

**PHARMACEUTICAL AIDS: A REVIEW**

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**ABSTRACT**

Pharmaceutical aids are the substances which have no or little pharmacological effect but they are essentially used in the preparation of pharmaceutical dosage form (like tablet, injection, emulsion, ointments etc). Pharmaceutical coloring agents are added to pharmaceutical dosage form to enhance its sensory characteristic of patient. Pharmaceutical coloring agents are used at relatively low concentration to achieve the desired effect. They may be natural or synthetic. Pharmaceutical coloring agents undergo toxicological analysis. Flavoring agents also contribute to the overall sensory quality of pharmaceutical dosage form. Flavoring agents refer to a mixed sensation of taste, touch, smell, sight and sound. All of which involve a combination of physiochemical and physiological action that influence the perception of substances. Preservatives are commonly used as additives in pharmaceutical formulation. Some liquid medicinal preparations are susceptible for microbial growth because of the water present in the formulation. Preservatives are used to protect such pharmaceutical formulation. Preservatives avoid degradation and alteration of pharmaceutical product.

**INTRODUCTION**

Pharmaceutical aids are those substances or material which have not any of their own pharmacological action. But pharmaceutical aids are the essential element for pharmaceutical preparation. Pharmaceutical aids play an important role in the formulation of preparation, preservation and transportation. Pharmaceutical aids have no specific effect on human body. Pharmaceutical aids used in the formulation of pharmaceutical product to mask the bitter taste or odor of the formulation. So that the patient compliance towards the medicine increased. Different pharmaceutical aids are used in the formulation of different dosage form like tablet, capsule, emulsion, suspension etc. Coloring agents, flavoring agents, sweetening agents, emulsifying agents, suspending agents, diluents, lubricants are the examples of pharmaceutical aids.<sup>[2]</sup>

A good pharmaceutical aid should have the following characteristics.

- ✓ They should be inert and non-reactive.
- ✓ They should be non-toxic.
- ✓ They should be cost effective.
- ✓ They should be chemically stable.
- ✓ They should have sufficient capacity to mask the bitter taste or odor of the formulation.

**Applications**

- ✓ Pharmaceutical aids are used to increase the shelf life of formulation.

- ✓ They prevent the chemical reaction in the formulation
- ✓ They preserve the formulation from any microbial contamination.
- ✓ They mask the bitter taste or odor of formulation.
- ✓ With the help of pharmaceutical aids, we can make the formulation in different color, flavour, taste.
- ✓ They increased the patient compliance.
- ✓ Pharmaceutical aids help to increase the bioavailability of the formulation or active pharmaceutical ingredients.
- ✓ Pharmaceutical aids help in the manufacturing of formulation and preserve the formulation for a long time.<sup>[1]</sup>

**Classification**

Pharmaceutical aids can be classified as follows.

- 1) Based on their origin
  - a) Animal sources
    - i) Lactose
    - ii) Gelatin
    - iii) Lanolin
    - iv) Honey
  - b) Vegetable sources
    - i) Turmeric
    - ii) Acacia
    - iii) Starch
    - iv) Peppermint
  - c) Mineral sources
    - i) Silica
    - ii) Talc

- iii) Kaolin
- iv) Paraffin
- d) Synthetic sources
  - i) Boric acid
  - ii) Lactic Acid
  - iii) Polysorbate
  - iv) Polyethylene glycol
- 2) Based on dosage form
  - a) Used in solid dosage form
    - i) Colloidal silicon di oxide
    - ii) Clay
    - iii) Silica gel
    - iv) Castor oil
  - b) Used in liquid dosage form
    - i) Water
    - ii) Alcohol
    - iii) Ethanol
    - iv) Phosphate buffer
- c) Used in semi-solid dosage form
  - i) Sodium benzoate
  - ii) Cholesterol base
  - iii) Lanolin
  - iv) Petroleatum
- 3) Based on Function
  - a) Anaesthetic
    - i) Chloroform
    - ii) Ether
    - iii) Halothane
    - iv) Nitrous oxide
  - b) Laxative
    - i) Xantham gum
    - ii) Karaya
    - iii) Bran
  - c) pH modifier
    - i) Citric acid
    - ii) Sodium hydroxide
    - iii) Hydrochloric acid
    - iv) Sodium phosphate
  - d) Astringent
    - i) Alum
    - ii) Cinnamon
    - iii) Zinc sulphate
    - iv) Copper sulphate
  - e) Carminative
    - i) Ginger
    - ii) Fennel
    - iii) Coriander
    - iv) Clove
  - f) Nutrient sources
    - i) Agar
    - ii) Lactose

