PHARMACEUTICAL INCOMPATIBILITIES

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Introduction

"It is defined as when two or more ingredients of a prescription are mixed together, the undesired changes that may takes place in the physical, chemical or therapeutic properties of the medicament is termed as incompatibility."

Classification of Incompatibility

3 classes of drug incompatibility

Physical incompatibility

Chemical incompatibility

Therapeutic incompatibility

Physical Incompatibility/ Pharmaceutical Incompatibility

- It is a evidence that failure of the drug combine properly.
- In physical incompatibility involves interaction between two or more substance which leads to change in colour, odour, taste, viscosity & morphology.
- It is a result of insolubility & immiscibility, precipitation, liquefaction, adsorption & complexation of solid materials.

Physical incompatibilities can be corrected by one or more methods viz.

- Order of mixing
- Alteration of solvents
- Changes in the form of ingredients
- Alteration of volume
- Accurate choice of emulgent & suspending agent
- Addition

Examples of physical incompatibilities

Immiscibility

Immiscibility is the result of the mixture of two or more immiscible liquids or an immiscible solids with liquid.

e.g. oil & water

Rectifying method...

- Vigorous shaking

Choice of emulgentor Solubilizing agents..

Examples of physical incompatibilities

Insolubility

Changes in pH, milling, surfactant, chemical reaction, co-solvent are the factors that affect the solubility.

- **e.g.** –if mucilage of acacia & alcohol are put together they form precipitation of acacia by the alcohol. For that reason acacia not be used with alcohol for mucilage preparation.
- In the suspension contains diffusible solids in that type of the suspension uses the thickening agents. If thickening agents are not used then particles settle quickly & dose cannot be maintained.

Chemical Incompatibility

- Chemical incompatibility is also called as immediate incompatibility.
- After compounding it shows immediate incompatibility.
- It occurs due to oxidation-reduction, acid base hydrolysis or combination reactions & those noticed by effervescence, decomposition, colour change.
- Chemical interaction occurs between the ingredients & a toxic & inactive product will beformed.

Examples of Chemical Incompatibility

Formation of precipitate

- Most alkaloid salts are soluble in water but alkaloidal bases practically insoluble in water & are freely soluble in organic solvents.

e.g. strychnine HCl aromatic spirit of ammonia purified water to 100ml

- In that case, strychnine HCl is an alkaloid salt & aromatic spirit of ammonia is an alkaline substance.
- Those, two insoluble mixture combine with each other that time forms the precipitate of strychnine.

In this case, strychnine HCl solution should be dissolved in half quty. of water & aromatic spirit of ammonia dissolved in the remaining quty. of water.

- Then mix both the mixture slowly.

Gas formation

- e.g. carbonates or bicarbonates with an acid or acidic drug resulting in the evolution of carbon dioxide.
- So those compounds compounded in open container to avoid explosion.

Colour Changes

- Colour changes due to changes in pH.
- It can be prevented by properly buffering the vehicle.

Ionic Reaction

- Many organic compounds associated with a large cation or anions.
- Interaction of such ions of opposing types may yield compound which may totally lack the useful properties of the interacting molecules.
- e.g. cream prepared using cationic emulgent may crack if mixed with a cream prepared using an anionic emulgent.

Therapeutic Incompatibility

• Therapeutic incompatibility is also called as drug interactions.

 In that modification of the therapeutic effect of one drug by the prior concomitant administration of another.

• It occurs due to when drug or excipients, which are antagonist to one another & are prescribed together.

- Also therapeutic incompatibility occurs due to following reasons viz...
- Overdose
- Wrong dosage form
- Contraindicated drug
- Drug interaction
- Wrong dosage form
- There are some drugs which have similar names.
- E.g. digoxin & digitoxin
- **Digitoxin** is a cardiac glycoside. It is a phytosteroid and is similar in structure and effects to **digoxin**(though the effects are longer-lasting). Unlike **digoxin**(which is eliminated from the body via the kidneys), it is eliminated via the liver, so could be used in patients with poor or erratic kidney function.

Contraindicating Drugs

- Some drugs are not prescribed for lactating mother because it will excrete into milk.
- E.g. Phenytoin, Phenobarbitone, Chloramphenicol etc.

Drug Interaction

- e.g. tetracycline is inactivated by the milk due to the presence of calcium.
- It forms insoluble complex with milk and not show any effect on systemic circulation.