PHARMACOGNOSY DEPARTMENT

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İrfan ATA

Fall Term

Pharmacognosy I Theoretical
Pharmacognosy I Practical

Pharmacognosy III Theoretical
Pharmacognosy III Practical

Spring Term

Pharmacognosy II Theoretical

Pharmacognosy II Practical

Pharmacognosy I

Carbohydrates

- Monosaccarides
- Oligosaccarides
- Polysaccarides
- **Glycosides** (Cardiac gly., Saponins, Cyanogenic gly., Glucosinolates, Anthraquinone containing drugs)

Pharmacognosy II

- **Glycosides** (Flavonoids, Anthocyanins, Iridoids, Coumarines)
- Tannins
- Lipids
- Waxs
- Terpenoids
- Essential oils
- Resins
- Latexs

Pharmacognosy III

- Alkaloids
- Alkaloids derived from tryptophan, Alkaloids derived from ornithine and lysine, Alkaloids derived from nicotinic acid, Alkaloids derived from phenylalanine and tyrosine, terpenoid alkaloids and steroidal alkaloids))
- Lectins
- Protits
- Enzymes


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Optional courses

- Herbal teas
- Aromatherapy
- Marine natural products
- Vitamin rich natural products
- Herbal narcotics and phscycotrops
- Biological activities of natural products
- Phytomedicines I
- Phytomedicines II
- Natural products used in oncology
- Nutraceuticals
- Standardization and chromatographic analysis of herbal products

Practical courses

Practical courses run in parallel with theoretical courses are;

- Isolation of active substances
- Microscopical analysis
- Qualitative analysis
- Pharmacopoeia analysis
- Assays

Pharmacognosy Graduate Programme

- Pharmacognosy Master's Programme (Academia, Drug Industry, Research and Control Laboratoires)
- Phytotherapy Master Programme (Pharmacies, Herbal Drug Industry, Agriculture of medicinal plants)
- Pharmacognosy Doctora Programme (Academia, Drug Industry, Research and Control Laboratoires)



Pharmacognosy Master's programme (PMsP)

- This programme provides the knowledge to deepen and improve the knowledge in the field of pharmacognosy at the level of expertise, depending on the qualifications of the undergraduate level.
- PMsP provide the necessary knowledge to archieve more accurate and more accurate results using modern and advanced principles, theories, techniques and methods in the field of pharmacognosy.

Pharmacognosy Master's programme (PMsP)

- PMsP provides the knowledge to develop and validate analytical methods for sensitive and accurate determination of active ingredients and commercial preformulations containing raw materials.
- PMsP provides knowledge of working principles of some devices used in the field of pharmacognosy.
- PMsP provide the ability to comprehend interdiciplinary interaction with which pharmacognosy releated.

Obligatory courses of PMsP

- Extraction methods-Theoretical
- Extraction methods-Practical
- Chromatography applications for plant secondary metabolites-Theoretical
- Chromatography applications for plant secondary metabolites-Practical
- Literature survey methods-Theoretical
- Literature survey methods-Practical

Optional courses of PMsP

- Pharmacopoeia analysis
- Extraction methods
- Opium alkaloids
- Vitamin rich natural products
- Natural antioxidants
- Homeopathy
- Biological activities of natural products
- Aromatherapy
- Phytotherapy
- Nutraceuticals
- Plant secondary metabolites

Courses of optional PMsP

- Essencial oils and terpenes producing in Turkey
- Natural products in pharmaceuticals
- Immunostimulant plants
- Hallucinogenic, allergenic and teratogenic plants
- Phytocosmetic
- Drogs used in traditional therapy
- Herbal baths
- Methods of preparation of drugs
- Animal originated drugs
- Regulation of herbal medicines

PHARMACOGNOSY

- The word *Pharmacognosy* is derived from;
- *pharmacon* …..a drog/ a poison (Greek)
- *gignosa* …..to acquire knowledge (Greek)
- *cognosco*….to know about (Latin)

pharmacon not only means poison, but also medication…the difference lies in the dose.

History

- The term «pharmacognosy» was used for the first time by the Austrian physician SCHMIDT in his book named «Lehrbuch der Materia Medica» in 1811.
- Also it was used by SEYDLER in a work entitled «Analecta Pharmacognostica» in 1815.

