- **Dosage form design**

Drug:

- Agent intended for use in diagnosis, mitigation, treatment, cure, or prevention of disease in humans or animals.
- ***New drugs*** derived from plant or animal sources, or as by-products of microbial growth, or through chemical synthesis, molecular modification, or biotechnology.

- The process of drug discovery is complex.
- It need scientific specialists: **organic**, **physical**, and analytical chemists; **biochemists; molecular biologists; bacteriologists**; **physiologists; pharmacologists; toxicologists; hematologists; immunologists; endocrinologists; pathologists; biostatisticians; pharmaceutical scientists; clinical pharmacists; physicians**; and many others.

- After discover new drug it undergoes:

1. **chemical and physical** characterization.
2. **biologic** effect must be gathered.
3. **Basic pharmacology**.
4. **mechanism of action** .
5. **toxicologic** features.

6-Drug site and rate of **absorption**.

7-**distribution** and concentration within body.

8-**Duration** of action.

9-Rate of **elimination**.

10-Metabolic degradation and activity of any of metabolites must be obtained.

Study :

1. **Short and long-term effects of drug** on body cells, tissues, and organs.
2. **Efffect of drug on fetus of pregnant animal** or its ability to pass to a nursing baby through breast milk of its mother.

3. Many new drug has been removed because it cause high adverse effects.

- **4-Effective routes of administration** (e.g., oral, rectal, parenteral, topical).
- **5- dosages recommended** for varying ages (e.g., neonates, children, adults, geriatrics), **weights**, and **states of illness** .

- **It has been said that the only difference between a drug and a poison is the dose.**

dosage forms formulated :

tablets, capsules, injections, suppositories, ointments, aerosols,.

- Each dosage units contain specified quantity of medication for accuracy of dosage administration.

In addition to **active ingredients**, a pharmaceutical formulation contains number of **non therapeutic ingredients**.

Pharmaceutical ingredients:

- Fillers.
- Thickeners.
- Solvents.
- suspending agents.
- tablet coatings.
- **Disintegrants**.
- **penetration enhancers**.
- **Stabilizer**.
- **Preservatives**.
- **Flavors**.
- **Colorants**.
- **sweeteners**.

To ensure stability of drug in formulation:

- **Chemistry**.
- **physical pharmacy**.
- **Microbiology**.
- **pharmaceutical technology** applied.
- The formulation must be such that all components are **physically and chemically compatible**, including **active** therapeutic agents, the **pharmaceutical ingredients**, and **packaging materials**.

Formulation must be

1. **preserved against decomposition** due to chemical degradation.
2. **protected from microbial contamination** and destructive influences of excessive **heat, light**, and **moisture.**
3. Drug must **released from dosage form** in proper quantity .
4. possess **attractive flavor, odor, color**, and texture .
5. product must be **effectively packaged.**
6. **completely labeled according to legal** regulations.

- The medication must be taken in
- **sufficient quantity**,
- **specified intervals**,
- **duration** .
- The effectiveness of medication should be reevaluated at regular intervals dosage, regimen, schedule.
- **side effects** should be evaluated and decisions made as to the continuance, adjustment, or major change in drug therapy.

Before taking medication:

- side effects
- foods, beverages, and/or other drugs may **interfere with effectiveness** of medication.
- effectively uses medication,
- patient monitoring.

THE HERITAGE OF PHARMACY

- **When the drug discovered?**
- **Drugs, existed as long as humans**.
- The use of drugs, began long before recorded history, for **primitive man to relieve pain** of wound by bathing it in **cool water** or by soothing it with a **fresh leaf** or protecting it with **mud**.
- early humans learn that certain therapy was more effective than others, from these beginnings came the practice of drug therapy.

THE FIRST APOTHECARY

- History: knowledge of drugs and application to disease meant **power**.
- Successes attributed to

1. **Experience**,
2. **Appropriate drug selection**,
3. **Natural healing**.
4. **Effect of drug**.
5. **Placebo effects**.

