

# Drug formulation: Drug Leaching, Stabilizer, Binder and flesh colour enhancers



# Definition

- **Leaching:** It is the process of a solute becoming detached or extracted from its carrier substance.
- **Drug leaching:** It is the process of drug's active ingredient becoming detached from its carrier substance.

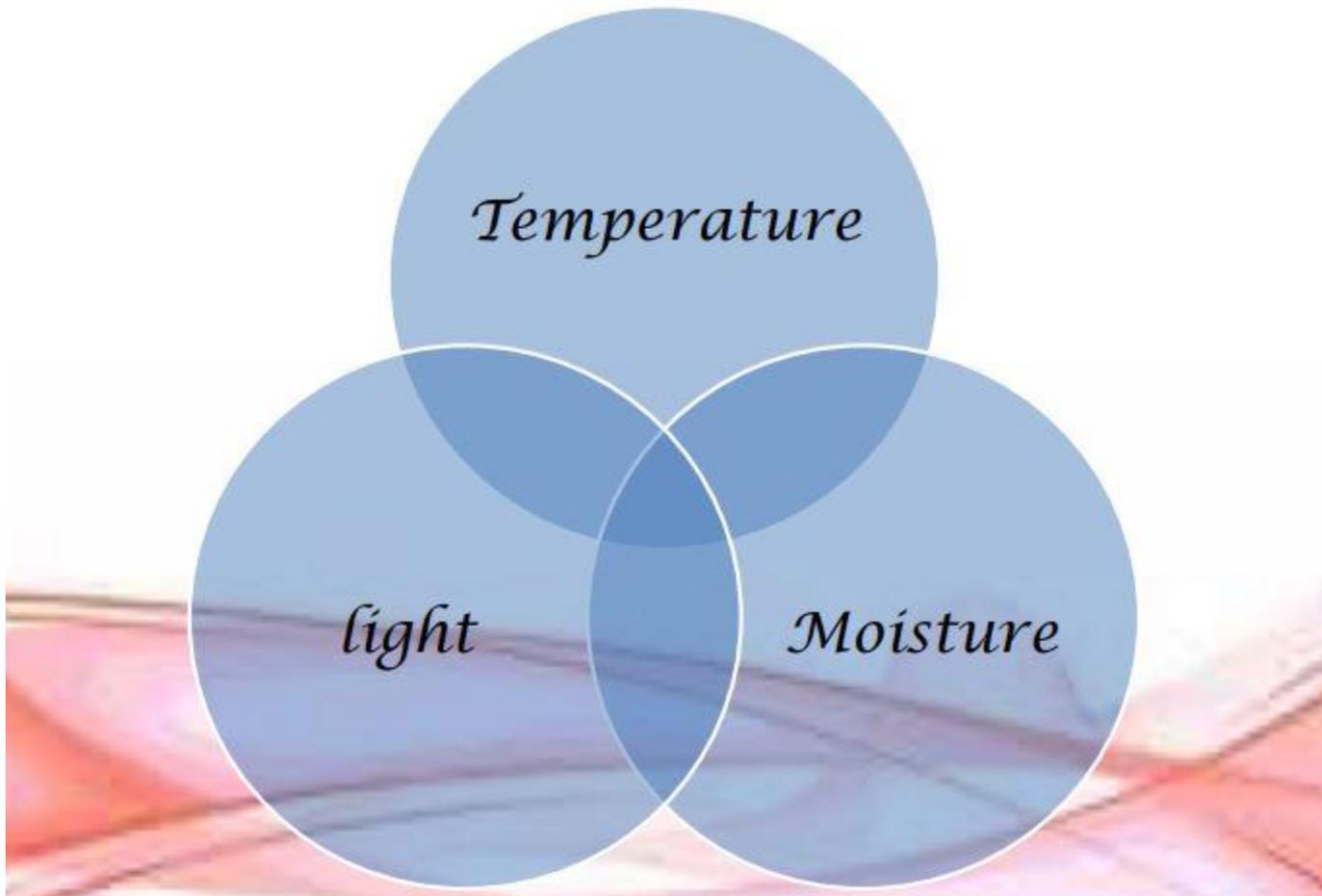
# Drug stabilizers

- **Drug stabilizers** are chemical agent which used to help the active pharmaceutical ingredient (API) maintain the desirable properties of the product until it is consumed by the patient.

