ABSTRACT

Organoleptic agents are one of the important members of pharmaceutical aids. Pharmaceutical aids are the components which have no medicinal value but these are essential to formulate any drug into medicine with lucrative look so that it can be easily acceptable by the patients. Organoleptic additives promote appearance and palatability of pharmaceutical dosage forms. If the product does not have acceptable colour, flavor and taste the patient would try to avoid using it. There is a definite psychologic basis for drug therapy in which the colour, flavor and taste of pharmaceutical preparation can play their own part. Mostly the drugs are of bitter and arid taste which are been prescribed by the physician for oral administration by tablets or syrups. These medications are being avoided by patients through oral route because taste buds don’t welcome these through oral route due to their unpleasant taste. If these dosage forms are being incorporated by organoleptic agents to improve their colour, flavour and taste then these are gladly accepted by patients (pediatric and geriatric). Human has sense of organs: eye, ear, nose, throat (ENT). Eye accepts lucrative coloured matters, ear accepts well harmony, nose accepts attractive smell and throat accepts palatable taste from taste buds of tongue. Colourful medicine with acceptable flavour with lucrative taste is always ready to consume by any patient.

KEYWORDS: API (Active Pharmaceutical Ingredient), Drug, Medicine, Formulation, Colour, Flavour, Taste bud, FDA, FD&C, Dyes, Lake Dyes, Mottling, Pitting.
INTRODUCTION

Organoleptic agents are as follows

1. Colouring Agents: These agents are used to provide distinctive colour with pleasing appearance or elegance to the dosage form. Colour helps the manufacturer to control the product during its preparation as well as serving as a means of identification to the user. Colouring agents may be soluble in the solvent system or suspended as insoluble powders. All colouring agents used in pharmaceutical formulations must be approved and certified by (FDA) Food Drug and Administration and FD&C (Food Drug and Cosmetics Act).

Types of colouring agents

a. Natural Colour

(i) 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 TiO$_2$. 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 TiO$_2$. 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.

(ii) Plant Colour: The colouring principles from plants are obtained by extraction. [β-Carotene, Alizarin, Indigo].

Indigo: This is obtained from plant _Indigofera tinctoria_. 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.\[1\]
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.

![β-Carotene](image1)

![Alizarin](image2)

![Indigo](image3)

(iii) 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.

b. Synthetic Colour:

![Tyrian Blue](image4)

![Cochineal](image5)

These colouring agents are mostly obtained from coal tar dyes and also used in food & beverages to enhance their appearance without toxicity. It is mainly used today under drug and cosmetic act:

Artificial Colour: Caramel, Coal tar dyes

Caramel: It is a dark brown material obtained by controlled thermal application on carbohydrates. It is also known as burnt sugar. The process of caramelization consists of heating sugar slowly to around 170 °C (340 °F). As the sugar heats, the molecules break down and re-form into compounds with a characteristic color and flavor.

Coal tar dyes: These are obtained from petrochemicals and coal. These are mostly aromatic azo dyes.
Figure 2: Artificial colours

Alizarin cyanine green F
Tartrazine
Orange G
Erythrosine
Sunset Yellow FCF
Fast Green FCF
Allura Red FCF
Indigotine
Ponceau 4R
Table-1: Colours and Name

<table>
<thead>
<tr>
<th>Colour</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>Naphthol blue black</td>
</tr>
<tr>
<td>Blue</td>
<td>Brilliant blue FCF</td>
</tr>
<tr>
<td>Red</td>
<td>Amaranth</td>
</tr>
<tr>
<td>Green</td>
<td>Alizarin cyanine green F</td>
</tr>
<tr>
<td>Yellow</td>
<td>Tartrazine</td>
</tr>
<tr>
<td>Orange</td>
<td>Orange G</td>
</tr>
<tr>
<td>Pink</td>
<td>Erythrosine</td>
</tr>
<tr>
<td>Orange</td>
<td>Sunset Yellow FCF</td>
</tr>
<tr>
<td>Turquoise</td>
<td>Fast Green FCF</td>
</tr>
<tr>
<td>Red</td>
<td>Allura Red AC</td>
</tr>
<tr>
<td>Indigo</td>
<td>Indigotine</td>
</tr>
<tr>
<td>Strawberry red</td>
<td>Ponceau 4R</td>
</tr>
</tbody>
</table>

