Drug Chemistry and Technology Basics,
Cleaner Production and Mega-Trends in Pharmaceutical Industry

Introduction

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Literature Sources

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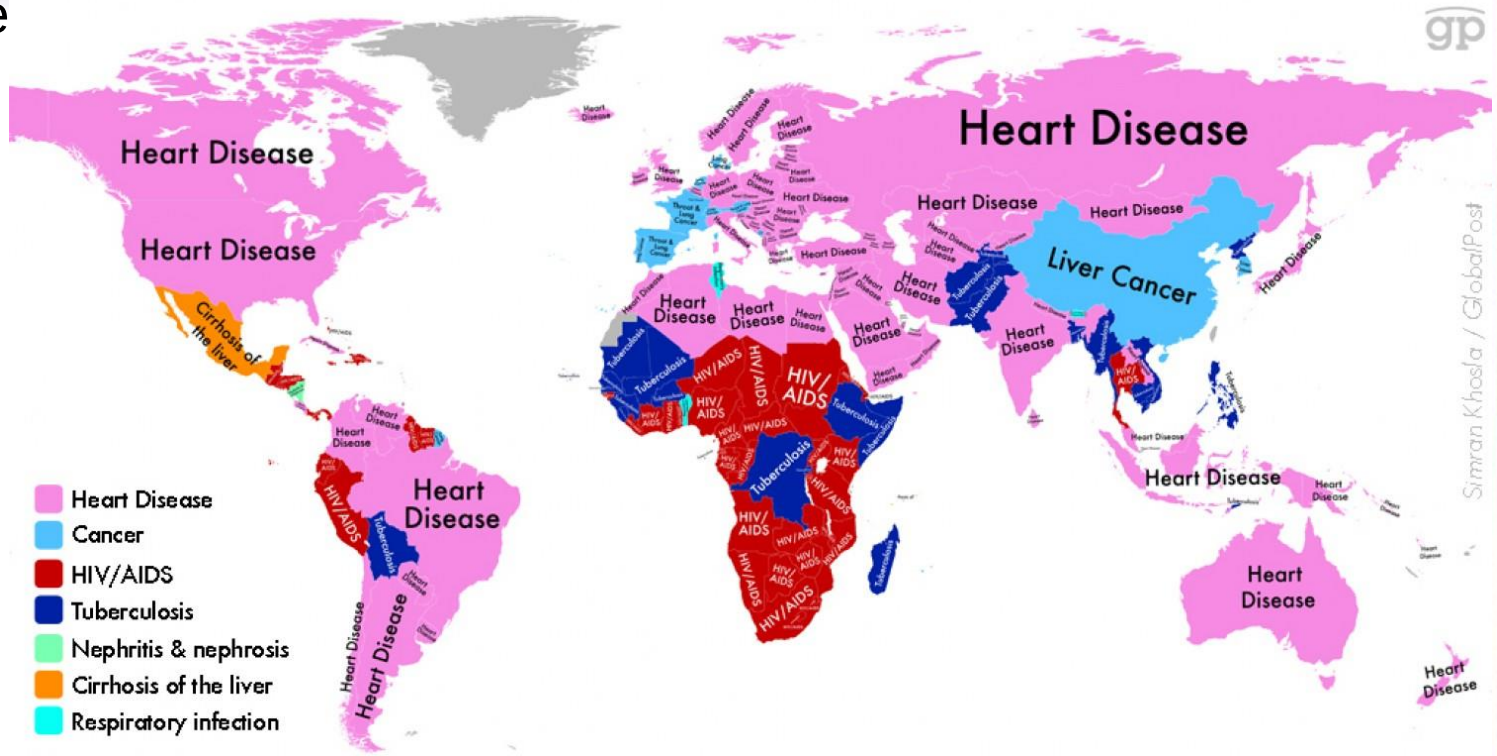
LECTURES

1. Introduction
2. Terminology of Drugs
3. Drug Design and Quality Standards
4. Falsification of Medicines
5. Quality Assurance in Medicines
6. Control by Pharmacopeias
7. *Trends in Pharmaceutical Industry