#### Organoleptive aids-

Organoleptive aids are those agents which are used to enhanced the appearance of formulation and patient compliance. Organoleptic aids includes flavouring agents, coloring agents, sweetening agents.

#### Coloring Agents

Coloring agents are used to give the color to the formulation and enhanced the appearance of formulation. Coloring agents are used to give the color to food, cosmetics and pharmaceutical preparations.

Coloring agents must have the following characteristics.

- ✓ Coloring agents must be non-toxic.
- ✓ Coloring agents must not have any its own pharmacological action.
- ✓ Coloring agents must be free from harmful impurities.
- ✓ Small amount of coloring agents must be sufficient to provide the color to formulation.
- ✓ Coloring agents must be stable in the presence of sun light, microbes and tropical temperature.
- ✓ pH of coloring agents must be stable.
- ✓ Colouring agents must be compatible with API as well as excipients.<sup>[5]</sup>

#### Classification

Colouring agents can be classified as follows.

- 1) Natural colors
  - a) Mineral origin colors
    - i) Titaniium di oxide
    - ii) Red ferric oxide
    - iii) Yellow ferric oxide
    - iv) Carbon black
  - b) Plant origin colors
    - i) Indigo
    - ii) Carrot
    - iii) Beta carotene
    - iv) Chlorophyll
    - v) Annatto seed
    - vi) Saffron
  - c) Animal origin colors
    - i) Tyrian blue
    - ii) Cochineal
    - iii) Carmine
- 2) Synthetic colors
  - a) Caramel
  - b) Coal tar dyes
  - c) Lake dyes

#### 1) Natural Colors

Natural colors are obtained from plant and animals.

**a) Mineral origin colors-** The pigments or colors are obtained from minerals. These are used in the manufacturing of medicine and cosmetics. These pigments are used internally as well as externally in the formulation of medicines and cosmetics. **For examples-** Titanium di oxide is a naturally occurring oxides. Titanium di oxide used in the manufacturing of various cosmetics like sunscreen. **Red ferric oxides** and **yellow ferric oxides** are the others colors which are derived from minerals. **Carbon black** is a pigment which are mainly used in the formulation of drinking preparation. It protects the preparation from sunlight.

**b) Plant origin colors-** Plant origin colors are obtained from plants. **Indigo** obtained from the plant of Indigo tinctoria. The color spectrum of Indigo is between 420-

450. **Beta carotene** is derived from carrot, spinach and broccoli. Beta carotene is a rich source of vitamin A. **Chlorophyll** is any of several related pigments found in the mesosomes of cyanobacteria and in the chloroplast of algae and plants. **Annatto seeds** is an orange red condiment and food colorant derived from the seeds of The achiote tree, native to tropical regions. **Saffron** is derived from the flower of *Crocus sativa*, commonly known as the saffron crocus. The vivid crimson stigma and styles, called threads are collected and dried for use mainly as colorant agents.

Coloring Agents	Produce color
Chlorophyll	Green
Annatto seeds	Yellow to orange
Indigo	Blue
Saffron	Yellow
Beta carotene	Red to orange

c) **Animal origin colors**- These colors are derived from animals. **Tyrian blue** is an animal origin colors which are derived from snail. Thousands number of snail are used for the extraction of colors. Cochineal, is used to produce red color in medicines and various cosmetics. This color is obtained from the insect which lived in the plant of cactus. These insects are dried in the presence of sunlight, make the powder of these dried insects by grinding. Now this powder is dissolved in water to obtained red color. Nowadays, cochineal is widely used in the manufacturing of medicines and cosmetic. Carmine also known as carmine lake or crimson lake. carmine is obtained from the aluminium complex derived from carminic acid. Carmine used to produce bright red color to pharmaceutical preparation and cosmetics.

