International Journal of Pharmaceutical Chemistry and Analysis 2023;10(3):150–155

Content available at: https://www.ipinnovative.com/open-access-journals

International Journal of Pharmaceutical Chemistry and Analysis

Journal homepage: https://www.ijpca.org/

Review Article

Natural flavoring agents used in pharmaceutical industry

Apurva A. Salunkhe[1], Firoj A. Tamboli[2,*], Manasi S. Zade[1], Yash R. Ghadge[3], Monali D. Kore[4], Amruta D. More[5]

[1]*Dept. of Pharmaceutical Quality Assurance, Bharati Vidyapeeth College of Pharmacy, Kolhapur, Maharashtra, India*
[2]*Dept. of Pharmacognosy, Bharati Vidyapeeth College of Pharmacy, Kolhapur, Maharashtra, India*
[3]*Dept. of Pharmaceutical Quality Assurance, D.Y. Patil Institute of Pharmaceutical Sciences and Research, Pune, Maharashtra, India*
[4]*Dept. of Pharmaceutical Chemistry, Dattakala College of Pharmacy, Swami Chincholi, Maharashtra, India*
[5]*Dept. of Pharmaceutical Chemistry, Sahyadri College of Pharmacy, Solapur, Maharashtra, India*

ARTICLE INFO

Article history:
Received 14-07-2023
Accepted 22-08-2023
Available online 15-09-2023

Keywords:
Excipients
Active ingredients
Prodrug
Flavours

ABSTRACT

In accordance with the International Pharmaceutical Excipients Council (IPEC), excipients are any component used during the production procedure or included in a finished medicinal formulation but which is not an active ingredient or a prodrug. The USP-NF defines Forty different types of additives for usage in medicines. Another of the classes, organoleptic compliance, gives medicines flavor and color. Medicine is made more palatable by adding flavors. Again, depending on where they originate, these tastes are classified as natural, artificial, or natural and artificial (N&A). To deliver not only tastes but also a delightful flavor, flavoring agents are used in pharmaceutical preparations such edible syrup, oral suspension, herbal remedies, pills, tablets that can be chewed, bubbly tablets, easily dispersed tablets, and ODT. They are used to boost patient compliance or enhance the taste of therapeutic dosage forms.

1. Introduction

An individual compound or a combination of compounds of manmade or natural origin that, when consumed or taken orally, can produce a taste or aroma (i.e., fragrance) are referred to as flavoring agents by the USP. A flavoring component constitutes a single of the additives in various pharmaceutical compositions. Additionally, flavorings or flavorants are other names for flavoring compounds. Keep in mind that flavor is written in British English, not American English.[1] The term "flavor" refers to a variety of sensory experiences, including taste, touch, smell, sight, and sound. These experiences all entail physiological and physio-chemical processes that affect how substances are perceived. Many synthetic or replica flavors have been developed as a result of the development of technology in the flavor industry. Cough syrups, laxatives, sedatives, antibiotics, vitamins, and preparations for kids as well as elderly people all come in a variety of flavors that effectively mask unpleasant tastes without sacrificing physical or chemical stability.[2]

In accordance with the UK Food Law, A natural flavor is one that is obtained physically, enzymatically, or microbiologically from a material of plant or animal-based origin and that was either unprocessed or had undergone a method that is usually employed in the manufacturing of meals for consumption by humans. Flavor is the physical impact of a food or other material, and it is mainly defined by the chemical senses of smell and palate. The U.S. Code of Federal Regulations regulates a "natural flavorant"

* *Corresponding author*.
E-mail address: drfatamboli@gmail.com (F. A. Tamboli).