- Even today, placebo therapy with inert chemicals is used successfully to treat individual patients in which subjects' responses to actual drug and placebo are compared and evaluated.

- As time passed, early civilizations, the **priest-magician or priest-physician became the healer of the body as well as of the soul.** Pharmacy and medicine are indistinguishable .

EARLY DRUGS

- The most famous **Ebers papyrus**:

60 feet long and a foot wide dating to **16th century** BC. This document, now preserved at University of Leipzig, named for German Egyptologist Georg Ebers, who discovered it in the **tomb of a mummy** and partly translated it during the last half of the **19th century**.

hieroglyphics,

- **1550 BC**, Egyptians used some drugs and dosage forms that are still used today.

- The text of the Ebers papyrus contains more than **800 formulas** being described and more than **700 drugs**.

- **Numerous ancient tablets**, scrolls, **3000 BC .**
- The drugs are **botanical**, **mineral** and **animal** drugs noted.
- 1- botanical substances as **acacia**, **castor** bean and **fennel** .
- 2-minerals as **iron oxide, sodium carbonate, sodium chloride, and sulfur.**
- **3-**Animal excrements were also used in drug therapy.

- The vehicles; beer, wine, milk, and honey.

- **Egyptians** used **mortars and pestles**, **hand mills**, **sieves**, and **balances** in their compounding of **suppositories**, **gargles**, **pills**, **inhalations**, **troches**, **lotions**, **ointments**, **plasters**, and **enemas**.

INTRODUCTION OF THE SCIENTIFIC VIEWPOINT

- Hippocrates, a Greek physician
- His works included **hundreds** of drugs.
- **pharmakon** mean **purifying remedy** for good only.

- his work in medical science ,teachings that become a part of modern medicine, Hippocrates called **Father of Medicine**.

EARLY RESEARCH

- Swede Karl Wilhelm Scheele (1742-1786), most famous of all pharmacists because of his discoveries.; **lactic acid, citric acid, oxalic acid, tartaric acid, and arsenic acid**.

- 1- He identified **glycerin**,
- 2- invented new methods of preparing **calomel and benzoic acid**,
- 3- discovered **oxygen.**

- **The isolation of morphine from opium by German pharmacist Friedrich Sertürner.**

- examples of **drugs isolated from natural source**

1. **Paclitaxel** with antitumor activity derived from Pacific yew tree employed in treatment of metastatic carcinoma of ovary.
2. **digoxin,** a cardiac glycoside, from Digitalis lanata.

DRUG STANDARDS

- **uniform standards to ensure quality**. This need led to the development and publication of monographs and reference books.

- Organized sets of monographs or books of standards are called pharmacopeias or formularies.

THE UNITED STATES PHARMACOPEIA AND THE NATIONAL FORMULARY

- **The term pharmacopeia comes from the Greek pharmakon, meaning drug, and poiein, meaning make**,
- and the combination **indicates any recipe or formula or other standards required to make or prepare a drug.**
- The term was first used in **1580** in Italy.

- In Great Britain,

1. **London**.
2. **Edinburgh**.
3. **Dublin**.

were official until 1864, when they were replaced by **British Pharmacopoeia** (BP).

- **American pharmacopeia** was -called Lititz Pharmacopeia.
- It was a 32-page booklet containing information on **84 internal** and **16 external** drugs and preparations.

- In 1808, the **Massachusetts** Medical Society published a **272-page** pharmacopeia containing information or monographs on **536 drugs** and pharmaceutical preparations.
- Included monographs on many drugs in America, which were not described in European pharmacopeias.
- **In 1872 synthesis of salicylic acid** from phenol , the synthesis of group of analgesic compounds including acetylsalicylic acid (**aspirin**), which was introduced into medicine in 1899.
- National Formulary (NF) on June 30, 1906,

- Before 1940, NF, like USP, revised every 10 years.
- After that date, new editions appeared every 5 years, with supplements issued.
- The first combined USP XX and NF XV, became official on July 1, **1980**.

products and preparations

- “**products**” refer to **manufactured drugs**
- “**preparations**” to **compounded drugs**.