The Most Common and Dangerous Diseases

- heart disease
- malignancy
- diabetes
- HIV/AIDS
- malaria
- tuberculosis
- lung disease
- viral hepatitis



- infectious diseases of the digestive system
- nervous system disease
- *rare (orphan) disease (any disease that affects a small percentage of the population, most genetic, e.g. cystic fibrosis (mucoviscidosis), phenylketonuria)

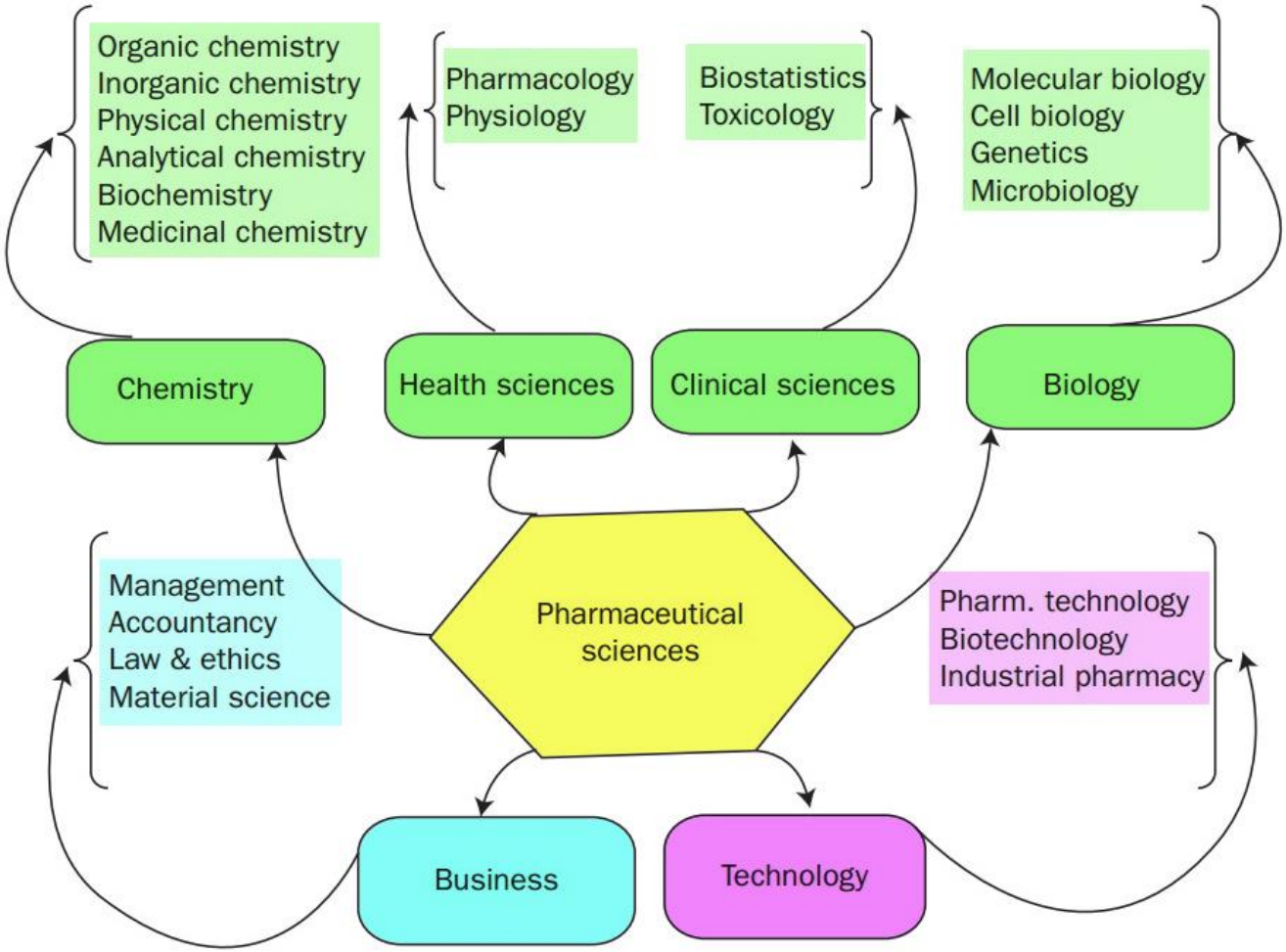
The Most Common and Dangerous Diseases

One new market in the U.S. and European economies is **geriatrics**

People are becoming increasingly old, while at the same time healthcare spending is increasing with age. Thus, there are many new medicines under development that specifically aim at treating older people, targeting diseases such as:

- ✓ diabetes,
- ✓ rheumatoid arthritis,
- ✓ **Alzheimer's,**
- ✓ **Parkinson's disease,**
- ✓ depression,
- ✓ gastrointestinal disorders,
- ✓ osteoporosis,
- ✓ bladder/kidney disorders

The Multidisciplinary Nature Of Pharmaceutical Sciences



The Core Functionality Of Pharmaceutical Sciences

Drug discovery	Chemistry, biochemistry, biology, microbiology, biotechnology, biostatistics
Drug delivery	Pharmaceutics, pharmacokinetics, drug analysis, biomaterials
Drug action	Toxicology, molecular biology, pharmacology, pharmacodynamics, biochemistry
Clinical studies	Clinical sciences, biostatistics, medical sciences
Regulatory affairs	Law, ethics, pharmacy
Manufacturing	Chemistry, industrial pharmacy, engineering
Quality control	Analytical sciences, microbiology
Drug costing	Accounting
Drug promotion	Medical sciences, business management, commercial art
Marketing & sales	Communication, marketing, management

Pharmaceutical Research and Development (R&D)

The pharmaceutical industry is research-based

Since the first blockbuster pharmaceutical, ***cimetidine (*****antiulcer drug*****)****, was launched by GlaxoSmithKline in the 1970s, both industry and regulators have been convinced that the "****blockbuster model" for the industry*** *was the long-term way forward: drug discovery and development was known to be high risk, expensive and time consuming, and that after patent expiry, generic manufacture would dramatically reduce the price of novel pharmaceuticals. However, new 'blockbuster' pharmaceuticals would continue to be invented at regular intervals and the profits made during their patent life would be more than sufficient to fund the necessary R&D for future products. Thus, the industry as a whole would continue to deliver innovative pharmaceuticals which would be available to all at low prices after a short patent life*

Blockbuster drug – a drug that has made more than US$1 billion/year

Pharmaceutical Technology

Pharmaceutical Technology – the application of scientific knowledge or technology to pharmacy, pharmacology, and the pharmaceutical industry

It includes methods, techniques, and instrumentation in the manufacture, preparation, compounding, dispensing, packaging, and storing of drugs and other preparations used in diagnostic and determinative procedures and in the treatment of patients

Pharmaceutical Technology

The pharmaceutical industry uses different technologies, such as **freeze drying, spray drying,** and **sublimation**, to formulate fast dissolving or mouth dissolving tablets

There is a new dosage form under development called **chronotherapeutic technology**, which would control drug release according to circadian rhythms and the timing of the symptoms of certain diseases, such as ulcers, asthma, and cardiovascular disease

Needleless injections are possible through technology, an engineering process by which scientific needs are met

Needle-free Injection Technology

Pharmaceutical Economics

Pharmaceutical economics, also known as **pharmacoeconomics**, deals with supply and demand of pharmaceutical products, as well as the cost-benefit evaluation of new and existing drugs

Primary concerns of the field include expanding drug accessibility, reducing the price of drugs and improving the cost-effectiveness of new drug therapies

The pharmaceutical industry is based on research, technology, investors, and ethics, and is the most profitable industry in the world

The pharmaceutical **R&D** accounts for 10% of the total cost of overall healthcare costs in the USA; other costs include **the services of physicians**, **hospital care**, and **administration**

Health Technology Assessment (HTA) and Pharmacoeconomics

Health technology assessment is the systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies

The Modern Market Of Medicines

- Bayer (*Germany*)
- Teva (*Israel*)
- Takeda (*Japan*)
- Pfizer (*USA*)
- Merck & Co (*USA*)
- Sanofi-Aventis (*France*)
- AstraZeneca (*Britain, Sweden*)
- GlaxoSmithKline *(United Kingdom)*

