

History of Pharmacology

Ancient Medicine

- Chinese medicine is the earliest and records dated about 2500 B.C. available today give an idea about the medical knowledge of Chinese.
- In Chinese medicine, the use of Ephedra or *Ma huang* as a tonic has been reported.
- Ayurveda or Indian Medicine is equally ancient. To form the science of life namely Ayurveda, Charaka, Sushruta and Vaghbhata (the great three classics) made a compilation of old and new drugs in the cure of diseases.
- The *Charaka Samhita* is believed to have arisen around 400-200 BCE. This work is considered a redaction of an older and more voluminous work of *Agnivesha Samhita* (46,000 verses). *Dridhabala*, living about 400 A.D, is believed to have filled in many verses of missing text (perhaps up to 20%). The language of Charaka is Sanskrit and its style is poetry, with meter and melody to serve as a memory aid. Most of their theoretical edifice concentrates on the branch of Ayurveda called ***Kayachikitsa*** (internal medicine), largely based on the theory of the internal fire - of digestion - or internal medicine, in modern terms.

The Sushruta Samhita presents the field of Ayurvedic surgery (Shalya). This branch of medicine arose in part from the exigencies of dealing with the effects of war. *Ashtanga Sangraha* and *Ashtanga Hridayam* are the work of a person named Vaghbhata.

- Egyptian medicine is also very ancient. The *Ebers Papyrus* (a kind of medical encyclopaedia) dated about 1500 B.C. gives a collection of drugs prevalent in Egypt at that time, their classification and their use. Some of the drugs employed now such as, castor oil and pomegranate bark are mentioned in this papyrus.

Fig. 1

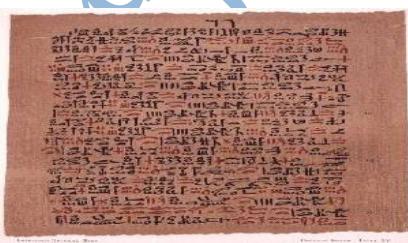


Fig. 2

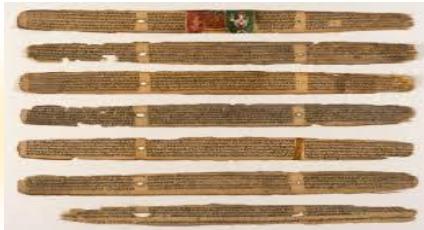


Fig. 1: *Ebers papyrus*: prescription for asthma treatment. (Source: U.S. National Library of Medicine/National Institutes of Health)

Fig. 2: Palm leaves of the *Sushruta Samhita* or *Sahottara-Tantra* stored at Los Angeles County Museum of Art (Source: http://collections.lacma.org/sites/default/files/remote_images/piction/ma-31972784-.jpg)

Pre-Christian Era

- Greek medicine is said to be the origin of modern medicine and therapeutics. *Hippocrates* in fifth century B.C. separated medicine from religion and was known as the **father of medicine**.
- He laid down certain principles on which modern medicine is built. According to *Hippocrates* the four elements of nature namely water, fire, air and earth gave rise to the four humors of the body namely blood, phlegm, yellow bile or urine and black bile. Any imbalance in one or more of these humors inflicted sufferings.
- **Galen** (*Aelius Galenus or Claudius Galenus*) was a famous Greek physician, surgeon and philosopher in the Roman Empire who practiced in Rome. In Galen's view, an imbalance of each humor (the bodily liquids) corresponded with a particular human temperament (blood—sanguine/cheerful, black bile—melancholic/pensive sadness, yellow bile—choleric/bad-tempered or irritable, and phlegm—phlegmatic/calm). Among Galen's major contributions to medicine was his work on the circulatory system. He was the first to recognize that there are distinct differences between venous (dark) and arterial (bright) blood. His name is still used to refer some drugs as *galenical drugs*. He was the **father of polypharmacy** (the concurrent use of multiple medications).
- Galenical drugs are pharmaceuticals compounded by mechanical means, mostly of the vegetable material.

