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Pharmaceutical Aids

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Abstract: ***Pharmaceutical aids are the drugs and 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 colouring agents undergoes toxicological analysis. Flavouring agents also contribute to the overall sensory quality of pharmaceutical dosage form. Flavouring agents refers to a mixed sensation of taste, touch, smell, sight and sound. All of which involve combine 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. In this article we will be studying about the substances needed in the preparation, preservation and storage of pharmaceutical products and how are they classified into different categories and why are they necessary in preparation and does that help to the pharmacist.***

Keywords: Pharmaceutical Aids

1. Introduction

Pharmaceutical aids are those substances or material which have not any its 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. These may be required for such purposes as preservations, stabilization, acidification, alkalization, suspending, excipient, adsorption, absorption, filtration, prevention of oxidation, stabilization, complexation etc. Pharmaceutical aids may remain in the final product in which case they do not exert any specific action on the body when the product is administrated or they may get removed during processing but come in close contact with the product at some stage. Different pharmaceutical aids are used in the formulation of different dosage form like tablet, capsule, emulsion, suspension etc. Colouring agents, flavouring agents, sweetening agents, emulsifying agents, suspending agents, diluents. Lubricants are the examples of pharmaceutical aids.(1)

Characteristics of a good pharmaceutical aids:

Classification Pharmaceutical aids can be classified as follows.

1) Based on their origin:-
   a) Animal sources: i) Lactose ii) Gelatine iii) Lanolin iv) Honey
   b) Vegetable sources: i) Turmeric ii) Acacia iii) Starch iv) Peppermint
   c) Mineral sources: i) Silica ii) Talc
2) Based on dosage form
   a) Used in solid dosage form:- i) Colloidal silicon dioxide 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) Petrolatum(2)

1.1 Colouring Agent

Colouring agents are mainly used to impart a distinctive appearance to the pharmaceutical dosage forms. 'e can also say that the colorants are the cosmetics for the pharmaceutical preparations, because the aesthetic appearance of dosage forms can be enhanced by using suitable colorants. The main categories of dosage form that are colored are& tablets (either the core itself or the coating.), hard or soft gelatine capsules & (the capsule shell or coated beads), oral topical creams, toothpastes, ointments and slaves. The elegance and eye appeal of a colored product is "aluable, especially for children whom it is often used to treat with syrups, tablets, or capsules, to a"oid and allow treatment at home

Classification of coloring agents

On the basis their origin it is divided into two parts:

1) Synthetic:-Tartrazine, Azorubine, brilliant blue, erythrosine.
2) Natural:-

Animal: eg. carmine, tyrian purple.
Animal Colour: These are obtained from animal source. Tyrian Blue: It is obtained from oxidizing of a colourless secretion from the gland of snails. Cochineal: This is obtained from an insect Coccus cactus a brilliant red colour carminic acid.

Plants: eg. Annatto, caramel, lycopene
Plant Colour: The colouring principles from plants are obtained by extraction. [β Carotene, Alizarin,Indigo]. Indigo: This is obtained from plant Indigo feratinctoria. The color spectrum is 420-450nm. The colour wavelength is in between blue and violet (VIBGYOR). The colour is considered one of the seven colours of rainbow or optical spectrum. World Journal of Pharmacy and Pharmaceutical Sciences β-Carotene: It is a carotenoid comes under natural pigments. It is responsible for many of the yellow and orange

colour of fruit and vegetables. β-Carotene is found in plenty in carrots. Dark green vegetables such as spinach and broccoli are another good source. In these the orange colour is masked by green colour of chlorophyll. This can be seen in leaves; in autumn, when the leaves die, the chlorophyll breaks down, and the yellow/red colour of most stable carotenoids can be seen. These can protect body against oxidative damage and can protect from UV light and enriched in source of Vitamin A.[3]

Mineral: eg. malachite, cinnabar, aragonite.

