em></td>
<td><em>Plantago lanceolata</em></td>
</tr>
<tr>
<td><em>Ptatyptila pica</em></td>
<td><em>Castilleja sulphurea</em></td>
</tr>
<tr>
<td><em>Meris alticola</em></td>
<td><em>Besseya plantaginea</em></td>
</tr>
<tr>
<td><em>Ceratomia catalpae</em></td>
<td><em>Catalpa bignonioiides</em></td>
</tr>
</tbody>
</table>
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Members of the Rubiaceae family (relatives of Morinda citrifolia) has iridoids in abundant quantity.

So in Asperula odorata is asperuloside acid (AA).

Its deacetil compound is one of the most important iridoids in TNBB (DAA)
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Basic iridoid research is commenced by a pharmacist named

Prof. Emile Bourquelot (1851-1921)

who was researching and teaching at the University of Paris. He was also a pioneer in the field of enzymology; therefore his students named him lovingly „professeur Bourquelase”.

He said often that iridoids are playing a very important role in the healing of different illnesses.
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Structure identification of the iridoids started also a half century ago – in the beginning of the ’60es.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Research showed the exact structure of iridoids – that is the structure of their glycosid parts.
A typical iridoid is **loganin**, which is found in the seeds of *Strychnos nux-vomica* relatively abundantly (4-5% w/w). (The well-known alkaloid of the same plant is strychnine).
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Loganin,
C_{17}H_{26}O_{10}
The structures of

**plumericin** (antimicrobial effects, from *Plumeria multiflora*)

and **allamandin** (antineoplastic effect, mainly by leukemia, from *Allamanda cathartica*)

are very similar, too.

This materials are well-researched and have a long history. Their structure was identified many decades ago (plumericin’s in 1951, allamandin’s in 1974) by Little JE *et al.*, and Kupchan SM *et al.*, respectively.
If the cyclopentane ring is popened than we get the group of secoiridoids.

A very important and well-known secoiridoid is secologanin which is common in the sweet-smelling plant family of Caprifoliaceae.
Secologanin is the precursor of many alkaloids: about one quarter (25%) of all alkaloids are synthetised from it.

Among these alkaloids are such important ones which was (and sometimes still can) to be found in pharmacies, and which were used for healing for very long times. (*Cinchona*- and *Ipecac*-alkaloids). (kinin=fever and emetin=cough).
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoids in folk medicine
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Medicinal plants, containing iridoids and secoiridoids are treasured remedies of the folk medicine and are used mostly for very long times.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Some time-, and research- proven iridoid effects are:

1. painkiller, antidoloricum (Verbena off.)
2. against inflammations, antiphlogisticum (Euphrasia off., Verbena off.)
3. against cramps, antispasticum (Valeriana)
4. against cancer, antineoplasticum (Morinda citrifolia, Allamanda catarthica),
5. antibacterial (Plantago lanceolata)
6. booster of the immune system (Harpagophyton)
7. lowering the level of blood sugar (Morinda citrifolia)
Eyebright (\textit{Euphrasia officinalis}; Augentrost in German) is very good against all kind of eye inflammations and has a mild laxative and diuretic effect, too. It contains eufroside, aucubin and catalpol.

It’s interesting that \textbf{aucubin} is active only in its aglycon form (in the presence of the enzyme \(\beta\)-glucozidase).
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Eyebright (*Euphrasia officinalis*)
Valerian (Baldrian in German), *Valeriana officinalis* contains the iridoid valepotriate which is a potent tranquillant. The name of this plant in hungarian is „cats’ root”.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Valeriana officinalis
**IRIDOIDS – A PHARMACISTS PROSPECTIVE**

*Valeriana officinalis* is a good exemple to show the complex and synergistic effects of plants; beside its good iridoid content

- its valerenic acids are inhibiting the enzyme which disintegrates GABA (Gamma Amino Butyric Acid, an important neurotransmitter in the brain with tranquilizing effect) so there remains more GABA

- and the extract of *Valeriana, (Tinctura valerianae* in the pharmacy) contains also GABA, too.
But *Tinctura valerianae* (either the *aetherea* or *spirituosa*) has a horrible taste and an unpleasant odor – some would name it *pungent stench*; they are right, believe me…
IRIDOIDS – A PHARMACISTS’ PROSPECTIVE

...but cats have an opposite opinion.