USP AND NF MONOGRAPHS

- **The USP and NF adopt standards for drug substances**
- **Chemical Abstracts Service** (**CAS**).
- The CAS registry number **identifies each compound**.

OTHER PHARMACOPEIAS

- **Homeopathic Pharmacopeia of the United States (HPUS).**
- **International Pharmacopeia (IP).**
- Homeopathy from Greek **homoios, mean similar, and pathos, mean disease.**
- the basis of homeopathy is **law of similars**, or **like cures like**: that **is, a drug that produces symptoms of illness in healthy persons will also be capable of treating those same symptoms and curing the disease.**

- Embodied in homeopathic approach are :
- (1) **test drug on healthy persons** to find the drug's effects so that it may be employed against same symptoms in ill person.
- (2) use only minute doses of drugs in dilutions expressed as “1×” (a 1:10 dilution), “2×” (a 1:100 dilution), and so on;.
- (3) administration of one drug at a time.
- (4) treatment of entire symptom complex of patient, not just one symptom.

- **International Organization for Standardization** (ISO)
- **quality control (QC),**
- **quality assurance (QA)**
- **quality management (QM),.**
- **World Health Organization (WHO).**
- American Pharmaceutical Association (APhA)

- In 1938 the new drug sulfanilamide :and distributed as elixir using the solvent diethylene glycol :diethylene glycol poisoning.

THE FEDERAL FOOD, DRUG, AND COSMETIC ACT 1938

- **FDA**: Food drug administration.
- Either **accept** or **deny** permission to **manufacture** and **distribute** a new product after reviewing data on product:

1. **Methods of assay.**
2. **Quality standards.**
3. **Formulation** and manufacturing processes.
4. Preclinical (animal, tissue, or cell culture). studies including pharmacology and toxicology
5. Clinical trials on human subjects.

- **OTC: non prescription drugs: sold without prescription.**

- thalidomide, recommended as a **sedative and tranquilizer**, was being **sold OTC** in Europe. 1960.
- apparent **lack of toxicity**
- Thalidomide given to women during pregnancy produced birth defects.
- A pharmaceutical company was awaiting FDA approval for marketing in the United States
- Some were born without arms or legs; others, with partially formed limbs. The more fortunate were born with only disfigurations of the nose, eyes, and ears.

- **investigational new-drug application** (IND) with the FDA before the drug may be clinically tested on human subjects.
- WHO now considers thalidomide to be the standard treatment for the fever and painful skin lesions associated with **erythema nodosum leprosum** (ENL) in patients with **leprosy**

COMPREHENSIVE DRUG ABUSE PREVENTION AND CONTROL 1970:

1. **Schedule I: Drugs with no accepted medical use**, with a high potential for abuse. **heroin**, **LSD**, **marijuana**
   (***Any nonmedical substance that is being abused)***.
2. **Schedule II**: **Drugs with accepted medical uses and a high potential for abuse. Lead severe psychological** or physical dependence **morphine**, **cocaine**, **methamphetamine**

3. **Drugs with accepted medical uses and a potential for abuse less than those listed in schedules I and II** that if abused may lead to **moderate psychologic** or physical dependence. **codeine, hydrocodone.**

4. **Schedule IV**: **Drugs with accepted medical uses and low potential for abuse.** lead to limited physical dependence or psychologic dependence . **diazepam**, **oxazepam.**

5. **Schedule V: Drugs with accepted medical uses and low potential for abuse** lead to limited physical dependence or psychologic dependence .

dihydrocodeine, diphenoxylate.

- 1979, United States FDA introduced **classification of fetal risks due to pharmaceuticals**. **risk versus benefit.**

The FDA-assigned pregnancy categories :

- **Category A:** Adequate studies **no risk to fetus in first trimester** (and no evidence of risk in later trimesters).
- **Category B:** Animal studies failed to demonstrate risk to fetus, and there are **no adequate and well-controlled studies in pregnant women.**
- **Category C:** Animal studies shown **adverse effect** on fetus and there are no adequate studies in humans, but potential benefits may **warrant use of the drug in pregnant women** despite potential risks.