2) **Synthetic colors**- Synthetic colors are synthesized by using different chemicals in the laboratory. Synthetic colors are used in the formulation of various medicines as well as cosmetics. Synthetic colors produced a good appearance to the formulation. They have not any harmful effect on human body. **Caramel** is a Synthetic color also known as invert sugar. Caramel is obtained by the process of caramelization. In this process the sugar is heated at 170. The **coal tar dyes** are made by combining various aromatic hydrocarbons like toluene, xylene, benzene. Coal tar is brown or black liquid of extremely high viscosity. Lake pigments are derived by the precipitation of dyes with metallic salt. These are water soluble dyes.

According to drug and cosmetic act, 1940 there are three types of coloring agents.

a) **FD & C colors**- These colors are used in formulation or manufacturing of medicine, food & cosmetics.

b) **D&C colors**- These are those dyes and pigments which are used in manufacturing of those medicines and cosmetics which come in contact with mucus membrane.

c) **External D&C colors**- These colors are used in the formulation of those medicines and cosmetics which are externally applied on skin.<sup>[4]</sup>

### Applications

**1. Increases acceptability**- By use of Colouring agents in formulation, we can increase the patient acceptability for the medicine. Colouring agents are also used to prevent variable appearance of same formulation in different batches. A good appearance of formulation also improves patient compliance.

**2. To identify the formulation**- Colouring agents also helps in the identification of medicine. Use of different colour in different strengths of same medicine (API), helps to differentiate the medicines at various stages of manufacturing process.

**3. To provide stability of formulation**- Some of colouring agents have specific quality to stabilize the formulation when added in coating or gelatin shell in the manufacturing of tablet or capsule.<sup>[4]</sup>

### Flavoring Agents

Flavoring agents are used in formulation to mask the unpleasant and bitter taste. Flavoring agent play an important role to mask the better taste, odor of the formulation. Flavoring agent increases the patient compliance. Flavoring agents mainly used in the formulation of those medicines which are administered by oral route. In case of oral administration patient recognised, the taste of medicine very rapidly. Sometime patient split the medicine due to their unpleasant taste or odor. So that addition of flavoring agent in the manufacturing of medicines is very essential. Generally, 0.5-0.75 percent of flavoring agent are used in the manufacturing of medicines. Generally flavoring agents are changeable in nature so that a lot of precaution have to taken in the addition of flavoring agents in formulation. If the flavoring agents dissolve in water, this type of flavoring agent mixed in the aqueous component of the formulation while if the flavoring agents are not dissolved in water, this type of flavoring agents mixed in the non-aqueous component of formulation.<sup>[7]</sup>

### Selection of flavoring agent

1. The selection of flavoring agent in the formulation depends on the API and excipient present in the formulation. Flavoring agent mask the taste as well as odor of the formulation. Any person or patient is more sensitive to order as compared to taste.

2. Selection of flavoring agent for formulation also depends on the odor and taste that is previously present in the formulation. Different types of flavoring agents are used in different medicinal dosages form like solid, liquid or semisolid dosage form.

3. Selection of flavoring agent also depends on the type of dosage form whether it is solid, liquid semisolid dosage.

4. Age actor is also considered while selecting flavoring agents for any formulation.

5. Selection of flavoring agents also depends on the type of application, whether it is used externally or internally.<sup>[7]</sup>

### Classification

Flavoring agents can be classified as follows.