History

- 19th century: the chemical structures of many of the isolated compounds were determined
- 20th century: the discovery of important drugs from the animal kingdom, particularly hormones and vitamins
- Microorganisms have become a very important source of drugs

The era of pure compounds

- 1803 Isolation of morphine from opium
- 1820 Strychnine
- 1921 lobeline
- 1810 quinine
- 1831 atropine
- 1848 papaverine
- 1860 cocaine
- 1869 digitoksine
- 1875 pilokarpin
- 1918 ergotamine
- 1930 digoksine
- 1931 reserpine
- 1935 tubocurarine
- 1935 ergometrine
- 1949 sennoside
- After 1940 Vitamins, antibiotics, anticancer drugs

PHARMACOGNOSY

- Pharmacognosy limits its field of investigation to natural starting materials: it is simply the descendant of «materia medica» , a dicipline which, since Dioscorides's treatise by that name, and until the birth of synthetic chemistry, dealt with mineral, animal, and plant starting materials.

PHARMACOGNOSY

- By the time, mineral substances lost their appeal. Those that are still in use are well known-defined substances, just like synthetic organic substances.
- Not only hormones, enzymes, but also substances elaborated by micro-organisms. Some do not hesitate to include biotechnology and genetic engineering.
-

PHARMACOGNOSY

- Under these conditions, *Pharmacognosy* is the study of raw materials and substances intended for therapeutics, and of biological origin, in other words obtained from plants, animals or by fermentation from microorganisms.

The pharmacognosy defined currently is as follows;

- **Pharmacognosy is the study of medicines derived from natural sources.**
- The study of the physical, chemical, biochemical and biological properties of drugs, drug substances of natural origin as well as the search for new drugs from natural sources. (The American Society of Pharmacognosy)

Ginseng

Biological and geographical sources of drugs

- Although pharmacognosy is principally concerned with plant materials, there are a small number of animal products which are traditionally encompassed within the subject; these include such items as beeswax, cod liver oil, lanoline, woolfat, gelatin, some vitamins, etc.
- In addition, marine organisms, many of the animal kingdom, are receiving increasing attention.

Biological and geographical sources of drugs

- Current estimates of the number of species of flowering plants range between 200.000 and 250.000 in some 300 families globally.
- Despite a rapid expanding literature on phytochemistry, only a small percentage of the total species have been examined chemically, and there is a large field for future research.

Biological and geographical sources of drugs

- Materials having no pharmacological action which are of interest to pharmacognosist are natural fibres, flavouring and suspending agents, colourants, disintegrants, stabilizers, filtering and support media.
- Other areas that have natural associations with the subject are poisonous and hallucinogenic plants, allergens, herbicides, insecticides and molluscicides.

Pharmacognosy

Recently it includes;

- Modern isolation techniques,
- Phrmacological testing procedures to prepare purified substances,
- Cultivation and propagation by tissue culture



PHARMACOGNOSY

- Pharmacognosy is closely related to botany and plant chemistry and, indeed, both originated from the earlier scientific studies on medicinal plants.
- As late as the begining of the 20th century, the subject had developed mainly on the botanical side, being concerned with the description and identification of drugs, both in the whole state and in powder, and with their history, commerce, collection, preparation and storage.

PHARMACOGNOSY

- A great proportion of the natural products are used drugs
- The study of drugs used by traditional healers is an important object of pharmacognostical research
- Crude drugs/raw materials:

  It is used for those natural products such as plants or part of plants, extracts and exudates which are not pure compounds

PHARMACOGNOSY

- Such branches of pharmacognosy are still of fundamental importance, particulary for pharmacopoeial identification and quality control purposes, but rapid developments in other areas have enormously expanded the subject.
- The use of modern isolation techniques and pharmacological testing procedures means that new plant drugs usualy find their way into medicine as purified substances rather than in the form of galenical preparations.



Fields of Pharmacognosy

- **Medical ethnobotany:** the study of the traditional use of plants for medicinal purposes;
- **Ethnopharmacology:** the study of the pharmacological qualities of traditional medicinal substances;
- **Phytotherapy:** the medicinal use of plant extracts
- **Phytochemistry:** the study of chemicals derived from plants including the identification of new drug candidates derived from plant sources
- **Marine pharmacognosy:** the study of chemicals derived from marine organisms

Phytochemicals

All plants produce chemical compounds as part of their normal metabolic activities.

These phytochemicals are divided into;

- Primary metabolites: such as sugars, fats which are found in all plants
- Secondary metabolites: compounds which are found in a smaller range of plants, serving a more specific function (alkaloids, glycosides, etc)

Phytochemicals

- Undoubtedly, the plant kingdom still holds many species of plants containing substances of medicinal value which have yet to be discovered; large numbers of plants are constantly being screened for their possible pharmacological value (particularly for their anti-inflammatory, hypotensive, hypoglycemic, amoebicidal, anti-fertility, cytotoxic, antibiotic and anti-parkinsonism properties).
- Pharmacognosists with a multidiciplinary backround are able to make valuable contributions to these rapidly developing fields of study.