Figure-3: Lake Dye (Mordant is Aluminium)

Lake dyes: These are aluminium or calcium salts of any water soluble colour. A lake pigment is a pigment manufactured by precipitating a dye with an inert binder, or “mordant”, usually a metallic salt. Unlike vermilion, ultramarine, and other pigments made from ground minerals, lake pigments are organic. Manufacturers and suppliers to artists and industry frequently omit the lake designation in the name. Many lake pigments are fugitive because the dyes involved are unstable when exposed to light. Many lake pigments are azo dyes. They characteristically have sulfonate and sometimes carboxylate substituents, which confer negative charge to the chromophore (colored species). The metallic salt or binder used must be inert and insoluble in the vehicle, and it must be colourless or very neutral. The organic component of the dye determines which wavelengths are absorbed and reflected by the resulting precipitate. In ancient times chalk, white clay, and crushed bones were used as sources of the calcium salts. The salts that are commonly used today include barium sulfate, calcium sulfate, aluminium hydroxide, and aluminium oxide (alumina), all of which can be produced cheaply from inexpensive mineral ores. A mordant is a substance used to set dyes on fabrics or tissue sections by forming a coordination complex with the dye which then attaches to the fabric or tissue. It may be used for dyeing fabrics, or for intensifying stains in cell or tissue preparations. The term mordant comes from the present participle of French mordre, "to
bite”. In the past, it was thought that a mordant helped the dye bite onto the fiber so that it would hold fast during washing. A mordant is often a polyvalent metal ion. The resulting coordination complex of dye and ion is colloidal and can be either acidic or alkaline.

The colour concentration used in liquid preparation is 0.0005-0.001% and for powder 0.1%.

**Factors for selection of colours**
Certification of dye, Physical and chemical property of dye, pH stability, photo stability, lucrative.

**Precautions**
Mottling: Unequal distribution of colour, so to prevent this proper missing is suggested. When wet granulation takes place then drying process must be done in proper care to prevent colour migration.

Pitting: It is defect whereby pits occur on the surface of tablet core without any visible disruption of the film coating. Temperature of the tablet core is greater than the melting point of materials of formulation.

![Mottling and Pitting](image)

**Figure-4: Mottling and Pitting**

2. **Flavouring Agents**: These agents are usually used to mask the four basic taste sensations: saline, bitter, sour, sweet.

Flavouring is particularly significant in case of liquid dosage form for oral use. Chewable tablets of antacids, vitamins, antibiotics which are intended for mastication in the mouth are usually sweetened and flavoured to increase patient acceptance.
Table-2: Flavours and Taste

<table>
<thead>
<tr>
<th>Flavour</th>
<th>Taste</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mint/Vanilla/Custard</td>
<td>Alkaline</td>
</tr>
<tr>
<td>Lemon/Orange</td>
<td>Acid</td>
</tr>
<tr>
<td>Mint/Fennel</td>
<td>Butter</td>
</tr>
<tr>
<td>Butter Scotch/Apricot</td>
<td>Saline</td>
</tr>
<tr>
<td>Vanilla/Honey/Fruity</td>
<td>Sweet</td>
</tr>
<tr>
<td>Flavour</td>
<td>Colour</td>
</tr>
<tr>
<td>Cherry/Apple</td>
<td>Pint to red</td>
</tr>
<tr>
<td>Chocolate/Caramel</td>
<td>Brown</td>
</tr>
<tr>
<td>Lemon</td>
<td>Yellow to orange</td>
</tr>
<tr>
<td>Liquorices</td>
<td>Blue</td>
</tr>
</tbody>
</table>

Flavor oils are added to tablet granulation in solvents or are dispersed on clays and other absorbents or are emulsified in aqueous granulation agents.\(^2\)

Volatile oils as flavours: Clove, Fennel, Orange, Wintergreen oil, Rose, Jasmine, Lavender for floral smell to creams/lotions.