Mineral Colour: Frequently termed as pigments and are used to colour lotions, cosmetics and other preparation for external use. [Red and Yellow Ferric Oxide, Lead Chromate, Titanium Dioxide, Carbon Black].Titanium Dioxide: It is naturally occurring oxides of titanium TiO2. In cosmetics and skin care products, titanium dioxide is used as a pigment and a thickener. It is mostly used in sunscreen with a physical blocker because of its high refractive index, its strong UV light absorbing capabilities and its resistance to discoloration in UV light. Titanium reacts with oxygen to form a clear TiO2. This clear oxides filter out light waves producing brilliant colour. As the thickness of oxides varies produce colour. Red and Yellow Ferric Oxide: Iron oxide is a unique natural mineral produced through beneficiation and fine grinding of our exclusive domestic ore body. Iron oxide is light fast, chemically stable and colour controlled within narrowly define parameters iron oxide formulations are used in manufacturing virtually all coloured cosmetics and beauty products. [Foundations, Eye shadow, Lipstick, Mascara, Mineral Pigments, Lip gloss, Face powder, Blush & Pencil, Eye liners]. These are the products that use iron oxides as their primary colouring ingredient.

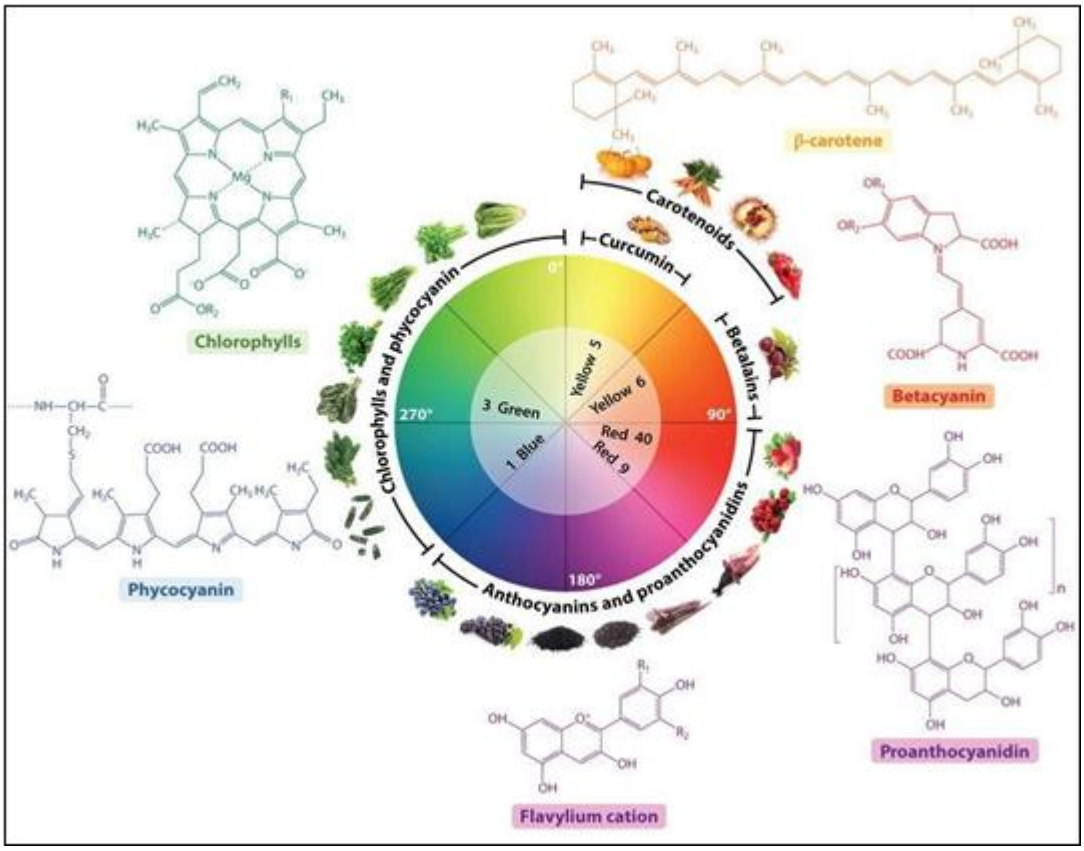


Figure 1: Colour and chemical structure compare four typical natural pigments: anthocyanins, betalains, carotenoids, and phycocyanins

On the basis of their solubility it is divided into two categories:

1) Colorant dyes (soluble in the medium):- Indigo carmine, brilliant blue, caramel.
2) Pigments (insoluble in the medium):- Cadmium pigment, chromium pigment, cobalt pigment.[4]

Pharmaceutical preparations are colored mainly for following reasons:

a) 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 appear

b) **For identification:** 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.
c) Standard preparations
d) Stability purpose
e) Also used as protective

Flavourants or flavouring agents:

Are mainly used for masking the unpleasant or unacceptable odor from formulation and provide more pleasant taste or flavour. There are four basic taste sensations are salty, sweet, bitter, and sour. Flavour added to drug solutions can make a medicine more acceptable to take especially if the drug has

an unpleasant taste. In the pediatrics dosages form flavour play a key role for administration of the drugs. Flavouring agents are more sensitive against the heat (thermolabile nature) so it cannot be added prior to an operation involving heat, they are often mixed with the granules as an alcohol solution. In market many coating tablet are present for masking the flavour.