Phytochemicals

- The use of single pure compounds, including synthetic drugs, is not without its limitations, and in recent years there has been an immence revival in interest in the herbal and homeopathic systems of medicine.
- The current return of phytotherapy was clearly reflected by the increased market of such products. In 2015 the latter, for Europe, reached a figure of 15 billion.

Pharmacognosy studies

Pharmacologically active constituents are responsible for the therapeutic activity of the drug.

In pharmacognosy, to study a plant is:

- To define its identity
- To describe its morphology and anatomy
- To know its origin and production methods,
- To determine its chemical composition
- To know pharmacological activity of the active principals

Medicinal plants

- A plant is said to be medicinal when «at least one part posseses therapeutic properties».
- It may be listed in a pharmacopoeia.
- It has curing or preventive properties for diseases.

e.g;

- Digitalis-medicinal plant
- Cynara-edible and medicinal plant

Medicinal plants

- A complete understanding of medicinal plants involves a number of disciplines including commerce, botany, horticulture, chemistry, enzymology, genetics, quality control and pharmacology.
- Pharmacognosy is not any one of these per se but seeks to embrace them in a unified whole for the better understanding and utilization of medicinal plants.

Classification of herbal drugs

- *Taxonomic:* The drugs are arranged according to the plants from which they are obtained, in classes, orders, families, genera and species.
- *Morphological:* The drugs are divided into groups such as the following: leaves, flowers, fruits, seeds, barks, rhizomes, roots, etc.
- *Pharmacological or therapeutic:* This classification involves the grouping of drugs according to the pharmacological action of their most important constituent or their therapeutic use.

However, it is important to appreciate that the constituents of any one drug may fall into different pharmacological groups.

Classification of herbal drugs

- *Chemical or biogenetic:* The important constituents, e.g. alkaloids, glycosides, volatile oils, etc., or their biosynthetic pathways, form the basis of classification of the drugs.

- This is a popular approach when the teaching of pharmacognosy is phytochemically based.

- Ambiquites arise when particular drugs possess a number of active principles belonging to different phytochemical groups, as illustrated by licorice, ginseng, valerian, etc.

Chemical classification

- Crude drugs are classified depending upon the active constituents
- Irrespective of the morphological or taxonomical characters, the drugs with similar chemical constituents are groupped together
- Advantage: it is a popular approach for phytochemical studies
- Disadvantage: ambiquities arise when particular drugs possess a number of compounds belonging to different groups of compounds.

- Raw materials and active substances which biological origin： **Drugs**

Active constituents

Supporting constituents

Scopes of Pharmacognosy

Scopes of Pharmacognosy

1. Isolation or analysis of phytochemicals (glycosides from digitalis leaves, morphine and codeine from opium latex)
2. Structure activity relationship (tubocurarine from Curare)
3. Drugs obtained by partial synthesis of natural products (steroid hormones from diosgenine)
4. Natural products as models for synthesis of new drugs (atropine for certain spasmolytics)
5. Drugs of direct therapeutic uses (ergot alkaloids, vincristine)

Scopes of Pharmacognosy

6. Cultivation and collection of medicinal plants (clove, cinnamon, opium)

7. Preparation of herbal formulations (asvas, aristas)

8. Development of tissue cultured plants

Pharmacognosy studies

- Definition of drugs/natural products
- To prepare extracts with different extraction technics
- Qualitative and quantitative analysis
- Standardization,
- Quality efficiency, reliability and storage of the drugs
- Biological activities of natural products

Pharmacognosy studies

On the other hand, pharmacognosy deals with the extraction, isolation, structure elucidation, qualitative and quantitative analysis and activity studies of the active compounds from natural products, especially plants.

Production of natural drug products

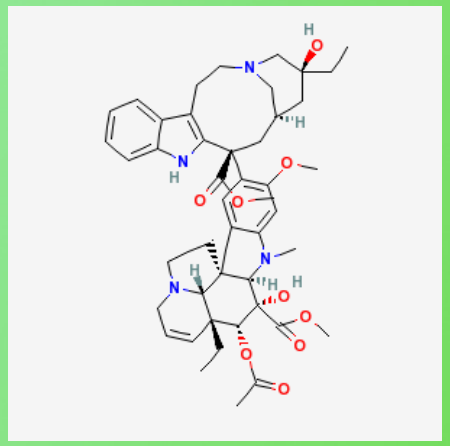
- Collection (wild)
- Cultivation, collection, harvesting, drying, garbling, packaging, storage and preservation e.g. Ginseng, ginkgo, peppermint
- Fermentation/recombinat DNA technology/genetically engineered drugs
- Cell culture techniques
- Microbial transformation
- Biologics