## **Factors affecting drugs stability:**

1. Environmental factors
2. Microbial contamination
3. Containers and packaging

# *Environmental factors*



# Temperature

- 3 types of storage temperatures
- 1. Room temperature: 25- 30 oC
- 2. Cold temperature / Refrigerator storage: 2-8 oC
- 3. Freeze storage: -10 to -20 oC

# Light (photolysis)

- The shorter the wavelength more the energy is absorbed per mole.
- It means: decomposition of drugs by light.
- Various sources of light are sunlight, metal halide lamps, fluorescent lamps, or other indoor lighting sources.
- These reactions can be induced by exposure to photolysis sources emitting in the 290–800 nm.
- **Photolysis is prevented by:**
  - ❖ Suitable packing in amber colored bottles.
  - ❖ Aluminum foil wrappers.

# MOISTURE

- It enhances the hydrolytic degradation.
- Packing materials such as Glass and Plastic are usually chosen to prevent exposure of drug product to high humid conditions.

## Microbial Instability:

### Sources of microbial contamination

- ✓ **Water-** gram-negative groups : Pseudomonas, Xanthomonas, Flavobacterium.
- ✓ **Air-** Mold spores: Penicillium, Aspergillus
  - Bacterial spores: Bacillus spp.
  - Yeasts.
- ✓ **Raw materials-** Micrococci

# Packaging and Stability



## 1. Glass

- Glass is resistant to chemical and physical change and is the most commonly used material.

## 2. Plastics



- The problems with plastic are:
- Migration of the drug through the plastic into the environment.
- Transfer of environmental moisture, oxygen, and other elements into the pharmaceutical product.
- Leaching of container ingredients into the drug.
- Adsorption of the active drug or excipients by the plastic

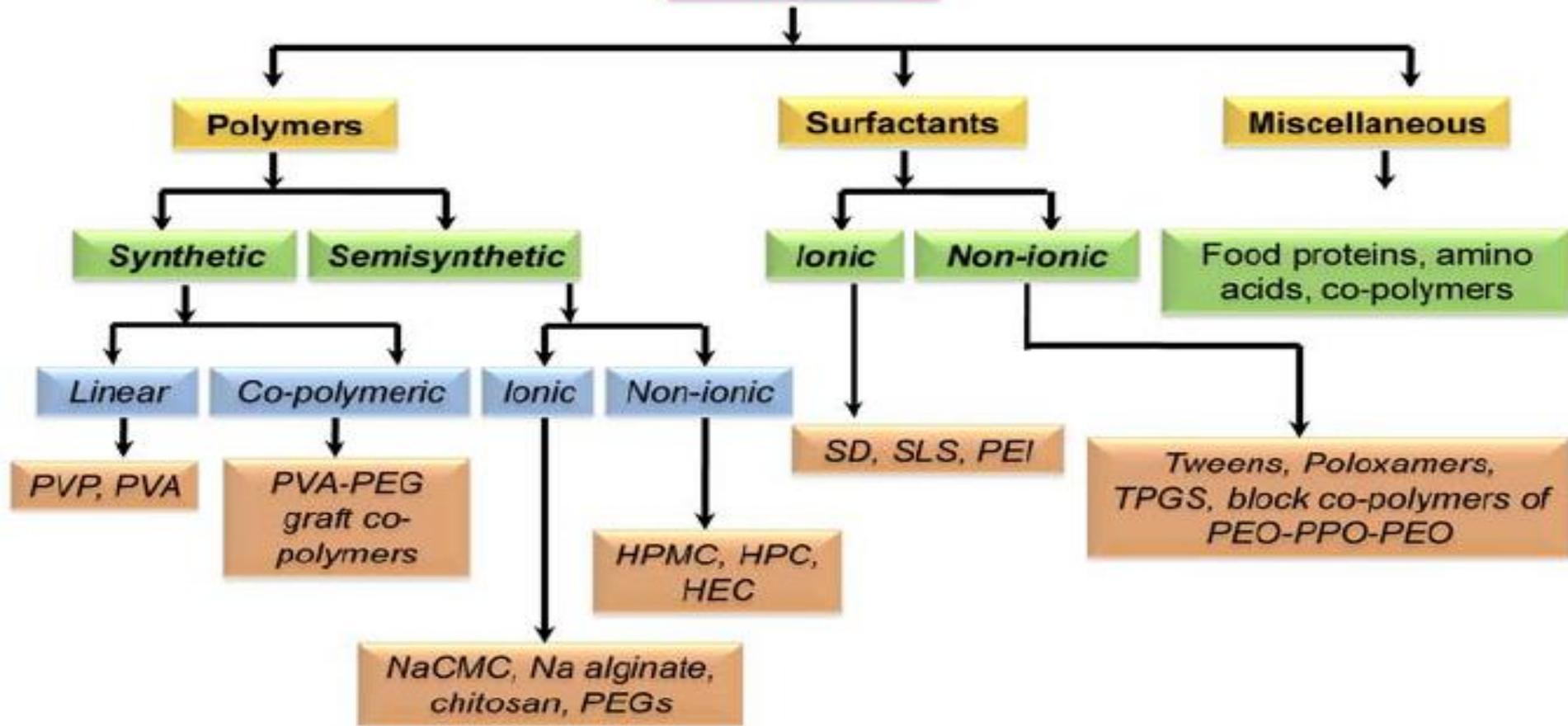
### 3. Metals:

- Various alloys and aluminum tubes may be utilized as containers for emulsions, ointments, creams and pastes.
- **Limitation:** They may cause corrosion and precipitation in the drug product.
- **Overcome:** Coating the tubes with polymers may reduce these tendencies.

### 4. Rubber:

- Rubber also has the problems of extraction of drug ingredients and leaching of container ingredients.

# Stabilizers



PVP (Povidone), PVA (Polyvinyl alcohol), PEG (Polyethylene glycol), HPMC (Hypromellose), HPC (Hydroxypropyl cellulose), HEC (Hydroxyethyl cellulose), NaCMC (Carboxymethylcellulose sodium), SD (Docusate sodium), SLS (Sodium lauryl sulfate), PEI (Polyeethylene imine), TPGS (D- $\alpha$ -tocopheryl polyethylene glycol succinate), PEO (Polyethylene oxide) and PPO (Polypropylene oxide).

# Drug binders

- **Binders:** binders are agent used in the drug formulation to hold the active pharmaceutical ingredient and inactive ingredients together in a cohesive mix.
- For example, solution binders are dissolved in a solvent, such as gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone (PVP), starch, sucrose and polyethylene glycol (PEG).

# Classification of binder

## Based on derivatives

### 1. Saccharides:

- a) **Disaccharides**- sucrose, lactose.
- b) **Polysaccharides**- starches, cellulose or modified cellulose such as microcrystalline cellulose and cellulose ethers such as hydroxypropyl cellulose (HPC).
- c) **Sugar alcohols**- xylitol, sorbitol or mannitol.

### 2. Protein- gelatine

3. **Synthetic polymers**- polyvinylpyrrolidone (PVP), polyethylene glycol (PEG) etc.