Mediaeval Medicine

- Paracelsus introduced inorganic chemicals like mercury into medicine. He called this '*Iatro Chemistry*' or medicinal chemistry.
- He induced practitioners to use *laudanum* (an opium preparation), Sulphur, Iron, Copper Sulphate, Potassium Sulphate, Mercurial, tinctures and fluid extract of various plants for treatment of diseases.

Revols in Medicine

- By the beginning of 19th century the principle of shotgun prescription flourished (Shotgun prescription is one that contains a number of substances with no therapeutic efficacy. It is a result of ignorant attempt to cure the disease, no matter what may be its nature).

- Gregory advocated methods like venesection, leeching emetics and drastic purgatives. Large doses of purgatives were given. The patient either survived or died. This sort of symptomatic treatment was referred to as allopathy meaning 'other suffering'. This term allopathy is now being used to refer modern medicine.
- Samuel Hahnemann introduced homeopathy meaning 'similar suffering' at the commencement of 19th century. In Greek, "homos" means same and "patheia" means suffering. He was known as the father of homeopathy. Homeopathy introduced by him had two newer principles that 'like cures like' and 'dilution potentiates the action of drugs'.

Modern Medicine

- Buccheim, a professor of Dorpat University who was known as the father of Pharmacology set up the first laboratory to study pharmacology. He discarded many remedies because rational scientific action or explanation could not be demonstrated in his laboratory.
- By the middle of the 19th century, modern medicine had brought to fight disease only one effective weapon i.e. immunization against smallpox.
- Later in quick succession came the anesthetics and antiseptics. In the last quarter, the causative organisms for malaria, plaque, cholera etc. were identified.
- Beginning in the 20th century, the fresh wind of synthetic chemistry began to revolutionize the pharmaceutical industry and with it the science of pharmacology.
- New synthetic drugs, such as barbiturates and local anesthetics, began to appear and the era of antimicrobial chemotherapy began with the discovery of arsenical compounds for the treatment of syphilis by Paul Ehrlich in 1909. He was known as the father of chemotherapy.
- Further breakthroughs came with the discovery of sulphonamides by Gerhard Domagk in 1935 and the development of penicillin during world war II.
- The addition of drugs to the therapeutic jungle is growing with rapid pace from the latter half of the 20th century

Scope of Pharmacology

- Pharmacology is the science which involves all aspects of the action of drugs on living system. It is the study of the therapeutic value and/or potential toxicity of chemical agents on biological systems. It targets every aspect of the mechanisms for the chemical actions of both traditional and novel therapeutic agents.
- Important and interrelated areas are: pharmacodynamics and pharmacokinetics.
- Pharmacodynamics is the study of how drugs act on the body while pharmacokinetics is the study of how the body acts on drugs. Pharmacodynamic and pharmacokinetic aspects of the action of chemical agents are applicable to all related areas of study, including toxicology and therapeutics.
- Toxicology is the study of the adverse or toxic effects of drugs and other chemical agents. It is concerned both with drugs used in the treatment of disease and chemicals that may present household, environmental, or industrial hazards.
- Therapeutics focuses on the actions and effects of drugs and other chemical agents with physiological, biochemical, microbiological, immunological, or behavioral factors influencing disease. Each of these areas is closely interwoven with the subject matter and experimental techniques of physiology, biochemistry, cellular biology, microbiology, immunology, genetics, and pathology. The ultimate goal of Pharmacology is to design chemical agents to cure, ameliorate, or prevent disease.