Contribution of plants to medicine and pharmacy

- 18th century drugs were based on plants
- 19th century a range of drugs was isolated:
  - 1805 morphine
  - 1817 emetine
  - 1819 strychnine
  - 1820 quinine

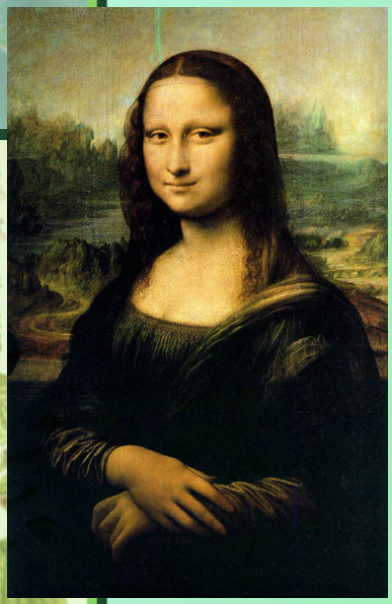
Famous plants/plant drugs?

Quinine



- *Cinchona* bark, South American tree
- Used by Incas; dried bark ground and mixed with wine
- First used in Rome in 1631
- Extracted 1820
- Large scale use 1850
- Chemical synthesis 1944
- Actual tree remains the most economic source

Belladonna -> atropine

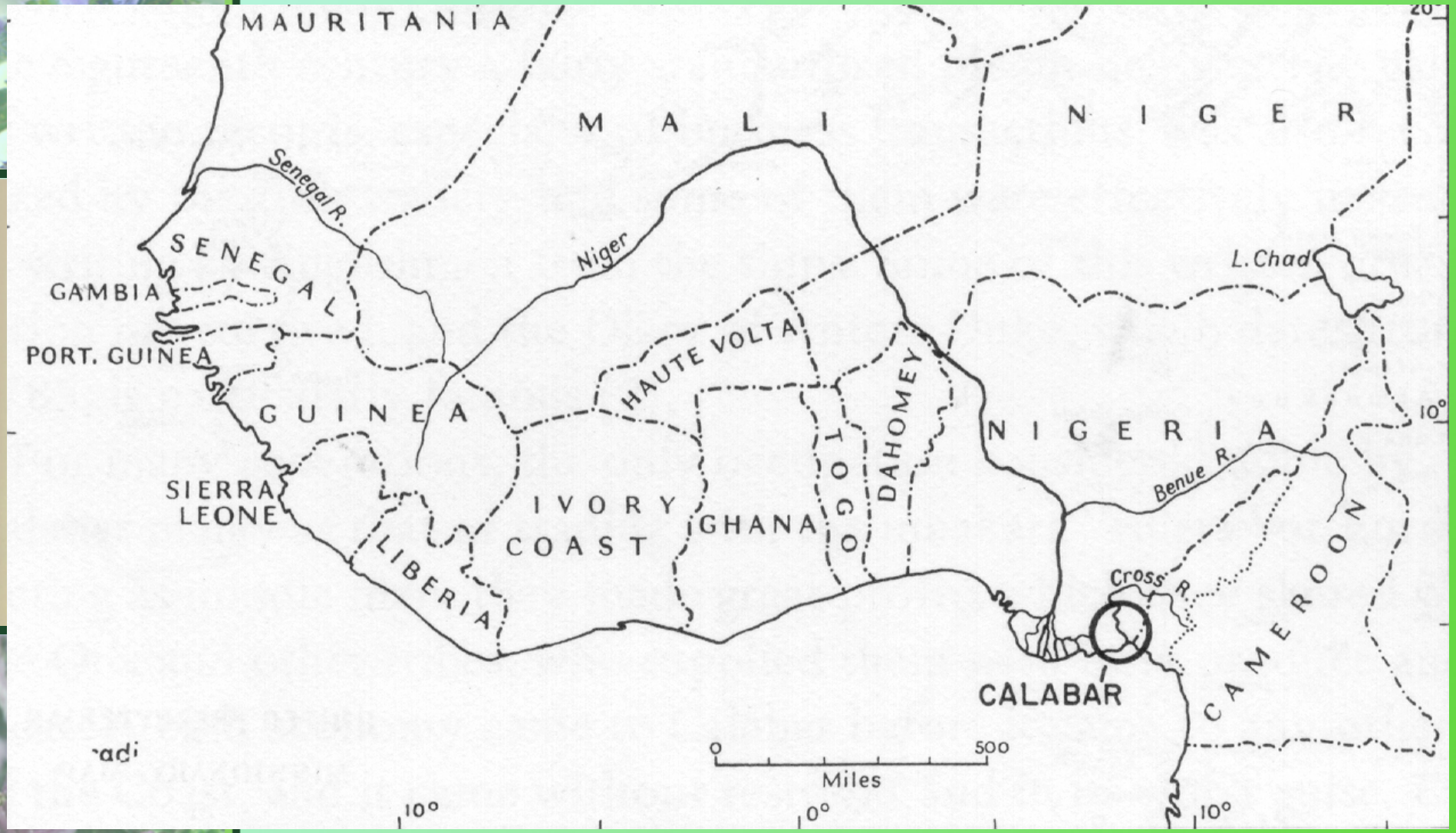


Anticholinergic syndrome:

- Hot as hell
- Blind as a bat
- Red as a beet
- Dry as a bone
- Mad as a hatter

Physostigma venosum

Calabar bean


MAURITANIA
MALI
NIGER
Senegal R.
Niger
L. Chad
SENEGAL
GAMBIA
PORT. GUINEA
GUINEA
HAUTE VOLTA
TOGO
DAHOMEY
NIGERIA
Benue R.
SIERRA LEONE
LIBERIA
IVORY COAST
GHANA
Cross R.
CAMEROON
CALABAR
0
500
Miles
10°
0°
10°
10°

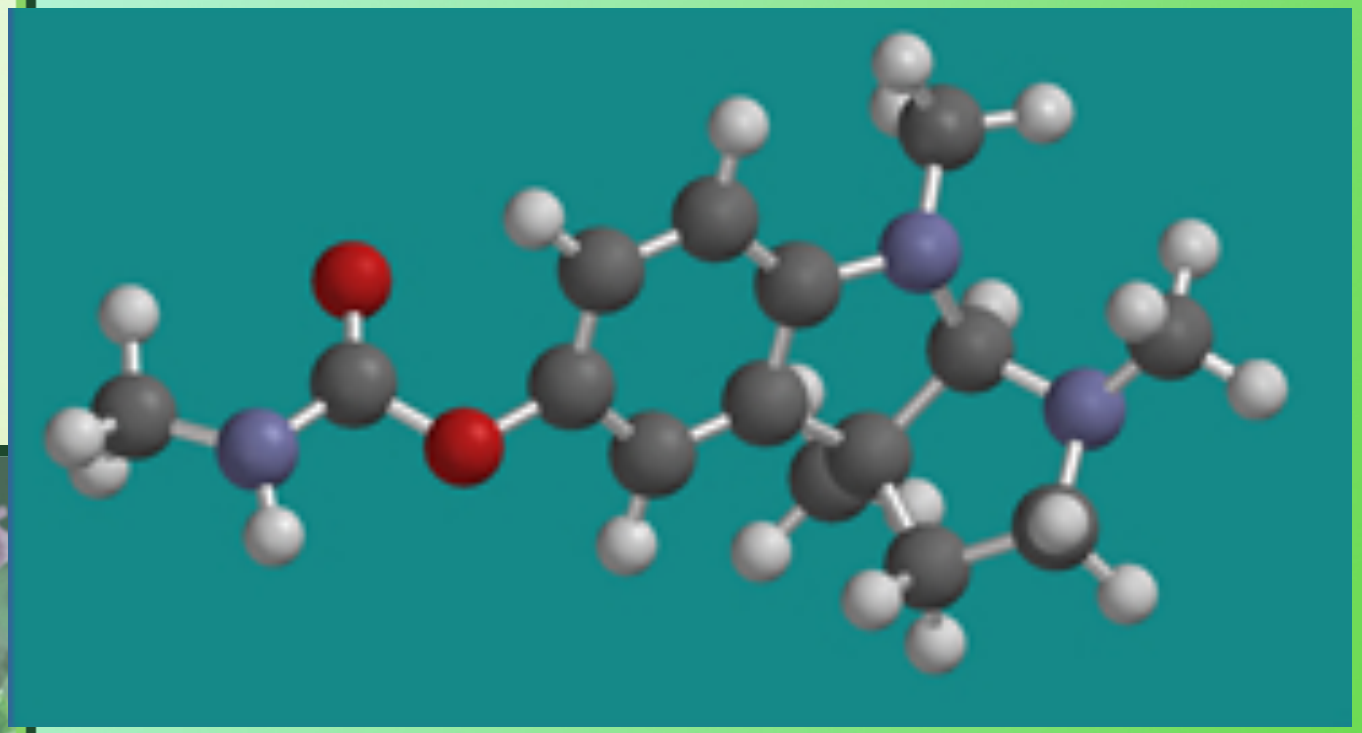
Efik People

Efik Law

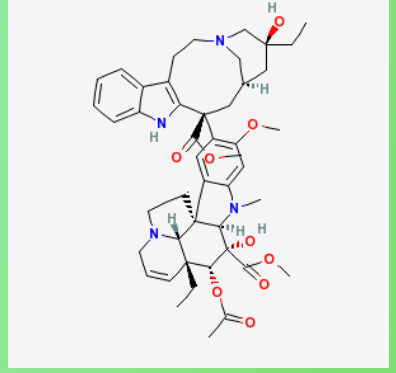
- Trial by ordeal
  - "A suspected person is given 8 beans ground and added to water as a drink. If he is guilty, his mouth shakes and mucus comes from his nose. His innocence is proved if he lifts his right hand and then regurgitates" (Simmons 1952)
- Deadly esere
  - Administration of the Calabar bean
- First observed by WF Daniell in 1840
- Later described by Freeman 1846 in a Communication to the Ethnological Society of Edinburgh

Physostigmine or Eserine

First isolated in 1864 by Jobst & Hesse



‘Taxol’



- Pacific Yew tree, *Taxus brevifolia,* bark
- 1964 activity discovered at NCI
- 1966 paclitaxel isolated
- Mitotic inhibitor
  - interferes with normal microtubule growth during cell div
- Used for cancer chemotherapy
  - lung, ovarian, breast, head & neck, Kaposi’s sarcoma



Taxol

- 1969
  - 1200kg bark -> 28kg crude extract -> 10g pure
- 1975 active in another in vitro assay
  - 1977 7000 pounds bark requested to make 600g
- 1978 Mildly active in leukaemic mice
- 1979 Horowitz; unknown mechanism
  - involved stabilising of microtubules
  - 1980 20,000 pounds of bark needed
- 1982 Animal studies completed

- 1984 Phase I trials
  - 12,000 pounds for Phase II to go ahead
- 1986 Phase II trials began
  - Recognised 60,000 pounds miniumum needed
  - Environmental concerns voiced

- 1988
  - An effect in melanoma
  - RR of 30% refractory ovarian cases