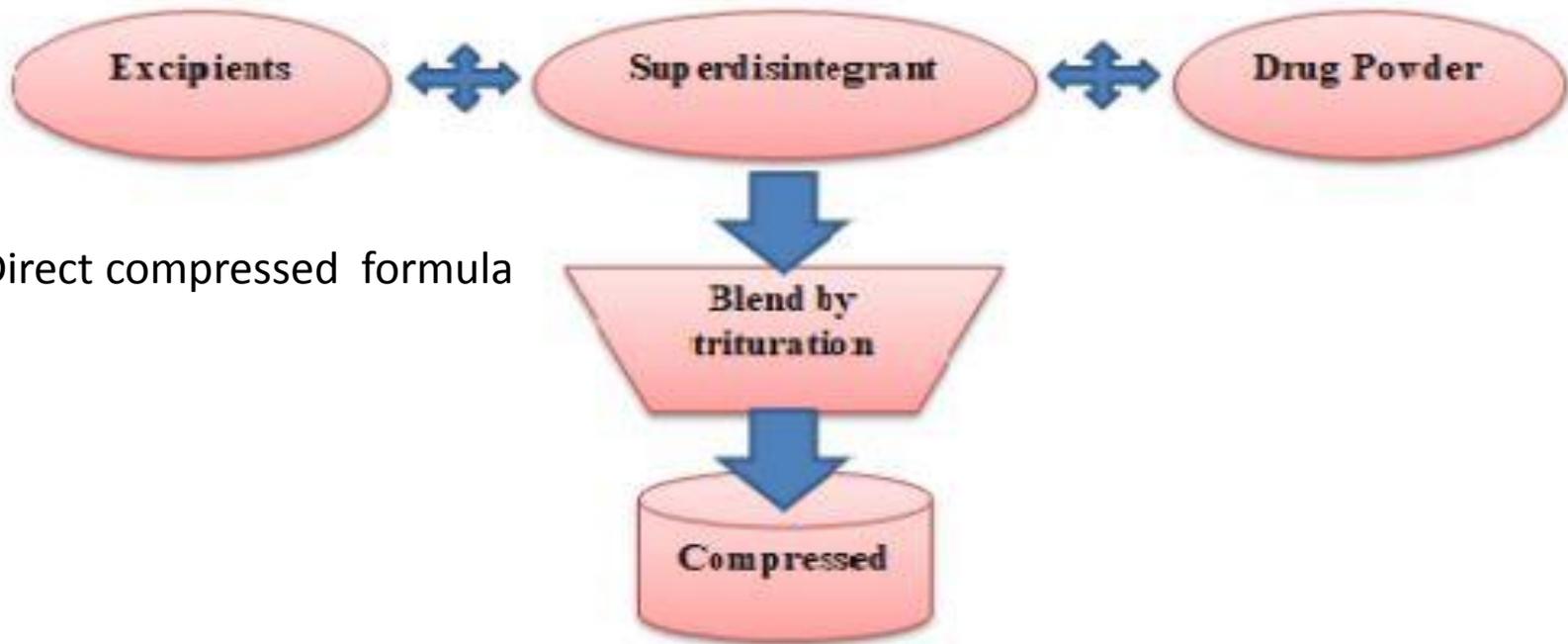
# Classified of binder according to their application:

## 1. Solution binders:

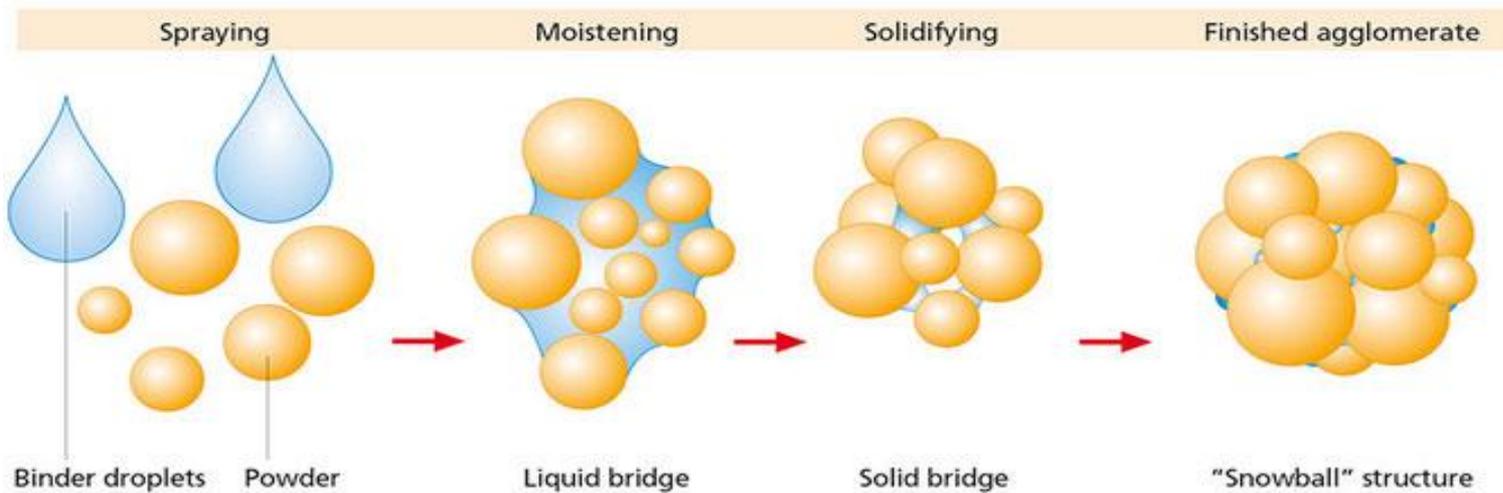
- ✓ Solution binders are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes).
- ✓ Examples include gelatine, cellulose, cellulose derivatives, polyvinylpyrrolidone (PVP) , starch, sucrose and polyethylene glycol (PEG).