- **Category D:** There is **positive** human **fetal risk** or **studies in humans**, **warrant use of drug in pregnant women** despite potential risks.

- **Category X:** Studies in **animals or humans** demonstrated **fetal abnormalities** :positive evidence of **human fetal risk**

- Every woman in the general population has a 3% to 5% risk of having a child with a birth defect or mental retardation.

MEDICATION EXPOSURES DURING PREGNANCY AND LACTATION

- Two factors consider when assessing teratogenic effect of medication:

1. **stage of pregnancy** at which the exposure occurred.
2. **Amount** of medication taken.

BLACK BOX WARNINGS

- Are the FDA's strongest labeling requirements for high-risk medicines.
- **abbreviated new-drug application (ANDA)**
- The FDA evaluates the **chemistry, manufacturing, control (CMC)** standards
- National Institutes of Health (NIH)
- The Center for Drug Evaluation and Research (CDER)

DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT OF 1994

- These products, include vitamins, minerals, amino acids, and botanicals, **legally are not considered drugs** if they have not been submitted for review on NDAs and thus have not been evaluated for safety and efficacy by the FDA. However, as with drugs, their safe use is a concern to the FDA.
- disclaimer must appear on the product: "**This product is not intended to diagnose, treat, cure, or prevent any disease.**"

- **The mission of FDA is to protect public health against risks associated with the production, distribution, and sale of food and food additives, human drugs and biologicals, radiologic and medical devices, animal drugs and feeds, and cosmetics.**

FDA

1. **Sets policies**, establishes standards, issues guidelines, and promulgates and enforces rules and regulations governing the affected industries and their products
2. **Monitors** for regulatory compliance through reporting requirements, product sampling and testing, and establishment inspections
3. **Establishes product labeling** requirements, disseminates product use and safety information, issues product warnings, and directs product recalls
4. Acts as the **government's gatekeeper** in making safe and effective new drugs, clinical laboratory tests, and medical devices .

DRUG PRODUCT RECALL

- Class I: the use of or exposure to a violative product will cause serious adverse health consequences or death.
- Class II: The use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or the probability of serious adverse health consequences is remote.
- Class III: The use of or exposure to a violative product is not likely to cause adverse health consequences.

- Bachelor of Science in Pharmacy (BS)
- the Doctor of Pharmacy (PharmD)
- RPh (registered pharmacist)
- American Association of Colleges of Pharmacy (AACP).
- (Master of Science [MS] or Doctor of Philosophy [PhD])
- The Board of Pharmaceutical Specialties (BPS)
- pharmacists serve as an expert source of drug information and participate in the selection, monitoring, and assessment of drug therapy.
- **“Clinical pharmacists”** participated with physicians in therapeutic decision making,

THE MISSION OF PHARMACY

- **Pharmacy** is health profession that concerns with the knowledge system that results in discovery, development, and use of medications
- **Medications** refers to legend and non legend agents used in the diagnosis, treatment, prevention, and/or cure of disease.
- Devices is equipment, process, biotechnological entities, diagnostic agent used to assist in effective management of medication regimen.
- Services refers to patient, health professional and public education services, screening and monitoring programs, that contribute to effective medication use by patients.

Code of Ethics for Pharmacists

- I. A pharmacist **respects the relationship** between the patient and pharmacist.
- II. A pharmacist promotes the good of every patient in a caring, compassionate, and confidential manner.
- III. A pharmacist **respects the autonomy and dignity** of each patient.
- IV. A pharmacist acts with honesty and integrity in professional relationships.
- V. A pharmacist maintains professional competence.
- VI. A pharmacist respects the abilities of colleagues and other health professionals.
- VII. A pharmacist serves individual, community, and societal needs.
- VIII. A pharmacist seeks justice in the distribution of health resources.