  - Annual destruction of 360,000 trees to treat all US cases
- 1989 NCI handed over to BMS
  - Agreed to find alternative production pathway
  - 1992 BMS given FDA approval & 5yrs marketing rights
  - Trademark ‘Taxol’ Generic paclitaxel
- 2000 sales peaked US$1.6 billion
  - Now available as generic

Alternative production of Taxol

- 1967-1993 all sourced from Pacific Yew
- Late 1970s synthetic production from petrochemical-derived starting materials
- 1981 Potier isolated 10-deacetylbaccitin from *Taxus baccata* needles
- 1988 published semi-synthetic route
- 1992 Holton patented improved process improving yield to 80%
- 1995 use of Pacific Yew stopped
- Now plant cell fermentation (PCF) technology used
- Also found in fungi
- Race for synthetic production -> docetaxel

Why do we need plants?

1. Source of drug molecules

- Most drugs can be synthesised
- Still more economical to use the plant

Papaver opium -> morphine, codeine (strong medicinal pain)

Ergot fungus –> ergotamine (headache), ergometrine (direct action on uterine muscle)

Why do we need plants

- *Compounds from natural sources play four significant roles in modern medicine:*

They provide a number of extremely useful drugs that are difficult, if not impossible, to produce commercially by synthetic means

Why do we need plants

2. Source of complex molecules that can be modified to medicinal compounds

- Examples:

  Droscera yam: molecule -> steroids

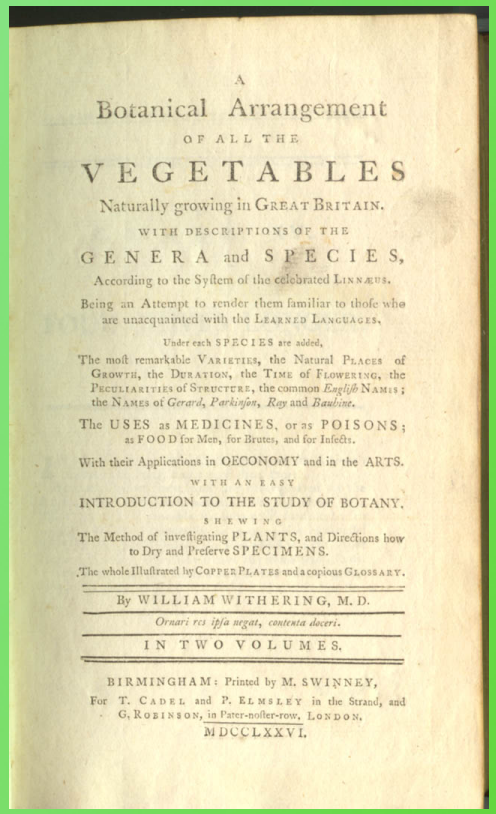
  Soya: saponins -> steroids

Why do we need plants

3. Natural sources also supply basic compounds that may be modified slightly to render them more effective or less toxic

Digitalis foxglove -> digoxin

(acts on cardiac muscle)



A

Botanical Arrangement

OF ALL THE

VEGETABLES

Naturally growing in GREAT BRITAIN.