Classification of flavouring agents:

It is classified into two categories:-

a) Natural flavouring agents:-Citrus fruit (lemon, orange), spice (cinnamon, pepper mint, ginger, onion), fruits (apple, banana).
b) Synthetic flavouring agents:- Benzaldehyde, cinnamicaldehyde, coumarin, ethylmethylketone.[5]

Table 1: Flavouring agents

	Natural Flavouring Substances	Nature-identical Flavouring Substances	Artificial Flavouring Substances
Nature / State	Completely Natural	Chemically identical to substances present in natural products	Completely artificial / synthetic
Process used for isolation	Physical / Microbial / Enzymatic	Chemical	Not isolated but made synthetically
Obtained from	Material of vegetable or animal origin either in the raw state or after processing (including drying, roasting and fermentation)	Aromatic raw materials or can be obtained syntheticall	Made synthetically and hence have not yet been identified in natural products

Sweetening Agent:

Sweeteners are defined as food additives that are used or intended to be used either to impart a sweet taste to food or as a tabletop sweetener. Tabletop sweeteners are products that consist of, or include, any permitted sweeteners and are intended for sale to the ultimate consumer, normally for use as an alternative to sugar. Foods with sweetening properties, such as sugar and honey, are not additives and are excluded from the scope of official regulations. Sweeteners are classified as either high intensity or bulk. High-intensity sweeteners possess a sweet taste, but are non- caloric, provide essentially no bulk to food, have greater sweetness than sugar, and are therefore used at very low levels. On the other hand, bulk sweeteners are generally carbohydrates, providing energy (calories) and bulk to food. These have a similar sweetness to sugar and are used at comparable levels.

Classification of sweetening agents:

1) Natural Sweetening agents:
   a) Saccharides:- e.g. i) Sucrose ii) Glucose iii) Honey
   b) Non-Saccharides:- e.g.i) Terpinoids, ii) Steroidalsaponins, iii)Proteins

2) Synthetic Sweetening agents:
   a) Aspartame
   b) Sucralose
   c) Saccharin

a) Sucrose:-

The sucrose, derived from Sanskrit word Sarkara, was being extracted from sugarcane in India, and hasbeen identified about 6000-10,000 BC as mentioned in Rig and Atharva Vedas. It was introduced in non-Asiatic continents by Alexander the Great . Sucrose is a Disaccharide sugar obtained mainly from the cane juice of saccharum Officinarum (Graminae) and from the roots of Beta Vulgaris (chenopodiaceae). Sucrose is most often prepared as a fine, white crystalline powder with a pleasing, sweet taste.

b) Honey:

Honey is a sugar secretion deposited in honey combs by the bees Apis indica (Indian Bee), Apismellifera, Apisdorsata (Rock Bee) and other species of Apis of family Apidae. Honey is the only sweetener obtained from animal source. The typical composition of honey is: moisture, 17.7%; total sugars, 76.4%; ash, 0.18%; and total acid (asformic acid), 0. 08%. Traditionally its use in food has been as sweetening agent several aspects of its use indicate that honey also functions as food preservative. Honey also contains tiny amounts of several compounds thought to function as antioxidants, including chrysin, pinobanksin, Vitamin C, catalase, and pinocembrin.

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.[6]

Preservative

A preservative is a substance or a chemical that is added to products such as food products, beverages, pharmaceutical drugs, paints, biological samples, cosmetics, wood, and

many other products to prevent decomposition by microbial growth or by undesirable chemical changes. In general, preservation is implemented in two modes, chemical and physical. Chemical preservation entails adding chemical compounds to the product. Physical preservation entails processes such as refrigeration or drying.[1] Preservative food additives reduce the risk of food borne infections, decrease microbial spoilage, and preserve fresh attributes and nutritional quality. Some physical techniques for food preservation include dehydration, UV-C radiation, freeze-drying, and refrigeration. Chemical preservation and physical preservation techniques are sometimes combined.

