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INCOMPATIBILITY

Definition

Incompatibility is defined as a change resulting and an undesirable product is formed, which may affect the safety, efficacy, appearance and stability of the pharmaceutical product.

Different types of incompatibility

1. Physical incompatibility
2. Chemical incompatibility
3. Therapeutic incompatibility

What is prescription incompatibility?

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.

Type # 1: Physical Incompatibility:

- Some physical properties of ingredients interfere in their coexistence. Pharmaceutical incompatibilities are usually of this type.
- The following physical properties of ingredients lead to this incompatibility:

Insolubility

When one or more ingredients are not soluble or poorly soluble in the vehicle e.g. Kaolin, calcium carbonate in aqueous solution.

Immiscibility

When two liquid ingredients in a preparation are not miscible e.g. Castor oil, liquid paraffin in aqueous solution.

Precipitation

When precipitation of one of the ingredients occurs e.g. volatile oils in aqueous solution if mixed with concentrated salt solution.

Liquefaction

When two solids are mixed together they may liquify e.g. Acetanilide, acetylsalicylic acid, phenacetin if mixed with resorcinol or urethane.

Examples of Physical Incompatibilities and their methods of correction:-

Immiscibility

Oil and water are immiscible with each other. They can be made miscible with water by emulsification .Example,

Rx

Castor oil - 15 ml

Water - 60 ml

Make an emulsion.

In this prescription castor oil is immiscible with water. To overcome this incompatibility an emulsifying agent is used to make a good emulsion.

Insolubility

In liquid preparation containing indiffusible solids such as chalk, aromatic chalk powder, acetyl salicylic acid, phenacetin, zinc oxide and calamine etc a suspending agent may be incorporated ,so as to increase the thickness of the preparation .It also helps to maintain uniform distribution of the insoluble substances for sufficient long time after shaking the bottle and facilitating uniform measurement of each dose. Example,

Rx

Phenacetin - 3 g

Caffeine - 1 g

Orange syrup -12 ml

water up to-90 ml

Make a Mixture.

In this prescription phenacetin is an indiffusible substance .Compound powder of tragacanth or mucilage of tragacanth is used as a suspending agent to make a stable suspension.

Precipitation

A drug in solution may be precipitated ,if the solvent in which it is insoluble is added to the solution e.g. resins are insoluble in water .When tincture containing resinous matter is added in water, resin agglomerates forming indiffusible precipitates .This can be prevented by slowly adding the undiluted tincture with vigorous stirring to the diluted suspension or by adding some suitable thickening agent.

Example :- Prepare and dispense 100 ml of the following lotion.

Rx

Tincture benzoin compound - 5.0 ml

Glycerin -15.0ml

Rose water in sufficient

quantity to make - 100ml

Tincture benzoin compound contain resins .The change in solvent system results in an unavoidable precipitate .Addition of tincture with rapid stirring yields a fine colloidal dispersion. So there is no need of any suspending agent.

Liquefaction

When certain low melting point solids are mixed together, a liquid or soft mass known as eutectic mixtures is produced. This occurs due to the lowering of the melting point of mixture to below room temperature .The medicaments showing this type of behavior are camphor, menthol, thymol, phenol, chloral hydrate and aspirin .These types of substances create problems when they are dispensed in powder form. These substances can be dispensed by any one of the following methods:-

1)Triturate together to form liquid and mixed with an absorbent like light kaolin or light magnesium carbonate to produce free flowing powder.

2) The individual medicament is powdered separately and mixed with an absorbent and then combined together lightly and filled in suitable container. example:-

Rx

Menthol-5 g

Camphor-5g

Ammonium chloride-30 g

Light magnesium carbonate-60 g

Make an insufflation.

In this prescription menthol, camphor and ammonium chloride get liquefied on mixing with each other .To dispense this prescription ,menthol, camphor and ammonium chloride are triturated together to form liquid .Add light magnesium carbonate and mix it thoroughly to make free flowing powder.

Type # 2. Chemical Incompatibility:

- Chemical incompatibility occurs when mixing two drugs changes the potency of their active ingredients. A drug that loses more than 10% of its potency when mixed with another drug is considered incompatible with that drug.

- This incompatibility involves some chemical interaction between the ingredients. There may be a chemical reaction, pH changes in dosage forms, interactions with preservatives or solvents in the dosage form, and combination of divalent cations with components of the mixture.

- Chemical incompatibility may be manifested in number of ways:

  - Precipitation,
  - Change in color,
  - Evolution of gas,
  - Gelatinization,
  - Inactivation without any visible change.

- It is an extremely bad practice to mix different drugs in the same syringe. Alkaloids, iodine, arsenic, iron, mercury and silver salts, salicylates, per-magnate, strong acids or alkalis and tannic acid are frequently incompatible with other agents and therefore should not be mixed, knowledge of incompatibility is useful as in the alkaloid poisoning, stomach lavage can be carried out with tannic acid or potassium per-magnate solutions or copper sulphate solution is administered in ingestion of phosphorus.

- In some cases chemically incompatible combinations are intentionally prescribed i.e. intentional incompatibility e.g. zinc sulphate and potassium sulphide are prescribed in Alba lotion (white lotion) to precipitate zinc sulphide which is the active agent used in the treatment of acne vulgaris. Chemical incompatibilities may involve different types of chemical interactions e.g. oxidation, reduction, hydrolysis etc.

Type # 3. Therapeutic (Pharmacological) Incompatibility:

- It occurs as a result of antagonistic (opposite) pharmacological effects in the patients or interfere with drug absorption following administration
- e.g., simultaneous administration of physostigmine and atropine in the eye. Physostigmine constricts the pupil, whereas, atropine dilates it.
- Incompatibility can also occur following oral administration.

- Antacids or dairy products will impair the absorption of tetracycline, whereas, kaolin will also produce similar effect when administered with erythromycin.

PHYSICAL & CHEMICAL INCOMPATIBILITY IMAGES