## 2. Dry binders:

- ✓ Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula.
- ✓ Examples include cellulose, methyl cellulose, polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG).



### Wet granulation



# Flesh colour enhancer compounds

- There are three main groups of pigments are responsible for the coloration of fishes, these are

1. **pteridines**

2. **melanins**

3. **carotenoids.**

Among them pteridines, melanins are produced endogenously but carotenoids can not synthesize endogenously so, it must be obtained through diet.

# Classification of carotenoids

- Carotenoids are classified according to their chemical structure are as follows:

## 1. Carotenes

## 2. Xanthophylls

❖ Carotenes- alpha-carotene, beta-carotene.

❖ Xanthophylls- Lutein, astaxanthin.

# Common carotene compound found in fish

Carotenoids commonly occurring in fishes with their colours are

- **Tunaxanthin** –yellow colour
- **Lutein** – greenish or yellow
- **Carotene** –orange colour
- **Zeaxanthin** – yellow or orange
- **Canthaxanthin**- orange or red
- **Astaxanthin** –red colour etc.

# Types of carotenoids used in diet

- It can be divided into types
  1. Synthetic carotenoids and
  2. Natural carotenoids.

## **Synthetic carotenoids:**

- ✓ **Lucanthin pink** (contain 10% astaxanthin), **CAROPHYLL Red** 10% (contain 10 % canthaxanthin.), **CAROPHYLL Pink®** (astaxanthin) are the examples of commercially used synthetic carotenoid powder.
- ✓ Nearly all commercial astaxanthin are produced synthetically.

# Natural sources of carotenoid compound

Three sources –

1. Microbial
2. Animal and
3. Plant based sources

## Microalgal sources:

- a) *Hematococcus pluvialis*
- b) *Dunaliella salina*
- c) *Arthrospira maxima* (spirulina)

All these microalgal sources of carotenoid are commercially available in market.

## **Animal based sources:**

- Astaxanthin is predominant carotenoid in crustacean by-product.
- Crustacean discards are utilize as natural astaxanthin source.
- Dried shrimp meal, red crab meal , krill meal, are commercially available as fish feed.
- However, it has certain disadvantage, high ash content and chitin reduce its digestibility for fish.
- So, the rate of inclusion in fish diet is severely limit.

## **Plant based sources:**

Plant-based sources of carotenoids are much cheaper than synthetic ,microalgal based and animal based carotenoids.

- Beside these plant-based sources are easily available.
- Thus researchers gives more emphasize on plant based sources.

Eg. Alfa-alfa (*Medicago sativa*),

Carrot (*Daucus carota*),

Marigold (*Tagetes erecta*) flower,

# **Role of carotenoid compound**

1. Colour enhancer in fish flesh
2. Ornamental fish colour or pigment enhancement
3. Vitamin A precursor
4. Antioxidant activity
5. Role in reproduction
6. Immuno stimulant