- Novartis (*Switzerland*)
- Hoffmann-La Roche (*Switzerland*)
- Gedeon Richter (*Hungary*)

The Modern Market Of Medicines

New Opportunities for Drug Development in China

Chinese manufacturers are very strong in their ability to copy foreign drugs, sometimes selling them under the foreign label

Almost 99 percent of the 3,000 pharmaceutical products manufactured in China are *copies of foreign products*, either legal generics or illegal counterfeits

It is important to note that R&D in China is a trend in the beginning. Many more R&D collaborations and institutes will be set up to make use of the vast gene pool in China (for clinical trials)

Drug Discovery and Development in India

Indian pharmaceutical companies' entry into the drug discovery and development field dates back to the early 1990s when India announced the signing of the World Trade Organization (WTO) agreement

Over the past few years, Indian pharmaceutical companies have been attempting to re-orientate their efforts toward developing *new innovative medicines*. However, the transition by Indian *generic-drug makers* will remain slow given the high risk levels associated with drug discovery

In Belarus

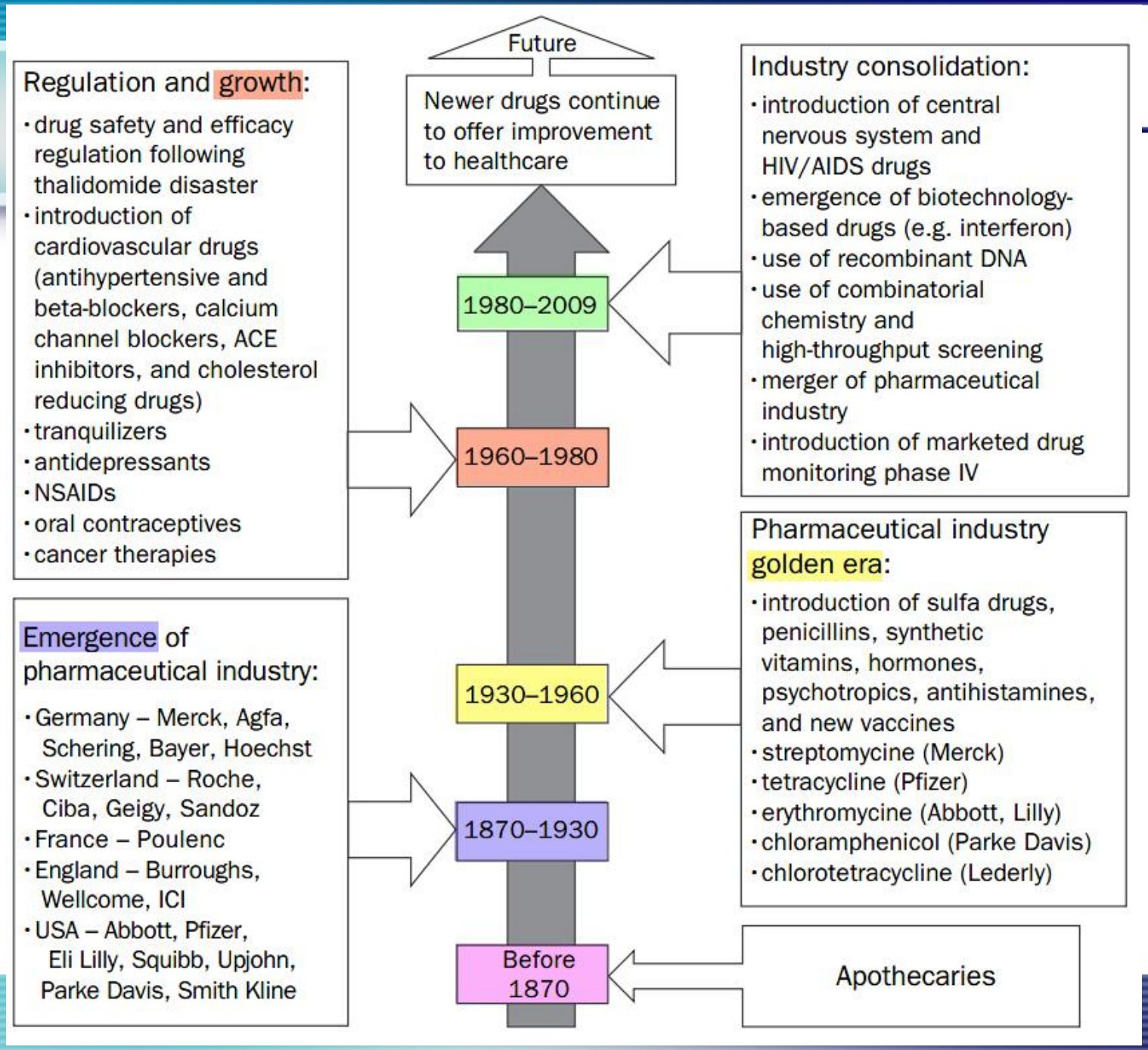
The main features of the development of the Belarusian pharmaceutical market:

I. expanding the range of manufactured drugs (mainly **generics**) for the treating of population with standard medicines against major widespread diseases with the aim of **increasing the share of Belarusian medicines** in the domestic market

II. focus on modernization of pharmaceutical companies, the transition to the constant and widespread use of international quality standards **GMP (Good Manufacturing Practice)**

III. the high level of **import drugs** in the pharmaceutical market (Germany, India, France, and others)

IV. Belarusian producers of drugs in general are focused on the domestic market, the bulk of the export of pharmaceutical products is sent to the CIS countries


Future
Newer drugs continue to offer improvement to healthcare
Regulation and growth:
• drug safety and efficacy regulation following thalidomide disaster
• introduction of cardiovascular drugs (antihypertensive and beta-blockers, calcium channel blockers, ACE inhibitors, and cholesterol reducing drugs)
• tranquilizers
• antidepressants
• NSAIDs
• oral contraceptives
• cancer therapies
Industry consolidation:
• introduction of central nervous system and HIV/AIDS drugs
• emergence of biotechnology-based drugs (e.g. interferon)
• use of recombinant DNA
• use of combinatorial chemistry and high-throughput screening
• merger of pharmaceutical industry
• introduction of marketed drug monitoring phase IV
1980–2009
1960–1980
Pharmaceutical industry golden era:
• introduction of sulfa drugs, penicillins, synthetic vitamins, hormones, psychotropics, antihistamines, and new vaccines
• streptomycine (Merck)
• tetracycline (Pfizer)
• erythromycine (Abbott, Lilly)
• chloramphenicol (Parke Davis)
• chlorotetracycline (Lederly)
Emergence of pharmaceutical industry:
• Germany – Merck, Agfa, Schering, Bayer, Hoechst
• Switzerland – Roche, Ciba, Geigy, Sandoz
• France – Poulenc
• England – Burroughs, Wellcome, ICI
• USA – Abbott, Pfizer, Eli Lilly, Squibb, Upjohn, Parke Davis, Smith Kline
1930–1960
1870–1930
Before 1870
Apothecaries

200 Years of Medicine

Antimicrobial Resistance

What is Drug

Drug (WHO) – Any substance or product that is used or intended to be used to modify or explore the physiological system or pathological state for the benefit of the recipient

Pharmaceutical drug (also a medication or medicine) – chemical substance used to treat, cure, prevent, or diagnose a disease or to promote well-being

The Apothecary or The Chemist by Gabriël Metsu (c. 1651–67)

Classifications of Drugs

Drugs can be classified in different ways according to:

– their mode of action

– their indications

– their chemical structure etc.

