What is Pharmaceutical Biology?

- Applied science dealing with living cells as host or producer of natural products with pharmacological activity
  - Naturally origin in living organisms
  - Biosynthesis
  - Biological activity and application
  - Improving production processes
Goal of this lecture series

- Nature as source for gene and drug discovery
- Biodiversity / Chemodiversity
- Synthetic Biology, Metabolic Engineering
- Drug regulation
- Economic value

Areas of Pharmaceutical Biology

- **Microbiology**
  - Bakteria
  - Fungi
  - Marine organisms

- **Botanica**
  - Taxonomy
  - Systematics
  - Ethnobotanics

- **Fytotherapy**
  - Phytopharmacology
  - Toxikology
  - Regulation of herbal medicinal drugs

- **Bioanalytics**
  - High Throughput Screening
  - Natural Product Chemistry
  - Standardisation
Natural Products in practise

From professional use to self medication

Nature is most important source for new drugs and therapeutic agents
Natural Products

- From microorganisms
  - *Streptomyces*
  - *Penicillium*
- From plants
  - Veele medicinale planten
- From animals
  - Corals
  - Marine organisms

Secondary natural products from plants in pharmacy

- Pure isolated compounds
  - morfine, digoxine, kinine, vinblastine, paclitaxel
- Semi-synthetics
  - podofyllotoxine → etoposide
  - artemisinine → arteether
- Synthetics (natural product is ‘template’)
  - E.g. atropine, morfine, cocaïne, tubocurarine
**Plant like drugs**

- Oldest form of pharmacotherapy
- Since 19th century isolation of natural productions
- Source for new drugs: chemical compounds from plants and their derivatives
- Fytotherapeutics
- Homeopathic medicines

**History**

Historic roots of traditional medicine
History

- Starch tablets from Mesopotamia (from 2500 b.c.)
**History**

**Theophrastus (300 B.C.)**
studied medicinal plants and is called father of botany

**History**

**Dioscorides**
Father of pharmaceutical biology and pharmacy
Writer of *Materia Medica*. Up to the 16th century a standard textbook
Hildegard von Bingen, 1098-1179

- Kloster medicine
- Liber Simplicis Medicinae
- Liber Compositae Medicinae
  - 280 plants described
  - Translation from Latin to German
  - First scientific use of plants

Klostermedicine

- No topic for medicine at universities
- First kloster founded 527 by Benedikt von Nursia
- Early and late middel age
- Medical nursery in Europe
- Based on plants
- Place of first medical library

- Bartolomaeus Anglicus (De proprietatibus rerum)
- Thomas Cantimpratensis (Speculum maius)
- Vinzenz von Beauvais
- Albertus Magnus
- Konrad von Megenberg (Buch von den natürlichen Dingen)
Avicenna, 979-1037

Abu Ali al-Husain ibn Sina-e Balkhi

- Persian medicus
- Author of 200 books
  - *al-Shifa* (the book of healing)
  - *Al-Qanun fi-l-Tibb* (The canon of healing)
- Eastern fytotherapie
  - Based on tradition of Aristoteles

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From history to presence

- Plants are essential for pharmacy
- Examples:
  - *Papaver somniferum*
  - *Podophyllum hexandrum*
  - *Artemisia annua*
From history to presence

- 40% of clinically used drugs are derived from nature

<table>
<thead>
<tr>
<th>Natural Product</th>
<th>Syntheticum</th>
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<tbody>
<tr>
<td>Caffeine</td>
<td>Sildenafil</td>
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<tr>
<td>Furanocoumarine</td>
<td>Chromoglycinzuur</td>
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<td>Morfine</td>
<td>Methadon, Pethidine</td>
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<td>Dicoumarine</td>
<td>Warfarine</td>
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<tr>
<td>Artemisine</td>
<td>Artemether</td>
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</tbody>
</table>

Microorganisms as source for drug discovery get more and more important

- Actinomycetes (Streptomyces) 60%
- Bacillaceae
- Pseudomonaceae
- Myxobacteria
- Enterobacteria
- Fungi imperfecti
  - *Penicillium*
  - *Aspergillus*
  - *Acremonium*
- Basidomycetes

1% only of microorganisms are known!
Natural Products from microorganisms

- Penicillin
- Streptomycine

Biodiversity

- What is Biodiversity?