https://doi.org/10.18231/j.ijpca.2023.027

as any natural oil, oleoresin, essence or extraction-based, protein hydrolysate, the distillate, or other by-product of the roasting process, heating, or breakdown by enzymes that includes flavoring elements that originate from a herb, fruit or beverage, plant-based or vegetable juice, consumable yeast, or any other mixture of these.[3] A flavouring is anything that imparts flavour to another material by changing the solute's properties, making it sweeter, sourer, tangier, etc. In the fragrance and flavor industry, the word also refers to edible chemicals and extracts that alter the flavor of food and food items by tempting to the sense of fragrance. The phrase is frequently utilized to describe the chemical responses of smell and flavor together.[4] Flavourings are volatile chemical compounds that enhance the flavour or aroma of food. They mostly use smell to function. According to the law, compounds that just have a sweet, sour, or salty flavour are not regarded as flavourings. Salt substitutes, sweeteners, acidulants, and flavour enhancers are frequently used in these.[5,6]

Flavoring agents classification:[1,3,7]

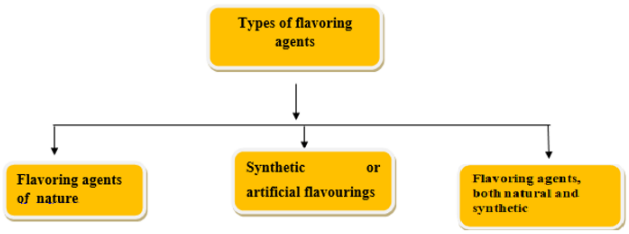

Fig. 1:

2. Based on the Sources

2.1. *Flavoring agent of nature*

Flavors that are naturally occurring using physiological, microbiological, or biochemical techniques to flavor products generated from unprocessed plant or animal components. They may be used in their unprocessed state or processed for usage by humans, however artificial flavoring agents are not permitted. The word "natural" flavoring compounds are either one sort of flavoring substance or a combination of flavoring materials that are obtained from plant or animal components through mechanical methods like roasting or heating or through chemical methods like the extraction process, the process of distilling enzymatic, or microbial activities. Complex volatile oil (anise oil), aldehyde (vanillin), ginger oil, peppermint oil, and lemongrass oil are a few examples of natural flavouring ingredients.[1,4,8–12]

Typical natural flavoring substances:[3]

Fig. 2: Natural flavoring agent

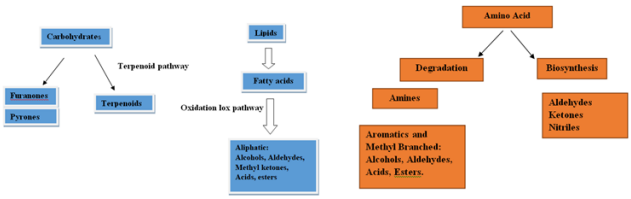

Fig. 3: Flavor synthesis from natural resources

2.2. *Synthetic or artificial flavorings*

Chemical compounds created using chemical procedures are known as artificial flavoring agents. These compounds may be structurally, chemically, and organoleptically identical to a flavoring ingredient that is already present in food. For instance, methanol and salicylic acid react chemically in the presence of heat, H+ ions from H_2SO_4, and salicylic acid to produce methyl salicylate (Wintergreen flavor).Additives to flavors artificial unknown flavoring ingredients in a natural food meant for consumption by humans. These are often created by fractional distilling natural chemicals, crude oil, or coal tar, along with extra chemical processing. They are combinations of several synthetic scent compounds, some of which may be exact

replicas of natural flavors. The ratios used to blend these flavors successfully mimic a natural fragrance.Including cinnamon aldehyde and benzaldehyde. Food additives known as artificial flavoring compounds are those that have not been found in natural products (figure 3). They can be distinguished from organic and nature-identical flavors by the fact that they are not found in natural products. [1,4,8–12]