- 1) Sweetening agents
  - a) Sucrose
  - b) Invert syrup
  - c) Sorbitol
  - d) Treacle
  - e) Saccharin sodium
- 2) Flavored Syrup
  - a) Fruit flavored syrup
  - b) Syrup with weak therapeutic activity
  - c) Cocoa syrup
- 3) Aromatic oils
  - a) Ginger
  - b) Peppermint
  - c) Clove
  - d) Cinnamon
  - e) Lemon
  - f) Orange
  - g) Dill
- 4) Synthetic flavor
  - a) Ketones
  - b) Lactone
  - c) Benzaldehyde
  - d) Vanillin
  - e) Esters<sup>[6]</sup>

**1. Sweetening Agent- Sucrose, invert syrup, treacle, sorbitol and saccharin sodium** are commonly used to provide sweetness to the pharmaceutical dosage form or preparation. Sucrose is used as sweetening agent in the formulation of linctuses, elixirs, syrup etc. Sucrose is also used in the manufacturing of tablet or in the coating material of tablet. Invert syrup is more sweeter than the simple syrup. Invert syrup is the mixture of glucose and fructose. Invert syrup is prepared by acidification of Sucrose.

**2. Flavored Syrup-** Fruit syrup, cocoa are the examples of flavored syrup. Those syrup which have low therapeutic index, also fall in category of flavored syrup. These syrups are used to provide flavor to the pharmaceutical preparations. **Fruit flavored syrup** is prepared by the juice of citrus fruit like lemon, orange, sweet lemon etc. **Cocoa syrup** used to mask the better taste of pharmaceutical preparation.

**3. Aromatic oils-** Different types of volatile oil are used to mask the unpleasant taste of pharmaceutical formulations. **For example-** ginger, cinnamon, clove, mint etc.

**4. Synthetic Flavor-** Synthetic flavors are derived by using different chemicals in laboratory. These synthetic flavors are used to mask the taste or unpleasant odor of formulation. **For example-** ketones, benzaldehyde, esters, lactone etc.<sup>[6]</sup>

### Applications

1. Flavoring agents are used to impart good taste and odor in the pharmaceutical preparation.
2. Flavoring agents increases the patient compliance towards the pharmaceutical dosage form.
3. Flavoring agents are essential component in the formulation of chewable tablet, buccal tablet and oral dosage form.
4. Chocolate flavor mainly used in the formulation of pediatric preparation.
5. Different types of flavors can be used in the formulation of geriatric preparation.<sup>[6]</sup>

### Sweetening agent

Sweetening agents are those agents which impart or provide sweet taste to the pharmaceutical preparation. Sweetening agent also helpful to increase the viscosity of liquid dosage form. Sweetening agents as well as flavoring agents both are essential ingredient of oral dosage form. In other words, we can say that the sweetening agents also mask the unpleasant taste of the pharmaceutical dosage form. **For example-** tablet, emulsion, suspension.

### Selection criteria

1. Sweetening agents should not have any interaction with the pharmaceutical preparation.
2. Sweetening agent should not have any chemical and physical interaction with API or excipient present in the formulation.
3. In case of diabetic patient, synthetic sugar must be used as sweetening agents because synthetic sugar contains zero calories.
4. Sweetening agents should be capable of producing sweet taste to formulation in a small quantity because we all consume huge amount of sugar in our daily routine life. **For example-** Sugar in the form of tea.
5. Sweetening agents must be stable.
6. Sweetening agent must not have any harmful effect to human body.<sup>[1]</sup>

### Classification

Sweetening agents can be classified as follows.

- 1) Natural Sweetening agents
  - a) Saccharides
    - i) Sucrose
    - ii) Glucose
    - iii) Honey
  - b) Non- Saccharides
    - i) Terpinoids
    - ii) Steroidal saponins
    - iii) Proteins
    - iv) Dihydrocalcones
    - v) Dihydroisocoumarins
    - vi) Volatile oil
    - vii) Polyols
- 2) Synthetic Sweetening agents
  - a) Aspartame
  - b) Sucralose
  - c) Saccharin

