Department of Pharmacy GP (Uttawar)

DRUG INCOMPATIBILITY

(Pharmaceutics II)
Unit 2

DEFINITION

- It is the result of prescribing or mixing two or more substances which are antagonist in nature and an undesirable product is formed which may affect the safety, purpose or appearance of the preparation.

CLASSIFICATION

Incompatibility can be classified into three groups-

1) Pharmaceutical or physical incompatibility
2) Chemical incompatibility
3) Therapeutic incompatibility

Physical incompatibility and chemical incompatibility together we can say physico-chemical incompatibility.

PHYSICAL INCOMPATIBILITY:

Interaction between two or more substances which lead to change in color, odor, taste, viscosity and morphology.

- A visible physical change takes place
- An unacceptable, non-uniform, unpalatable product is formed.
- Difficult to measure an accurate dose.
- Can be corrected by applying pharmaceutical skill.

MANIFESTATIONS OF PHYSICAL INCOMPATIBILITY:

- Insolubility of prescribed agent in vehicle
- Immiscibility of two or more liquids
- Liquification of solids mixed in a dry state

1. Insolubility:

The following factors affect the solubility of prescribed agent in vehicle and may render it less soluble:

1. *Change in pH*
2. *Milling*
3. *Surfactant*
4. *Chemical reaction*
5. *Complex formation*
6. *Co-solvent*

Example of insolubility:

- *Benzalkonium chloride*
- *Sodium lauryl sulfate*

2. Immiscibility of two or more liquids:

- Incomplete mixing

Example: Flavoring agent such as orange oil, lemon oil or their alcoholic solution are added in aquous preparation they may not mix well and droplets of the oils may b float on the water surface. They make the solution turbid, having a hazy appearance.

3. LIQUIFICATION OF SOLIDS MIXED IN A DRY STATE:

It means that when two solid substances are mixed together, conversion to a liquid state take place.

Example: Certain low melting points solids when mixed together liquefy due to formation of eutectic mixtures, they form a soft mass when mixed together thus the physical integrity of the preparation may be lost. Ex- menthol, thymol, aspirin form eutectic mixture when two of them are mixed together.

CHEMICAL INCOMPATIBILITY

Chemical Incompatibility:

Reaction between two or more substances which lead to change in chemical properties of pharmaceutical dosage form.

- ***Types of chemical changes:***

1. Oxidation

2. Hydrolysis

3. Polymerization

4. Isomerization

5. Decarboxylation

6. Absorption of Carbon-di-oxide

7. Combination

8. Formation of insoluble complexes

Chemical incompatibility is two types:

1. Tolerated
2. Adjusted

CONSEQUENCES OF PHYSICO-CHEMICAL INCOMPATIBILITY

- We can detect these by our naked eyes.

a) Turbidity
b) Precipitation
c) Crystallization/crystal growth
d) Aggregation
e) Solidification
f) Discoloration
g) Thickening
h) Change in color, odor and tastes, etc.

THERAPEUTIC INCOMPATIBILITY:

Therapeutic incompatibilities are unintentional pharmacodynamic or pharmacokinetic interactions that take place in vivo after administration of medicinal products.

Example: Amine containing drugs are incompatible with mono amino-oxidase inhibitors.

CAUSES:

It may be due to the administration of :

- Overdose or improper dose of a single drug.
- Improper Dosage form.
- Contraindicated drug.
- Synergistic and antagonistic drugs

DIFFERENT KINDS OF DRUG INTERACTION

Mainly two types of drug interaction:

1) Pharmacodynamic interaction
2) Pharmacokinetic interaction

Other interactions:

- ✓ ***Drug - Drug interaction***
- ✓ ***Drug - Excipient interaction***
- ✓ ***Excipient - Excipient interaction***
- ✓ ***Drug - Food interaction***
- ✓ ***Excipient - Packaging interaction***

Pharmacodynamic Interaction:

Pharmacodynamic interactions are those in which drugs having similar or antagonistic pharmacological effects or side effects are administered concurrently and situation in one drug is altered by another. These are of two types-