Divergence of life
Biodiversity

• Complex and high number of animals, plants and microorganisms
• Extraordinary high number of varieties

Biodiversity

• All organisms produce a different pattern of natural products

Chemodiversity
The beginning of wisdom is to give a name to the unknown

Botany

Carl von Linne
(Linneaus)

- Classification of nature according to common distinguishing marks
- Scientific nomenclature
- e.g. *Papaver somniferum* L.
Botany / Evolution

Charles Darwin

Founder the evolution theory.

Botany / Evolution

Giving a name based on relationships.
Possible through:
- Evolution
- Taxonomy
- DNA sequencing

Phylogenicity
Genetic origin of Chardonnay wine

Synonyms
Pinot Chardonnay, Beaunois, Morillon, Weißer Clevner and Feinburgunder

Phylogenetic origin of Chardonnay wine

Results:
- Pinot noir: known by Romans
- Gouais blanc: Origin in East Europe
- both well known in the middle age
- natural crossing of Pinot and Gouais Blanc


Chemodiversity

- Chemodiversity is the source for drug discovery
- But, how to find?
- High Through Put Analytics (HTPA)
- High Through Put Screening (HTPS)

We see later in the next chapter!

Ethnopharmacy

- Ethnobotany = traditional use of plants
- Ethnofarmacie = traditional use medicine / healing techniques

J. W. Harshberger
1869-1929
Ethnobotany - Ethnopharmacy

Homeopathie, Kneipp, Bach
TCM
Kampo
Ayuverda
Jamu
Traditionele Noordamerikanse Geneeskunde
Traditionele Afrikanse Geneeskunde
Traditionele Zuidamerikanse Geneeskunde

College 1/1 - 33
Ethnobotany - Ethnofarmacy

Natural drugs? Is it possible to have?

What is the most apparent way of treating sick people in the world?
That’s it!

Contrasts between 1st and 3rd world...
Natural drugs?

- Most people in the world are dependent on plants and herbal medicinal products
- More and more interest in traditional medicine in so called western world
- "Back to Nature" trend in industrial communities

Table 2: Comparison of Prevalence and Frequency of Use of Alternative Therapies Among Full Respondents, 1997 vs. 1998*

<table>
<thead>
<tr>
<th>Type of Therapy</th>
<th>Used in Past 12 mo</th>
<th>Same-Patient Use 12 mo</th>
<th>Mean No. of Visits per 12 mo</th>
<th>No of Visits per 1000 Population</th>
<th>Estimated Total No. of Visits in 1997 (in Thousands)</th>
<th>Total Visits, % [5]</th>
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<tbody>
<tr>
<td>Herbal medicine</td>
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<td>ART-16 alternative therapy</td>
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<td>Self report</td>
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</table>

*Percentage use of those who used that type of therapy. **Estimates indicate data not applicable.

Natural drugs?

- More of:
  - Fytotherapy
  - Homeopathy
  - Traditional art of healing

- More than **120** therapies are already accepted!
Use of medicinal plants

- Ca. 80% of world population is depended on.
- Synthetic drugs mostly too expensive
- Highly depended on cultural background
- WHO considers herbal medicinal products as essential part in the arsenal of medicines used today

Active constituents

- Some plants are well characterised, but mostly we do not much about constituents
- Plants may contain a toxic principle that is accepted as wanted active drug
- Synthetic drugs as single preparations are preferred
Ethnobotany - Ethnofarmacy

- Transfer from traditional medicine to clinically drugs works:
  - Artemisinine - Anti-malaria
  - Podofyllotoxine - Anti-cancer
  - Paclitaxel - Anti-cancer