Storage: 15-30°C, Relative humidity-45%.

Mainly 0.5 to 0.75% flavouring agents are used.

Factors: Can improve the palatability, Concentration of flavor, colour, sweetener. Type of preparation-internal or external, age of patient, General liking and disliking of consumer.\(^3\)

3. Sweetening Agents: These agents are used to impart sweetness in a pharmaceutical formulation. The four primary tastes are sweet, bitter, sour and saline and all other tastes are considered to be the admixture of one or more of these primary tastes in variable degrees.

Many sweetening agents are used to mask bitter taste and it must be dissolved either when taken in solution form or dissolved in saliva. It is used in the adjustment of taste in oral formulation because all drug for oral use may not having agreeable taste and often disagreeable taste is to be masked.
Sweetening Agents: Sucrose, Liquid glucose, Saccharin, Cyclamates, Sorbitol, Xylitol, Dextrose, Aspartame.

Sucrose/Sugar: Soluble in water and is available in highly purified form in reasonable cost, Physically and chemically stable at pH 4-8, Frequently used in conjugation with sorbitol, glycerin and other polyols which reduce the tendency of sucrose to crystalline.\(^4\)

**Table-3: Sweetening agents**

<table>
<thead>
<tr>
<th>Sweetening agent</th>
<th>Comparison to sucrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccharin</td>
<td>500 times</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>0.5 times</td>
</tr>
<tr>
<td>Xylitol</td>
<td>1 time</td>
</tr>
<tr>
<td>Dextrose</td>
<td>0.75 times</td>
</tr>
<tr>
<td>Aspartame</td>
<td>250 times</td>
</tr>
<tr>
<td>Sucralose</td>
<td>1000 times</td>
</tr>
</tbody>
</table>

Liquid glucose: Prepared by partial hydrolysis of starch with strong acid. Glucose syrup, also known as confectioner's glucose, is syrup made from the hydrolysis of starch. Glucose is a sugar. Maize (corn) is commonly used as the source of the starch in the US, in which case the syrup is called "corn syrup", but glucose syrup is also made from potatoes and wheat, and less often from barley, rice and cassava. Glucose syrup containing over 90% glucose is used in industrial fermentation, but syrups used in confectionery contain varying amounts of glucose, maltose and higher oligosaccharides, depending on the grade, and can typically contain 10% to 43% glucose. Glucose syrup is used in foods to sweeten, soften texture and
add volume. By converting some of the glucose in corn syrup into fructose (using an enzymatic process), a sweeter product, high fructose corn syrup can be produced.

![Glucose](image1.png) ![Sucrose](image2.png) ![Sodium Cylamate](image3.png) ![Aspartame](image4.png)

Figure-6: Sweetening agents

Saccharin: It is an artificial sweetening agent and synthetic compound which is 250-500 times sweet as sugar but gives bitter taste after taste. It is carcinogenic. It is available as saccharin sodium, saccharin calcium.

Cylamates: These are normally sodium or potassium salts of cyclohexane sulfamic acid and it are carcinogenic, so it has been banned. Sodium cyclamate is an artificial sweetener. It is 30–50 times sweeter than sucrose (table sugar), making it the least potent of the commercially used artificial sweeteners. It is often used with other artificial sweeteners, especially saccharin; the mixture of 10 parts cyclamate to 1 part saccharin is common and masks the off-tastes of both sweeteners. It is less expensive than most sweeteners, including sucralose, and is stable under heating.

Aspartame: It is the methyl ester of aspartic acid and phenyl alanine, which is less stable in moisture and hygroscopic in nature, stable in 3.5-5.