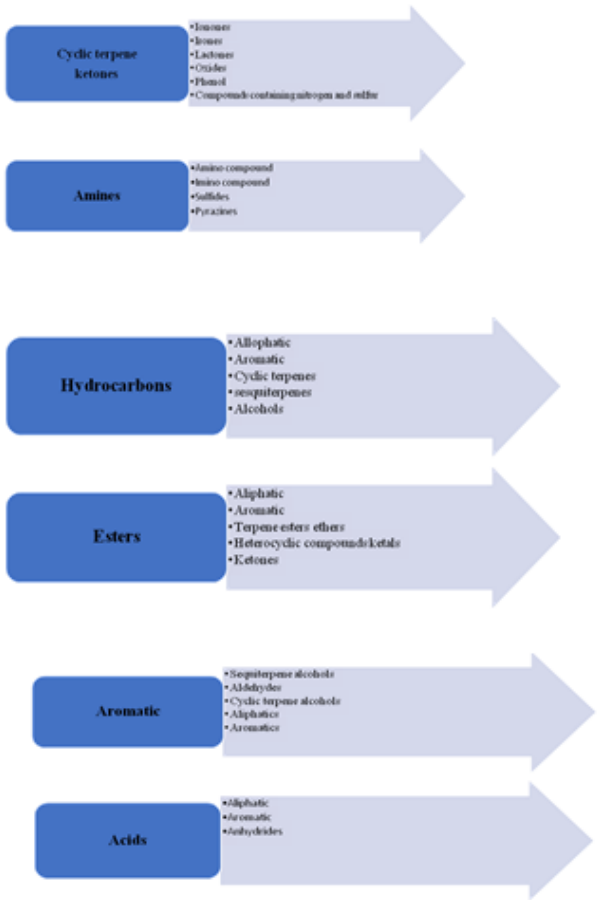

Fig. 4: Major aromatic compounds used in flavorings

2.3. *Flavoring agents, both natural and synthetic*

These comprise a combination of a variety of natural flavoring components and artificial flavoring compounds to enhance flavor balance and intensity.Improvingflavor balance and fullness, N&A flavor systems mix artificial and natural flavors. The wide range of flavoring chemicals available to the formulator from N&A Flavours is an advantage. [1,4,8–12]

3. On the Basis of Appearance

3.1. *Flavorings that are solid*

These flavoring substances can be purchased in solid form and can be either natural or artificial. As an illustration, consider mango, chocolate, and pineapple flavoring powders. [1]

Fig. 5: Natural and artificial flavoring agent

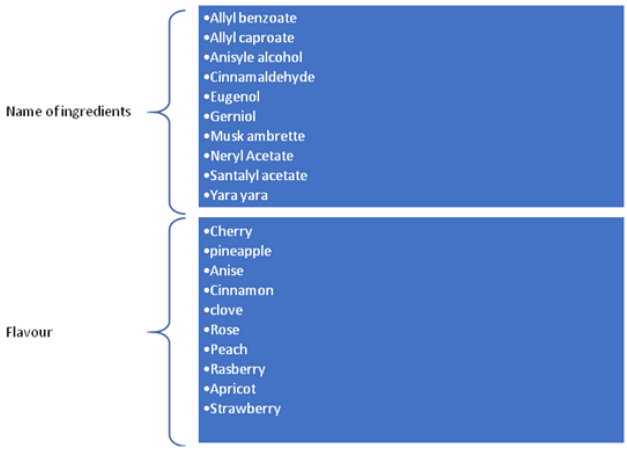

Fig. 6: *Commonly used N and A flavors:* [3]

3.2. *Flavoring agents for liquids*

These are flavoring agents that can be utilized in liquid form and can be either natural or artificial. For instance, essential oils like methyl salicylate, lemon oil, orange oil, and peppermint oil. [1]

3.3. *The following categories of flavoring agent are employed in the preparation*

1. *Sweetening agents:* Sugar (Sucrose), fructose syrup, treacle i.e. the sticky substance (which is utilized in the drug chlorodyne, which also includes morphine tincture BPC and chloroform), sorbitol, and saccharine sodium are a few examples of sweetening agents. [2,13]
2. *Flavored syrup:* Fruit-flavored sugar syrups and syrups with limited medicinal value, such cocoa syrup, which has the carminative effect (the capacity to

Table 1: Most commonly used flavours

Taste	Masking flavor
Salty	Glycyrrhiza (licorice) syrup, maple, butterscotch, cinnamon, raspberry, orange
Sour	Fruit, citrus, cherry syrup
Sweet	Berry, fruit, vanilla, and acacia syrup
Bitter	Raspberry syrup, glycyrrhiza (licorice), eriodictyon, wild cherries, chocolate-mint, walnut