WITH DESCRIPTIONS OF THE

GENERA and SPECIES,

According to the System of the celebrated LINNÆUS.

Being an Attempt to render them familiar to those who are unacquainted with the LEARNED LANGUAGES.

Under each SPECIES are added,

The most remarkable VARIETIES, the Natural PLACES of GROWTH, the DURATION, the TIME of FLOWERING, the PECULIARITIES of STRUCTURE, the common *English* NAMES; the NAMES of *Gerard*, *Parkinson*, *Ray* and *Bauhine*.

The USES as MEDICINES, or as POISONS; as FOOD for Men, for Brutes, and for Insects.

With their Applications in OECONOMY and in the ARTS.

WITH AN EASY

INTRODUCTION TO THE STUDY OF BOTANY,

SHEWING

The Method of investigating PLANTS, and Directions how to Dry and Preserve SPECIMENS.

The whole Illustrated by COPPER PLATES and a copious GLOSSARY.

By WILLIAM WITHERING, M. D.

Ornari res ipsa negat, contenta doceri.

IN TWO VOLUMES.

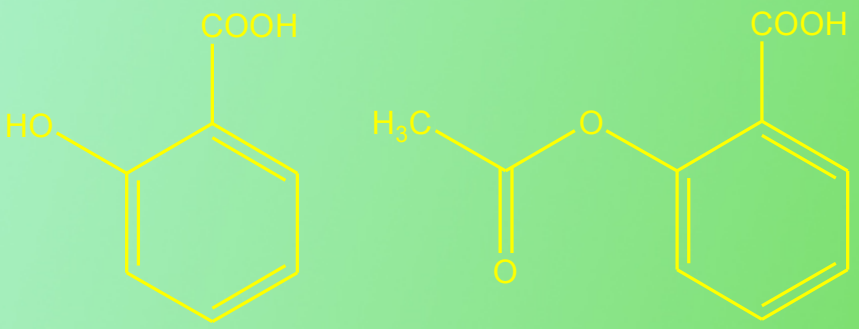
BIRMINGHAM: Printed by M. SWINNEY,

For T. CADEL and P. ELMSLEY in the Strand, and G. ROBINSON, in Pater-noster-row, LONDON.

MDCCLXXVI.

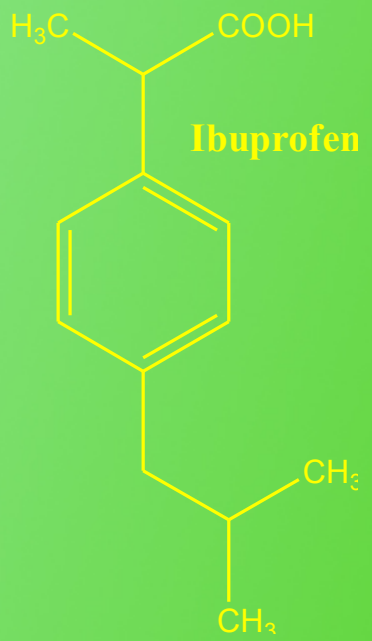
Why do we need plants?

4. Their utility as prototypes or models for synthetic drugs possessing physiologic activities similar to the originals



Salicylic Acid

Aspirin



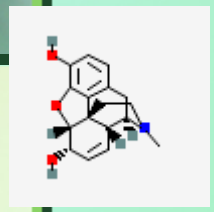
Ibuprofen

Why do we need plants?

5. Some natural products contain compounds that demonstrate little or no activity themselves but which can be modified by chemical or biological methods to produce potent drugs not easily obtained by other methods

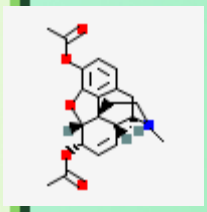
Baccatin III → **Taxol**

6. Source of compounds to use as templates for designing new drugs



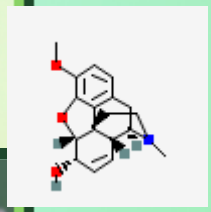
Morphine:

No better painkiller. Once structure worked out wanted to improve it. What is required?



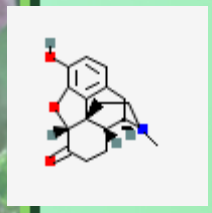
Diacetylmorphine (heroin):

OH group -> O-O-diacetyl. Still addictive?