Sucralose: It is a non-nutritive sweetener. The majority of ingested sucralose is not broken down by the body, so it is noncaloric. Sucralose is about 320 to 1,000 times as sweet as sucrose, twice as sweet as saccharin, and three times as sweet as aspartame. It is stable under heat and over a broad range of pH conditions. Therefore, it can be used in baking or in products that require a longer shelf life. The commercial success of sucralose-based products stems from its favorable comparison to other low-calorie sweeteners in terms of taste, stability and safety.\[^5\]
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.

Certain flavouring agents are more effective than others in masking or disguising the particular taste. Though the individuals’ choices vary, there are certain general concepts: cocoa flavours are preferred for masking taste of bitter medicinal agents; fruits or citrous flavour to combat sour or acid tasting API; and cinnamon, orange and raspberry flavour for saline medicinal ingredients. The age of the patient is too crucial in selection of the flavour.
Children like sweet candy like preparations with fruit flavour but adults may prefer less sweet preparation with a tart. The elderly persons may have liking for wine flavour. The oral solid dosage forms like capsules and coated tablets do not need flavouring agents in their formulation. On the other hand, the chewable or effervescent tablets do need flavours and also sweetening agents to improve acceptance. As the flavouring agents are often thermolabile, the time of addition of flavour in tablet formulation is critical. They cannot be added to an operation involving heat (drying of granules). They may be mixed with the granules prior to compression as alcoholic solutions. The flavouring agent in liquid dosage forms is added to the solvent or vehicle component of the formulation in which it is most soluble or miscible. The water soluble flavouring agents are added to the aqueous component of the formulation and poorly soluble are added to the alcoholic or other non-aqueous solvent component of the formulation. In multi-component systems, the appropriate solvent level of the flavouring agent is essential to keep them in solution. Sucrose, a low molecular weight carbohydrate, has been traditionally used as sweetening agent because of several advantages associated with it: very soluble in water, stable over a pH range of 4-8, increases viscosity which imparts a product a pleasant texture in the mouth. However, it is also associated with two issues: use in diabetic patients and its cryogenic properties. Polyhydric alcohols: sorbitol, mannitol and to some extent glycerin have sweetening properties and can be used in preparations for diabetic patients. In addition, there are many artificial sweeteners. They are sweeter than the sucrose and are suitable for patients who need to restrict their sugar intake. But there are several safety issues raised on some of them especially on: saccharin, aspartame and cyclamate. Saccharin does not undergo metabolism and its potential for causing cancer is determining factor for its use. Aspartame undergoes metabolism producing phenylalanine and the phenylalanine metabolism is a problem in persons with phenylketonuria. The increased serum level of phenylalanine amino acid can cause mental retardation and affect the foetus of a pregnant woman. Cyclamate is metabolized and its by products are excreted in kidneys. Its safety issues concern with possible carcinogenicity, possible causation of genetic damage and testicular atrophy. However, in addition of safety concern, they have the disadvantages of being imparting a bitter or metallic after taste. The colouring agents are included in the dosage forms not only to improve the attractiveness of the product, but also to enable easy product identification, particularly in poisonous materials. The presence of strongly coloured inert degradation product can be masked by the use of suitable colours. The natural colouring agents like carotenoids, chlorophyll, anthocyanins, riboflavines, caramel and extracts of beetroot have better acceptability. But they have the usual problems like variations in
availability and chemical composition leading to formulation difficulties. On the other hand, synthetic or coal tar dyes provide bright colours with greater stability. Many of these synthetic dyes are found to be hazardous to health because of their own chemical nature or the impurities present. Because of their toxicity or carcinogenicity tendency, they are regulated and only approved colouring agents can be used in pharmaceutical products. The Drugs and Cosmetics Act and the Rules of India specified what colouring agents can be included in dosage forms. The FDA of USA has classified the colouring agents according to their use: Colours for use in Foods, Drugs and Cosmetics; Colours - some of which for use in drugs, some of which in cosmetics and some are for medical devices; colours for use in externally used products (not in lips or other mucous surface of the body). 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.

REFERENCES
4. Ma J, Bellon M, Wishart JM, Young R, Blackshaw LA, Jones KL, Horowitz M, Rayner CK. Effect of the artificial sweetener, sucralose, on gastric emptying and incretin