Cats become delirious when they encounter with *Valeriana* (remember the hungarian name *cats’ root*)! – if they can they try to get the plant’s root, they chew it, but they like notoriously the similar *Nepeta cataria* also.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Nepeta cataria
Nepeta cataria has several iridoids: nepetalacton is good against fever (febrifugium) against cramps (antispasticum) and has antimicrobial effect and is a good and mild tranquillant.
Different iridoids are the key of the beneficial effects of many medicinal plants.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Simple iridoids: \((C_9 - C_{10})\)

- *Boschniakia rossica*
- *Teucrium marum*
- *Myoporum ssp.*
- *Actinidia polygama*
- *Nepeta cataria*
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Secoiridoid glycosids: \((C_{16} – C_{29})\)

- *Gentiana lutea*
- *Olea europaea*
- *Lonicera, Vinca rosea*
- *Swertia japonica*
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoid glycosids I. (C\textsubscript{15} – C\textsubscript{22})

- Vitex agnius-castus
- Antirrhinum majus
- Asperula odorata
- Aucuba japonica
- Catalpa, Plantago
- Catalpa speciosa
- Strychnos, Menyanthes
- Glandifora ssp.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoid glycosids II. (C_{15} – C_{22})
- Gardenia, Cornus
- Harpagophytum procumbens
- Strychnos nux-vomica
- Monotropa, Pyrola sp.
- Paederia scandens
- Plumeria acutifolia
- Gardenia sp.
- Verbena officinalis
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Nonglycosid iridoids: \((C_{11} – C_{22})\)

- Allamanda cathartica
- Valeriana, Centranthus
- Plumeria ssp.
- Genipa americana
- Plumeria multiflora
- Valeriana, Centrarthus
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Summarised: the iridoids

- are found in dozens of medicinal plants,
- are deeply rooted and effectively used in the folk medicine
- and their research is continued during 50-60, but sometimes more than 100 years.
But it’s not a simple task to apply evenly and effectively green and dry plant materials to the human body – I mean poor adsorption because poor gut flora, the problems of equal doses etc.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

And besides, as it was mentioned, iridoids are very bitter – that’s why they are in the plants.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Amarogentin
it’s the etalon of bitterness
IRIDOIDS – A PHARMACISTS PROSPECTIVE

So we should have a fruit, with good, at least with *tolerable* taste… from which we could make a liquid form: easy application, good bioavailability, and maybe more iridoids than in the modest cranberries (2).

We should develop a DESIGNER FRUIT, right?!
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Maybe with 5 or 6 iridoids? Much more than any other known fruit? A new champion?
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Me, as a pharmacist of decades, continuously learning and working cannot hide my joy, wondering – and kind of embarrassment – that a Great Designer already made this fruit and that I can be the part of this emerging miracle.
Morinda citrifolia has twelve iridoids (maybe more...). I can’t explain such difference between ordinary fruits and noni.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

But for the healthcare professionals who are now getting acquainted with Tahitian Noni® Bioactives surely iridoids are the most interesting…
IRIDOIDS – A PHARMACISTS PROSPECTIVE

...because iridoids

- have long and rock-solid research,
- TNBB has lot of them
- and their bioavailability is exceptionally good.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Good bioavailability in the human body is greatly determined by two important factors: solubility and physical / chemical stability.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

Iridoids in noni have

1) good solubility so they are easily adsorbed

2) they are very resistant to chemical degradation during manufacturing and shelf-life (but flavonoids aren’t!)
IRIDOIDS – A PHARMACISTS PROSPECTIVE

So TNBB is the world’s first – and still the only – fruit-based bioactive drink.
IRIDOIDS – A PHARMACISTS PROSPECTIVE

For a pharmacist it is very important that Tahitian Noni Bioactive Beverage™

- has a very profound quality insurance and quality checking system (GMP, GAP, GHP)
- was already researched in 14 human clinical trial
- and that its’s iridoid content is declared, constant and can be every time verified.
IRIDOIDS – A PHARMACISTS
PROSPECTIVE

Tahitian Noni Bioactive Beverage® has an innovative, modern design…
IRIDOIDS – A PHARMACISTS PROSPECTIVE

…and tartes *sooo* good! (It’s a subjective and a personal opinion).

Thank you for your attention!