1. Direct pharmacodynamic interactions.

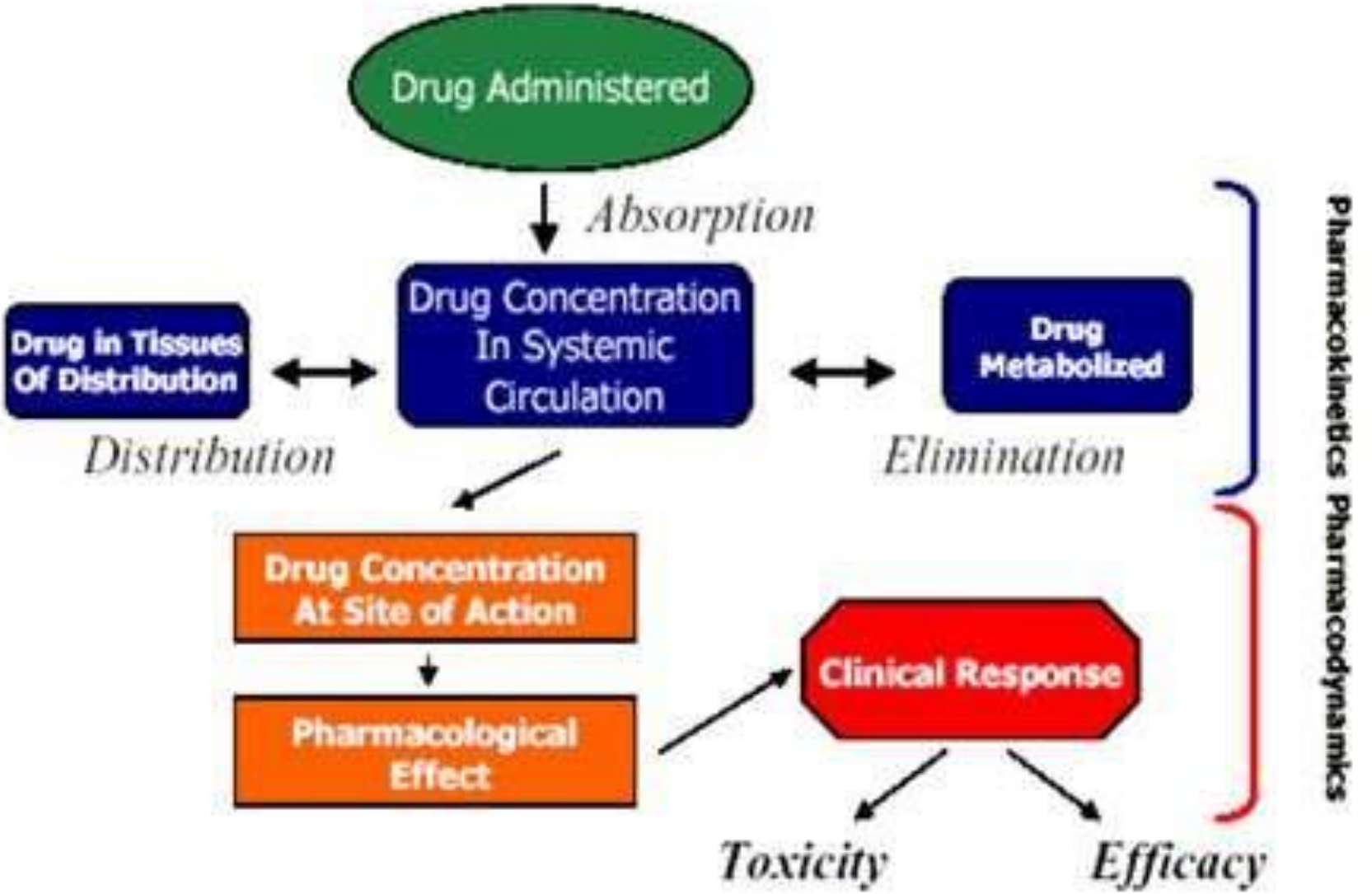
2. Indirect pharmacodynamic interactions.

Pharmacokinetic Interaction:

Pharmacokinetic interactions are those in which one agent alters the adsorption,distribution,metabolism and excretion of a second drug with a resultant change in the plasma concentration of the later agent.

There are some difference between Pharmacodynamic and pharmacokinetic interaction-

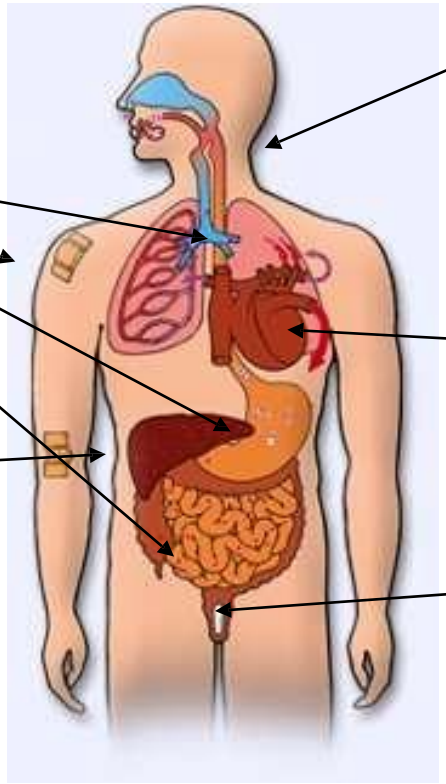
Pharmacodynamic vs. Pharmacokinetic



Pharmacokinetic interactions are classified as:

1. ***Absorption interactions***
2. ***Distribution interactions***
3. ***Metabolism interactions***
4. ***Excretion interactions.***

Drug absorption



Transport of the drug inside the body

Drug displacement (protein-binding)

Drug metabolism (biotransformation)

Drug excretion

DRUG-DRUG INTERACTION

- Drug-drug interactions occur when a drug interacts, or interferes, with another drug. This can alter the way of one or both of the drugs act in the body, or cause unexpected side effects.

- This action can be **synergistic** (when the drug's effect is increased) or **antagonistic** (when the drug's effect is decreased) or a new effect can be produced.
- Examples of this include the use of **codeine** with **paracetamol** to increase its analgesic effect. Or the combination of **clavulanic acid** with **amoxicillin** in order to overcome bacterial resistance to the antibiotic.

Table

IMPORTANT DRUG–DRUG INTERACTIONS	
Drug–Drug Interaction	**Potential Risk**
Amiodarone and haloperidol	This PK and PD interaction may cause arrhythmias
Bepridil and clarithromycin	PK and PD interaction may cause arrhythmias
Colchicine and clarithromycin	Colchicine toxicity
Conivaptan and ergot alkaloids	Ergot toxicity
Cyclosporine and ketoconazole	Cyclosporine toxicity
Cyclosporine and rifampin	Loss of immunosuppressive effect
Ramelteon and fluvoxamine	Ramelteon AUC increase over 100-fold
Simvastatin and ketoconazole	Statin toxicity
Sirolimus and clarithromycin	Marked increase in sirolimus levels with nephrotoxicity

AUC = area under the concentration curve; PD = pharmacodynamic; PK = pharmacokinetic.

More drug = More interactions

DRUG-EXCIPIENT INTERACTION

- Drug-excipient interaction occurs between the API and excipient materials.

  Example: Certain amine drugs (paracetamol) react with lactose (diluent) in the presence of Magnesium stearate to form brown color compound. This may cause darkening of the tablets and the integrity of the tablet maybe loss.

EXCIPIENT-EXCIPIENT INTERACTION

- This type of interaction occurs between two or more excipients in a drug molecule.

  Example: In proper addition of electrolyte such as- Ca++ or Mg++ ion in suspension containing sodium carboxymethyl cellulose (Na CMC) which will cause formation of Calcium/Magnesium CMC. The suspending agent will be destroyed and cannot perform its function.

DRUG-FOOD INTERACTION

- A drug-food interaction happens when the food we eat affects the ingredients in a medicine we are taking so the medicine cannot work the way it should. Example-

  1.Consumers taking **digoxin** for heart failure or ACE inhibitors for high blood pressure should be careful with salt substitutes, which most often replace sodium with potassium.

  2.Blood-thinning drugs such as **Coumadin®** (warfarin) interfere with vitamin K-dependent clotting factors. Eating too much green leafy vegetables, which are high in vitamin K, can decrease the ability of blood-thinners to prevent clotting.

Please share to your friends

Foods that may Affects Medication You Taking

Dairy Products

Coffee

Grapefruit Juice

Cokes

Alcohols

Tea

Charcoal-Broiled foods

Green Leafy Vegetables

Licorice

Ginseng

EXCIPIENT-PACKAGING MATERIAL INTERACTION

- In some pharmaceutical formulation excipient and packaging material may interact with each other and thus can cause ex-packaging interaction.

Example:

Many commercial glass products such as containers are made of soda-lime glass, and therefore have a substantial percentage of sodium ions in their internal structure. Since sodium is an alkali element, its selective removal from the surface results in a alkali leaching.

How TO Prevent Drug Interactions?

- We should tell our doctor about everything we are taking, including prescription drugs, OTC medications, vitamins and herbal supplements.
- We should read the consumer information sheet with our prescriptions and read it carefully.
- We should read the labels on OTC medications, paying special attention to the “Warnings”section.
- Before buying a new OTC medication, vitamin or herbal supplement, we should ask our pharmacist if there are any potential drug interactions with the prescriptions or not.


Thank you!