Each classification system will have its advantages and limitations and it usefulness will depend on the purpose, the setting used and the user's knowledge of the methodology

Classifications of Drugs

1. **by therapeutic use – nosological classification** (e.g., antidepressants)
2. **by pharmacologic profile** (e.g., selective serotonin reuptake inhibitors)

   Most texts use a combination of therapeutic and pharmaceutical classifications

3. **by chemical structure**
4. **Anatomical Therapeutic Chemical (ATC)** classification

   Don't confuse it with Anatomical Therapeutic (AT) classification developed by European Pharmaceutical Market Research Association (EPhMRA)

ATC Main Group

- A Alimentary tract and metabolism
- B Blood and blood forming organs
- C Cardiovascular system
- D Dermatologicals
- G Genito urinary system and sex hormones
- H Systemic hormonal preparations, excl. sex hormones and insulins
- J Antiinfectives for systemic use
- L Antineoplastic and immunomodulating agents
- M Musculo-skeletal system
- N Nervous system
- P Antiparasitic products, insecticides and repellents
- R Respiratory system
- S Sensory organs
- V Various

Structure of ATC Code

- **A** ALIMENTARY TRACT AND METABOLISM

(1st level, anatomical main group)

- A**10** DRUGS USED IN DIABETES

(2nd level, therapeutic subgroup)

- A10**B** BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS

(3rd level, pharmacological subgroup)

- A10B**A** BIGUANIDES

(4th level, chemical subgroup)

- A10BA**02** METFORMIN

(5th level, chemical substance)

Classifications of Drugs

5. **legal classifications of drugs** (these classifications are broken down based on their potential for abuse and if they have a legitimate medical use) (*Schedules I, II, III, IV, V of FDA*)

6. **original drugs** and **generics** (marketed after the expiry date of the patent for original drugs)

7. **allopathic** (suppress symptoms) and **homeopathic** (cause symptoms in a very small extent) drugs

Classifications of Drugs

8. **Commercial production of medicinal product** – a finished dosage form of a pharmaceutical product that has undergone all stages of manufacture, including packaging in its final container and labelling

and

Extemporaneous compounding – constructed into a drug individual chemical components that is usable by an individual patient (made by pharmacists at the pharmacy)

Nomenclature of Drugs

Most of drugs are known under **different names**

The number of such synonyms can reach more than 100:

Aspirin – **360**

Paracetamol – **413**

Ascorbic acid – **more than 430**

Why it is so?

Nomenclature of Drugs

Drug Names

Chemical
based on IUPAC nomenclature

Nonproprietary
OR
Generic Name
OR
Approved Name
OR
Official Name

Proprietary
OR
Brand Name
OR
Trade Name
OR
Commercial

International Nonproprietary Names

International Nonproprietary Names (INN) identify pharmaceutical substances or active pharmaceutical ingredients

Each INN is a unique name that is globally recognized and is public property

A nonproprietary name is also known as a **generic name**

The INN system is managed by the **World Health Organization (WHO)**

International Nonproprietary Names

The INN is issued by the WHO **for**:

- ✓ Active substance, NOT product
- ✓ International, NOT country-specific
- ✓ Non-proprietary, NOT company-specific

The INN has **important roles**:

✓ Allows doctor and other healthcare professionals to identify an active substance regardless of:

(i) which country(s) they currently practices and (ii) which company manufactures the product for that country

✓ Allows the global exchange of healthcare information

INN Lists

- ✓ New INNs are published in **WHO Drug Information**: 2 proposed and 2 recommended lists every year in English, French, Spanish and Latin
- ✓ All INNs are published in a **cumulative list** with additionally INNs in Arabic, Chinese and Russian
- ✓ About 8500 INNs have been published **http://www.who.int/medicines/services/inn/publication/en/index.html**
- ✓ On-line INN information**:** **Mednet – INN Extranet**

Comparison Of Naming Standards

International Nonproprietary Name (INN)	paracetamol (en) paracetamolum (la)
British Approved Name (BAN)	paracetamol
United States Adopted Name (USAN) United States Pharmacopeia (USP)	acetaminophen
Japanese Accepted Name (JAN) Japanese Pharmacopoeia (JP)	acetaminophen
Other generic names	acetamol
Proprietary names	panadol
IUPAC name	N-(4-hydroxyphenyl)acetamide
ATC code	N02BE01

Sources for Drugs

1

Minerals

- ✓ **iron is used in treatment of iron deficiency anemia**
- ✓ **mercurial salts are used in syphilis**
- ✓ **zinc oxide paste is used in wounds and in eczema**