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.

Classification of preservative:

A) On the basis of mechanism of action it is divided into three categories:-

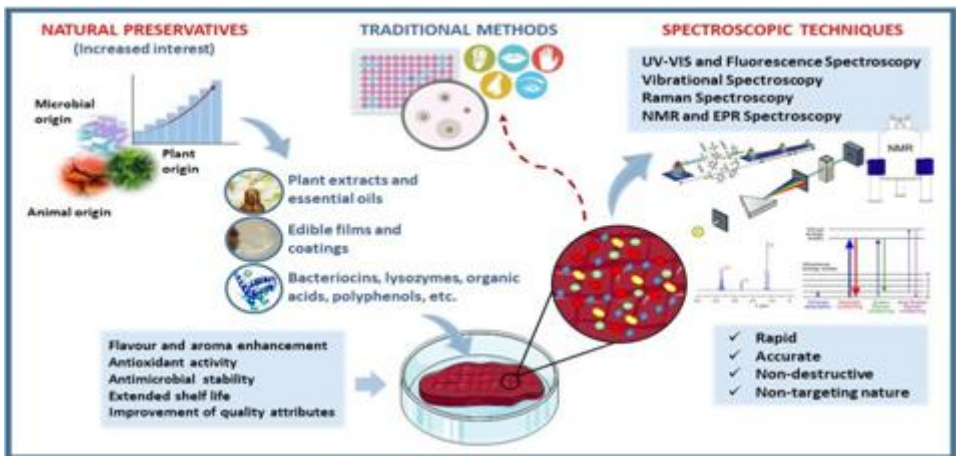
Antimicrobial agents—that agent which prevents the contamination (gram positive and gram negative) and degradation by microbes is as antimicrobial agents. These agents are active in low concentration. Example-phenolic compounds, parabens, propyleneglycol, BHT, BHA.

B) On the basis of their activity it is further divided into two parts.:-

1) Microbiostatic—that inhibits the growth and multiplication of the microbes. b. Microbiocidal—that agent direct kills the microbes.
2) Antioxidants agents—those agents which prevents the products oxidation or degradation in the presence of molecular oxygen. Generally API is more reactive towards the oxygen, so antioxidants are mix with the product and overcome the product reactivity. An *antioxidant* is the substrate that prevents the oxidation of molecules inside a cell. It is a well-known chemical process that allows the removal of electrons or hydrogen from a substance. Free radicals are produced during the biological oxidation reaction. Because the radicals are reactive, they start the chain reaction simultaneously. This can lead to the damage or even the death of a cell. Hence, antioxidant agents are capable of terminating a chain reaction by eliminating free radical intermediates. Example—ascorbic acid, citric acid, tocoferols, BHA, BHT.[7]
3) Chelating agents—those agents which form the cyclic compounds or complexes with the pharmaceutical ingredients and prevent the degradation of pharmaceutical formulation. Are chemical compounds whose structures permit the attachment of their two or more donor atoms (or sites) to the same metalion simultaneously and produce one or more rings. These molecules are also called "chelates" or chelating groups, and the formation of rings is called "chelation." These metal complexes have the ability to resolve into optically active (R&L) forms. Stability of metal complexes differs with pattern of complex formation and difference in stability becomes more relevant in the increasingly dilute solutions in biological systems such as serum or tissue. The toxico kinetics and toxico dynamics of metal and chelating agents are an integral part of an effective chelation therapy in addition to the following criteria, which also need to be fulfilled:
   - High affinity for the toxic metal
   - Low affinity for essential metals
   - Minimal toxicity
   - Lipid solubility
   - Good absorbability from the gastrointestinal tract. Example- EDTA, polyphosphates.