### Applications

- **Sucrose** is a disaccharide sugar. Sucrose is obtained from the juice of *Saccharum officinarum*. The second source of sucrose is *Beta vulgaris*. Sucrose is mainly used in the preparation of toffee, Biscuit, ice cream etc.
- **Aspartame** is mainly used in the food beverage.
- **Lactose** used to mask the unpleasant taste of the pharmaceutical preparations. Lactose is also used to enhance the stability of pharmaceutical products.
- **Saccharin** is a synthetic sweetening agent. Saccharin is 500 times more sweeter than sugar. Saccharin is widely used to provide sweet taste to the pharmaceutical preparation or product.
- **Sodium cyclamate** is a synthetic sweetening agent. Sodium cyclamate is 30-50 times more sweeter than sugar.
- **Sucralose** is 600 times more sweeter than sugar. Sucralose contain zero calories. Sucralose mainly used in food beverage and drinkable item like candy, coffee, soft drink etc.
- **Honey** is a sugar derived from the comb. Honey is derived from the different species of bees like *Apis indica*, *Apis mellifera*, *Apis dorsata*. Honey is only sugar that is derived from animal. Honey is also used as antioxidant. Honey is non-carcinogenic. Honey 10,000 times sweeter than sucrose. It is also safe for diabetic patients.
- Sweetening agents are used in the manufacturing of pharmaceutical preparations to enhance the sweet taste, which alternatively enhance the patient compliance. Sweetening agent is used in liquid dosages form to make the syrup base. This syrup base play an important role in the viscosity and consistency of the liquid preparations.
- Sweetening agents like sugar is also used to coat tablet pills etc.
- Liquid glucose is also known as glucose syrup. Glucose is derived by the hydrolysis of starch. Glucose syrup is used to provide softness and sweet taste to the pharmaceutical products.<sup>[3]</sup>

**Preservatives-** A preservative is a natural or synthetic substance that is added to pharmaceutical products to prevent decomposition by microbial growth or by undesirable chemical changes. Preservatives inhibit the growth of bacteria, yeast and molds that can cause disease.

### Characteristic of Preservatives

- It should be non-toxic.
- It should be chemically stable.
- It should produce the desired effect.
- It should protect the pharmaceutical product from microbial growth.
- It should not change the chemical nature of the drug.
- It should give its effect in small quantity that is potent<sup>[8]</sup>

**Classification-** Preservatives may be classified as follows.

- 1) On the basis of mode of action
  - a) Antioxidants
  - b) Antimicrobial agents
  - c) Chelating agents
- 2) On the basis of sources
  - a) Natural preservative
  - b) Artificial preservative<sup>[9]</sup>

#### 1) On the basis of mode of action

**a) Antioxidants-** Those agents which prevailed oxidation of drugs are called antioxidants.

**For example-** Vitamin E, Vitamin C, butylated hydroxytoluene, butylated hydroxy anisole etc.

**Applications-** Antioxidants such as vitamin E are used as preservatives in pharmaceutical product to protect the drug from oxidation and deterioration. They are used in concentration of 0.001- 0.05 percent.

**b) Anti-microbial agents-** Antimicrobial agents are those agents that prevent or kill the microbes are called antimicrobial agents. **For example-** methylparaben, Propyl paraben, Benzoic acid, Sodium benzoate etc.

**Applications-** Antimicrobial agents such as **Methylparaben** is used in almost all type of pharmaceutical formulation. It may be used either alone or in combination with other parabens. Methylparaben is most effective against yeast and mold. **Propyl paraben** as a preservative is used in cosmetics such as cream, lotion shampoo and soaps. **Benzoic acid** is used as preservative in concentration of 0.02 to 0.5% in oral medicine, 0.5% in parental product and 0.1 to 0.5% in cosmetics.

**c) Chelating agents-** Chelating agents, these are the agents which form the complex with the pharmaceutical ingredient and prevent degradation of pharmaceutical product. **For example-** di sodium ethylenediaminetetraacetic acid (EDTA), Poly phosphate, citric acid etc.

**Applications-** EDTA is used as preservative for pharmaceutical product.

#### 2) On the basis of sources

**a) Natural preservative-** These are the substance obtained from natural sources such as plant minerals and animals. **For example-** Sodium chloride, honey, lemon, Neem oil etc.

**Applications-** Natural preservative are used to protect the drug from microbial contamination.

**b) Artificial preservative-** These are the preservatives prepared by chemicals that are effective in small concentration. **For example-** Benzoate, sorbate.

**Applications-** Artificial preservative are used in almost all the drugs to prevent deterioration of drug from microorganism during storage.<sup>[10]</sup>

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