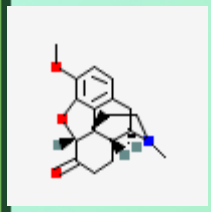
Codeine:

Methylate hydroxyl phenolic; O-Me. 1/5 analgesic capacity of morphine, useful to suppress cough reflex



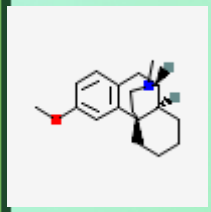
Dihydromorphinone:

Reduced =, oxidised 2y alc. Potential analgesic.



Dihydrocodeine:

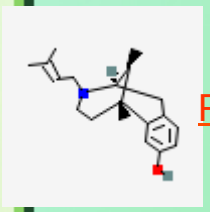
Me-ether of previous. More powerful than codeine, less than morphine.



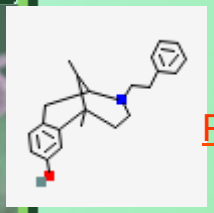
Dextromethorphan:

Good against cough reflex

Is lower ring necessary?

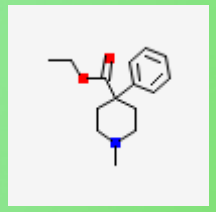


Pentazocin

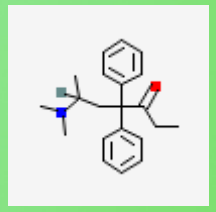


Phenazocine

Is middle ring needed?



Pethidine

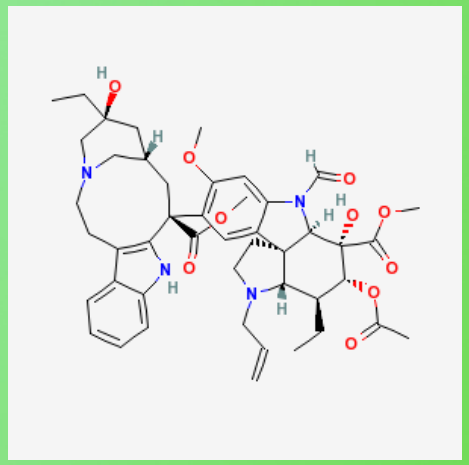


Methadone

Why do we need plants?

- 7. Source of novel structures
  - these might never be thought of

Catharanthus periwinkle -> vincristine (alkaloid dimer)



Why do we need plants?

- 8. Source of plant drugs
  - As a powder or extract
  - The pure compound is often not isolated because:
    - » Active ingredient is unknown
    - » Active ingredient is unstable
    - » Isolation process is too costly

- 250,-500,000 species of higher plants on earth
- <10% investigated and only for one activity
- Huge potential in plant kingdom

Future: intense screening

» Anticancer - NCI
» Antimicrobial
» Antiviral
» Antimalarial
» Insecticidal
» Hypoglycaemic
» Cardiotonic
» Antiprotozoal
» Antifertility - WHO

Herbal Remedy

- The term «herbal remedy» is used to describe a marketed product, whereas «herbal ingredient» refers to an individual herb that is present in a herbal remedy.
- «Herbal costituent» is used to describe a specific chemical constituent of a herbal ingredient. Thus, as examples, Valerian tablets are a herbal remedy, Valerian or Valeriana officinalis is a herbal ingredient, and valtrate is a herbal constituent of Valerian.

Future

80% world population rely on natural remedies

- Westernization of societies
  ('traditional' knowledge)
- Extermination of species
  - » conservation, retain gene pools
- Natural resources exhausted
  - » cultivation, artificial propogation

Conclusion

- Natural products;
- are very important to medicine
- exist in range of structures that one wouldn’t think of synthesizing
- can act as templates for new drug development
- untapped reservoir of new compounds

How do herbs differ from conventional drugs?

- While many conventional drugs or their precursors are derived from plants, there is a fundamental difference between administering a pure chemical and the same chemical in a plant matrix.
- It is this issue of the advantage of chemical complexity which is both rejected by orthodoxy as having no basis in fact and avoided by most researches as introducing too many variables for comfortable research.

How do herbs differ from conventional drugs?

- Herein lies the fundamental difference between the phytotherapist, who prefers not just to prescribe chemically complex remedies but often to administer them in complex formulations, and the conventional physician who would rather prescribe a single agent.
- Synergy is an important concept in herbal pharmacology. In the context of chemical complexity, it applies if the action of a chemical mixture is greater than the sum of the individual parts.
- One herbal medicine can be used for several diseases which is not the case for conventional drugs (at least one drug for each illness).

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