Branches of Pharmacology

- **Neuropharmacology** is the study of neurophysiological or neurobiochemical functions of the nervous system including the brain, spinal cord, and the nerves that are modified by drug action.
- **Cardiovascular pharmacology** concerns the effects of drugs on the heart, the vascular system, and those parts of the nervous and endocrine systems that participate in regulating cardiovascular function.
- **Molecular pharmacology** deals with the biochemical and biophysical characteristics of interactions between drug molecules and those of the cell. It is molecular biology applied to pharmacology and toxicology.
- **Biochemical pharmacology** is the study of action of drugs and drug metabolism, how drugs interact with, and influences, the physiology of the organism.
- **Behavioral pharmacology** studies the effects of drugs on behavior of organism. It includes topics such as the effects of psychoactive drugs on the phenomena of learning, memory, wakefulness, sleep and the behavioral consequences of experimental intervention in enzyme activity and brain neurotransmitter levels and metabolism.
- **Endocrine pharmacology** is the study of drugs that are either hormones or hormone derivatives, or drugs that may modify the sections of normally secreted hormones.
- **Clinical pharmacology** is the application of pharmacodynamics and pharmacokinetics to patients with diseases, it also includes pharmacogenetic component. Clinical pharmacologists study how drugs work, how they interact with the genome and with other drugs, how their effects can alter the disease process, and how disease can alter their effects. Clinical trial design, the prevention of medication errors, and the optimization of rational prescribing are critical components of clinical pharmacology.
- **Chemotherapy** is the area of pharmacology that deals with drugs used for the treatment of microbial infections and malignancies. Chemotherapeutic agents selectively inhibit the growth of, or kill, the infectious agent or cancer cell without seriously impairing the normal functions of the host.
- **Toxicology** is the science of adverse effects of chemicals/ drugs on living systems. It also includes problems of drug safety, effects of drug over dosage.

- **Pharmacy** is a separate discipline in the health sciences. It is the profession responsible for the preparation, dispensing and appropriate use of medication, and provides services to achieve optimal therapeutic outcomes.

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Terms & Definitions

Pharmacology Related Terms

- **Pharmacology** is the science that embraces the knowledge of the history, source, physical and chemical properties, compounding, biochemical and physiological effects, mechanism of action, absorption, distribution, biotransformation and excretion of drugs. It is also defined as an experimental science dealing with the properties of drugs and their effects on living system.
- **Pharmacodynamics** is the study of the biochemical and physiological effects of drugs and their mechanism of action. It is the response of the organism to the action of a drug in the absence of a disease. Pharmacodynamics is 'what the drug does to the body'.
- **Pharmacokinetics** is the study of the actions of the drugs in the body over a defined period of time. It deals with the absorption, distribution, biotransformation and excretion of the drug. Pharmacokinetics is 'what the body does to the drug'.
- **Pharmacometrics** is the study of the techniques used in the measurement of drug effects to the administered dose of drug.
- **Pharmacogenetics** is the study of genetically determined variations in animals that are revealed by the effect of drugs.
- **Pharmacogenomics** This term describes the use of genetic information to guide the choice of drug therapy on an individual basis.
- **Pharmacoepidemiology** is the study of drug effects at the population level. It is concerned with the variability of drug effects between individuals in a population and between populations.
- **Pharmacoconomics** aims to quantify in economic terms the cost and benefit of drugs used therapeutically.
- **Pharmacy** is the science that deals with the preparation, formulation, manufacture, standardization, preservation and dispensing of drugs. The term pharmacy also indicates the place where drugs are dispensed or sold.
- **Pharmacognosy** is the study of the source of drugs. It also deals with the physical and chemical properties of drugs.

- **Materia Medica** is an obsolete didactic subject that was concerned with pharmacy, posology (the part of medicine concerned with dosage), pharmacognosy and indications for therapeutic use of the drug.
- **Metrology** is the study of weights and measures as applied to the preparation and administration of drugs.
- **Chronopharmacology** is the study of how the effects of drugs vary with biological timing and endogenous periodicities.
- **Pharmacovigilance** is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.
- **Pharmacoepidemiology** is the study of the use of and the effects of drugs in large numbers of people.

