INDUSTRIAL PHARMACY-I

UNIT I-PREFORMULATION

CLASS1

TOPIC: Introduction to preformulation, goals and objectives, study of physicochemical characteristics of drug substances.

PREFORMULATION

It is defined as a phase of research and development process for an investigation of physical and chemical properties of a new drug substance alone or in combination with other excipients in order to develop safe and effective dosage form.

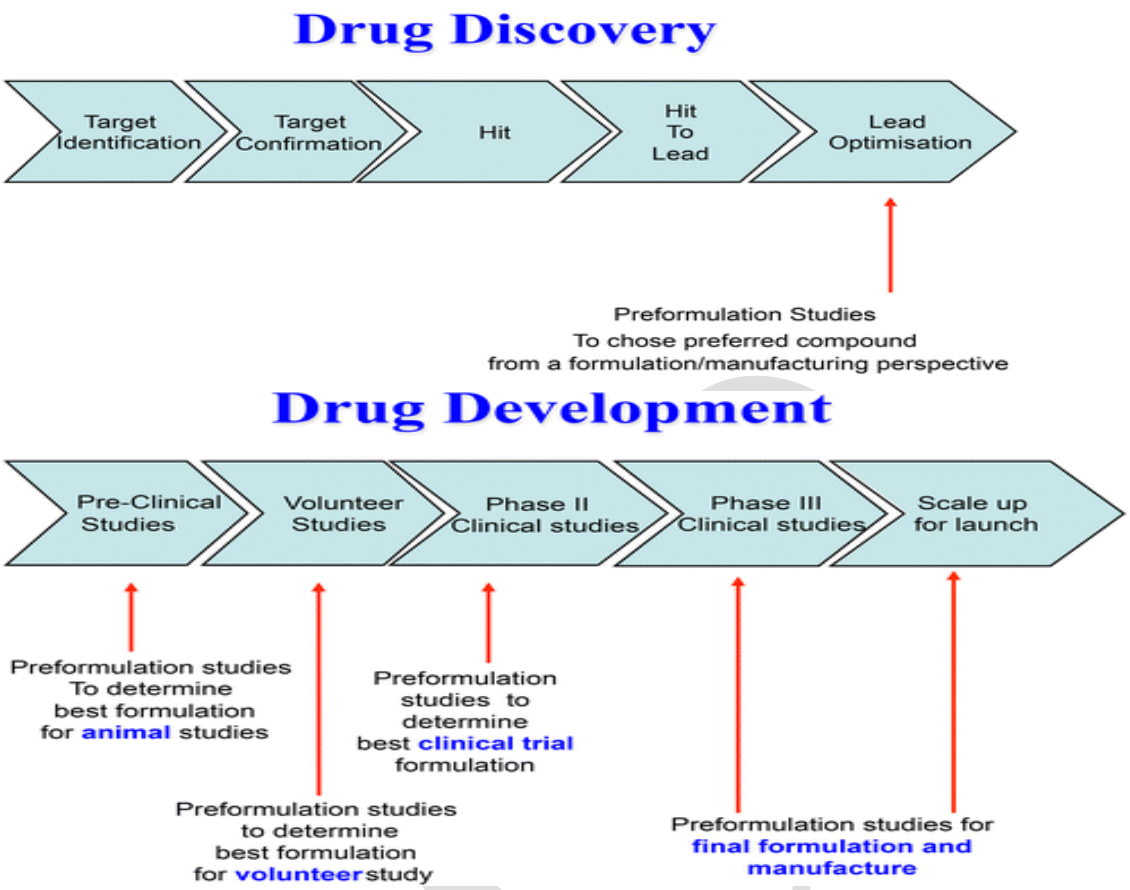
OBJECTIVES

The overall objective of preformulation testing is to generate information useful to the formulator

- ✓ To formulate stable and effective dosage form
- ✓ To increase drug stability
- ✓ To improve drug bioavailabilty
- ✓ Reduce drug-excipient incompatibility

APPLICATIONS

- ✓ It describes process of optimizing the delivery of drug through determination of physical, chemical properties of new drug molecule that affects drug performance and development of an efficacious stable and safe dosage form
- ✓ Provides rationale for drug design and molecular modification and biopharmaceutically stable and suitable dosage form



PRELIMINARY EVALUATION

Once pharmacological active compound has been identified,different project team have responsibility for assuring that compound enters into development process

Physical pharmacists obtain information on known properties of a compound,Medicinal chemist knows molecule weakness and various synthetic methods ,literature review is done to know stability and decay mechanisms.If any deficiency is detected then project team decide on molecular modification.For example salt form,prodrugs, solvates , polymorphs.

Salt formation:

Most salts of organic compounds are formed by the adddition or removal of proton to form ionized drug molecule which is then neutralized with counter ions.Organic salts are more soluble than unionized molecule,hence increases dissolution rate and bioavailability.

Br-,Cl-,I-,citrate,maleate etc are used as anions for salt formation

Ca,K,Na,Zn etc are used cations for salt formation

Ex: Ephedrine hydro chloride :addition of proton to the basic nitrogen atom on ephedrine resulting in a protinated drug molecule which is neutralized with chloride ion

Advantages

- Organic salta are more soluble than corresponding unionized molecule and offer a simple means of increased dissolution rate and bioavailability

Disadvantages

- Poor crystallinity
- Various degrees of salvation or hydration
- Instability due to unfavourable pH in crystalline micro environment

Prodrugs:

Prodrugs may be formed with any organic molecule having reactive functional group.

These are synthetic derivatives of drug molecule which on transformation yields active drug molecule.

Eg.,Erthromycin estolate is a prodrug which is inactive but when undergoes ester hydrolysis yields bioactive erythromycin

Amidon suggested water soluble prodrugs by adding selected aminoacids that are substrates for enzymes located in the intestinal brush border.

ORGANOLEPTIC CHARACTERS

❖ Colour,odour, taste of the new drug must be recorded

COLOUR	ODOUR	TASTE
Off-white	pungent	Bitter

Cream yellow	Acidic	Bland
tan	sulphurous	Intense
shiny	Fruity	Sweet
	Aromatic	Tasteless
	Odourless	

Once the optimum molecular form has been selected ,formulation development begins their task in development process.

Areas of preformulation:

1. Bulk characterization
   - Crystallinity
   - Polymorphism
   - Hygroscopicity
   - Micromeritic properties- particle characterization
     - Density and porosity
     - Powder flow properties
2. Solubility studies
   - solubility profile and common ion effect
   - pKa determination
   - effect of temperature
   - solubilisation
   - partition coefficient
   - dissolution
3. Stability studies
   - Solution stability
   - Solid state stability
   - Drug excipient compatibility