C) On the basis of sources it is divided into two parts:-

1) Natural preservatives:-. This means you can get natural preservatives from plants, animals, fungi, and algae. Salt and sugar are both natural preservative examples. Adding salt to meat is called curing and is how you make beef jerky, e.g. vinegar, honey, castor oil, salt, sugar.
2) Synthetic preservatives:-Artificial preservatives are chemical substances that are added to food during the manufacturing process. These chemical additives can slow down or restrict food deterioration caused by micro-organisms and oxidation reactions. e.g. sodium benzoate, BHA, BHT.[8]



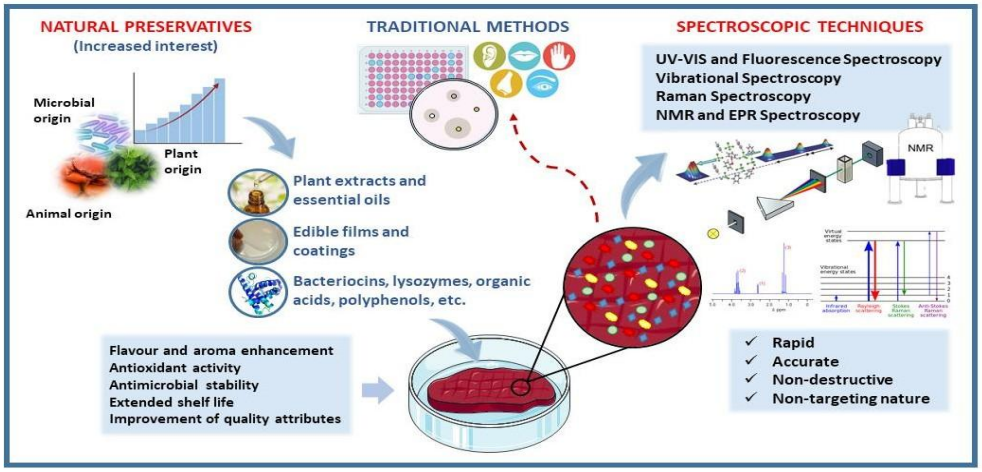


Figure 2: Natural and Spectroscopic preservatives

Application of preservatives

- Preservative enhance the stability and shelf life of the products, so it maintain the product activity for long time.
- It prevents the product by any microbial contamination increase their resistance power against the microbial growth.
- Many environmental factors affect the products property, for overcoming this activity preservative is also used.
- It also mixes with the food preparation for prevention their oxidation.[9]

2. Conclusion

The active pharmaceutical ingredients (API) are not used as such but are suitably formulated into dosage forms or drug delivery systems in an attempt to ensure safe, efficient, reproducible and convenient manner of drug delivery. The dosage forms are not API alone but contain many other additives. These additives are known as excipients. The pharmaceutical excipients are defined as substances (other than API) which have been appropriately evaluated for safety and included in a dosage form to: add in processing of dosage form during its manufacture; protect, support, or enhance stability, bioavailability or patients acceptability; assist in product identification; or enhance any other attribute of overall safety and effectiveness of the API during storage or use. While the API is the primary constituent of the pharmaceutical product, the pharmaceutical excipients contribute to the physical form, texture, stability, taste and overall appearance. The patients' medication adherence is most vital in therapy to get the optimum outcome. The medication adherence often closely related to the odour, taste and colour of the product. The proper combination of the flavour, fragrance and colour in a dosage form contribute to the acceptance of the pharmaceutical products. The flavouring, sweetening and colouring agents are grouped together as organoleptic excipients. The flavouring agents are included to improve the taste of the product either by providing a more pleasant taste or by masking the unpleasant taste. In general flavouring of liquid products requires better expertise than solid pharmaceutical dosage forms. Medications in liquid forms directly come in contact with taste receptor cells in the mouth and produce positive or negative taste sensation. The selection of the flavouring agents depends on many factors primarily on the taste of API and the age of the intended patient. There are four basic types of taste: salt, sour, bitter and sweet. The colour acceptable in one country may not be acceptable in another country. It is necessary that the current regulation relating to use of colouring agents in medicines be referred for formulating products meant for export. The nomenclature of the colours too causes confusion. The selection of colours and maintaining a reproducible colour of the product from batch to batch is a highly skilled job. The slight change in intensity of the colour raises doubt about the product in consumer's mind. While formulating, it is necessary to consider colour, odour, texture and taste together and not in isolation. The colour of pharmaceutical products must have a psychogenic balance with the taste and the colour must enhance the taste. Dosage form manufacturers must perform at least one test to verify the excipients' identity and to check conformity with specification for purity, strength and quality in order to ensure manufacturing of consistent and reproducible products. Though suppliers' test may be acceptable, at least one test is essential for validation. If the excipient manufacturer does not provide the result for specification test, it should be indicated on the certificate of analysis. The dosage form manufacturer needs to perform these tests. They need to comply with country's regulations in identifying these excipients.[10]

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