Drug Related Terms

- **Drug** is any chemical agent except food that is used to promote or safeguard the health of human beings or animals. It is also defined as any substance or product that is used or intended, to be used to modify or explore physiological systems or pathological states for the benefit of the recipient. The word drug is derived from a French word ‘Drogue’ meaning a dry herb.
- **Over the counter drugs** are those preparations that can be sold without any prescription because they can be adequately labeled for layman use.
- **Prescription drugs** are drugs that can be used only on the order of a licensed veterinarian/physician/dentist/surgeon based on a prescription. They are also known as legend drugs.
- **Essential drugs** are agents that satisfy the healthcare needs of majority of the population. They should therefore be available at all times in adequate amounts and in appropriate dosage form.
- **Pro-drugs** are drugs that are inactive or have a low order of activity in the form administered and are metabolized to the active form in the body.
- **Hard drugs** are drugs used for non-medical purposes that are liable to disable the individual seriously as a functioning member of the society by inducing severe psychological and/or physical dependence. e.g. Heroin

- **Soft drugs** are drugs used for non-medical purposes that are less dependence producing. There may be psychological dependence but not physical dependence, except with heavy dose. e.g. Amphetamine.
- **Nootropic drugs** are drugs that affect the intellect. These drugs are claimed to enhance learning, increase brain resistance to stress including hypoxia and stimulate brain metabolism especially in senile patients. e.g. Piracetam
- **Orphan drugs** are drugs or biological products useful for diagnosis/treatment/prevention of a rare disease condition for which there is no reasonable expectation that the cost of developing and marketing it will be recovered from the sales of that drug. E.g. Acetylcysteine. These drugs may be life saving for some patients, but are not commercially available.
- **Placebo** is a vehicle for cure by suggestion and is surprisingly often successful though only temporarily. It can be used as a control in scientific evaluation of drugs and to benefit or please a patient not by pharmacological actions but by psychological means (Latin: *Placebo* – I shall be pleasing or acceptable). Placebo reactor is an individual who report changes of physical and mental state after taking a pharmacologically inert substance.

Dose Related Terms

- **Dose of the drug** is an estimate amount of a drug, that when administered by a particular route to a certain species is most likely to produce a certain intensity of response. It is the quantity of medication to be administered at one time. Dosage is the determination and regulation of doses.
- **Possology** is the study of the medicine dosages, which varies with the species of animals, the intended effect of the drug and the individual tolerance or susceptibility.
- **Loading dose** is one or a series of doses that may be given at the onset of therapy with the aim of achieving the target concentration rapidly.
- **Maintenance dose** is a series of relatively small doses that follow the loading dose in order to maintain an effective concentration in the bio-phase.

Sources of Drugs

Plant Sources of Drugs

- Many drugs available from plants are even today used in the treatment of pathological conditions.
- With the increasing tendency for the use of alternate medicine, this source has gained more importance in the recent past.
- The pharmacological activities of plants are attributed to certain active principles in plants. They are - Alkaloids, Glycosides, Oils, Tannins, Saponins, Resins, Gums etc.

Alkaloids

- Alkaloids are nitrogenous substances obtained from various parts of the plant. Alkaloids containing oxygen are solids and comparatively non-volatile (cocaine) while those that do not contain oxygen are liquids and volatile (nicotine, lobeline and coniine).
- Alkaloids are insoluble in water while their salts (atropine sulphate, caffeine citrate) are soluble in water.
- Alkaloids are bitter to taste. They are incompatible with the alkalis, tannic acid and heavy metals.
- Alkaloids represent the waste products of plant metabolism and their names end with 'ine'.
- Alkaloids should be administered in small quantities and when given in excess they may produce death without much postmortem changes for diagnosis. (Adrenaline is considered as animal alkaloid)

Glycosides

- Glycosides are non-nitrogenous substances obtained from plants.
- The glycosides on hydrolysis yield two molecules namely a sugar molecule and a 'genine' or 'aglycone' molecule.
- Sugar helps in the dissolution of the preparation while the pharmacological action rests with the 'aglycone'.
- When the sugar molecule is glucose, the glycoside is known as glucoside.
- Cardiac glycosides digitalis, strophantus and squill play a major role in the treatment of congestive cardiac failure.

- Cyanogenetic glycoside is one in which hydrocyanic acid is released on glycolysis



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