Sources for Drugs

2

Tissues and organs of animals

- ✓ **insulin**
- ✓ **thyroid hormones medications**
- ✓ **enzyme preparations**

Insulin manufacture in the 1920s. beef pancreas is sorted and fed into a mincer

Sources for Drugs

3

Plants

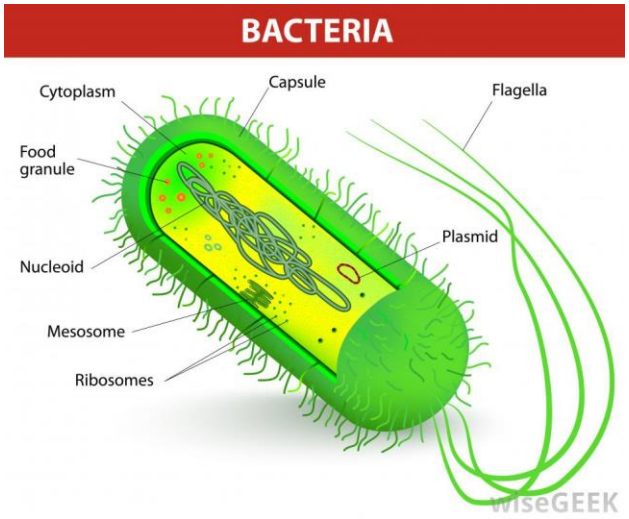
- ✓ **cardiac glycosides (*digitoxin* etc.)**
- ✓ **morphine**
- ✓ **reserpine**
- ✓ **atropine**

Sources for Drugs

4-5

Microorganisms

- ✓ **antibiotics: *penicillins, cephalosporins, macrolides* etc.**
- ✓ **hormones (*cortisone, prednisolone, insulin*)**



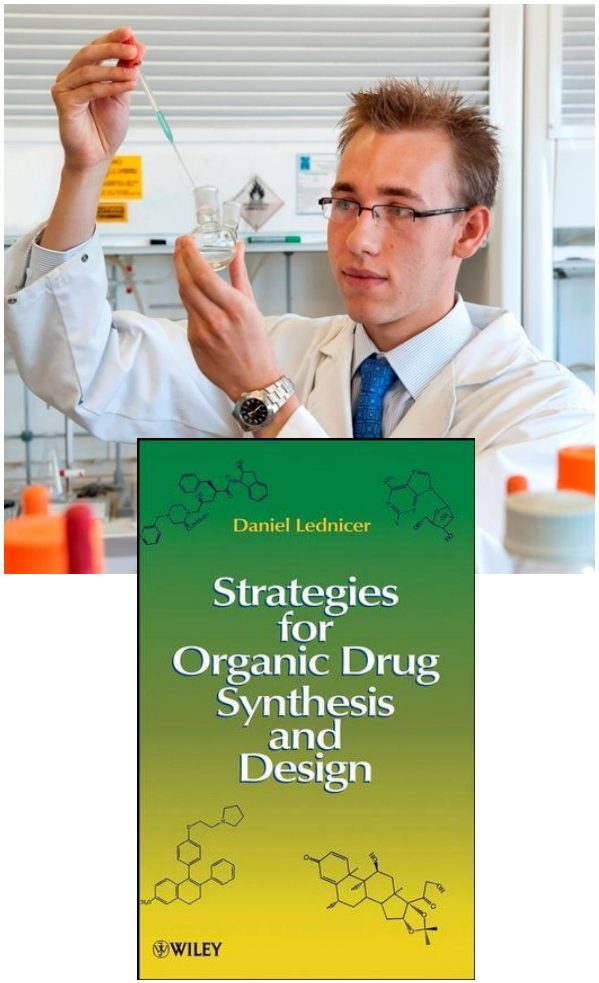
Recombinant bacteria are bacteria that have undergone genetic engineering. This means their DNA has been altered by the introduction of new DNA. Such bacteria have been of immense value in biological research, and for industrial and environmental uses.

Sources for Drugs

6

Chemical synthesis

- ✓ **sulfonamides**
- ✓ **acetaminophen**
- ✓ **acetylsalicylic acid**



Sources of Drugs

Thank You !

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