List of flavouring agents in pharmaceutical formulations: [1,3]

Table 2: List of flavouring agents in pharmaceutical formulations

Sr. No.	Flavoring agent names	Name of the Chemical and Maximum Amount
1.	Vanillin	The scientific name for vanillin is (4-hydroxy-3-methoxybenzaldehyde). Vanillin is used in tablets (which incorporates those containing caffeine and polythiazide), solutions (0.01-0.02% w/v), syrups, and powders as a medicinal excipient.
2.	Menthol (USP), Racementhol (BP)	In many pharmacological preparations, menthol is employed, particularly in antacid pills, solution, and expectorant tablets (antibacterial pills). It is utilized in topical therapies and has the ability to produce a hydrating or pleasant effect. 0.05-10.0% for topical formulations, 0.4% for toothpaste, 0.1-2.0% for mouthwash, and 0.3% for oral spray. 0.02-0.05% for inhalation. 0.003% for oral suspension. 0.005-0.015% for oral syrup.
3.	Grape	Methyl Anthranilate
4.	Apple	Ethyl 2-methylpentanoate, or manganite
5.	Banana	Isopentyl acetate, another name for isoamyl acetate
6.	Pear	Ethyl Decadienoate
7.	Coconut flavor	γ-Octalactone
8.	Cherry	Allyl Benzoate
9.	pineapple	Allyl Caproate or Allyl Hexanoate
10.	Orange	d-Limonene, Ethyl Butyrate
11.	lemon	3,7-Dimethyl-2,6-Octadienal
12.	Mango	It comprises the flavoring compounds listed below: A few examples of cultivar compounds used as taste enhancers include ethyl butanoate for (fruity mango), 3-hydroxy-4,5- dimethyl-2(5H)-furanone, ethyl-2-methybutanoate, (E,Z)-2,6-nonadienal, and 1-(E,Z)-undecatriene.
13.	Cinnamon	Cinnamaldehyde
14.	Peppermint	Menthyl Acetate shall make up not less than 5% of the peppermint flavor and not more than 50% of the overall menthol content.
15.	Ginger	Gingerol, d-Camphene And ß- Phellandrene
16.	Clove	Eugenol
17.	Lavender	Linalyl Acetate
18.	Rose	Geraniol and l-Citronellol
19.	Raspberry	Raspberry Ketone (4-(4-Hydroxyphenyl) butan-2-one)
20.	Strawberry	Ethyl Methylphenylglycidate
21.	Adipic Acid	Additionally referred to as hexanedioic acid, it is used to give food a sour flavor.
22.	Capric acid	To add a citrus-like flavor to medicinal products as a flavoring component.
23.	Malic Acid	It has a faint apple flavor and is employed to cover up bitter flavors and add sharpness(acidity).
24.	Fumaric Acid	mostly utilized as an acidulant and flavoring component in liquid medicinal form of administration.
25.	Sodium Metabisulfite	It gives preparations a distinct flavor at doses above around 550 ppm.
26.	Thymol/Thyme oil	Primarily utilized in cosmetics to add a strong, nearly mint flavor.
27.	Caraway	Carvone & Limonene
28.	Truffle	2,4-Dithiapentane
29.	Wintergreen	Methyl Salicylate
30.	Citric Acid Monohydrate	As a flavor booster for its acidic and sour nature.

Table 3: The choice of flavoring agents is made primarily on their taste

Flavoringingredients	Taste of Flavoring agents
Peach, Wintergreen, Butterscotch, Apricot, Maple	By virtue of the existence of anions and cations such KBr, NH4Cl, and sodium salicylate, foods have a salty flavor.
Vanilla, Fruit, and Berry flavor	Alfa-amino acids, polyhalogenated aliphatic compounds, and polyhydroxy compounds all contribute to the sweetness of the flavor.
Wild Cheery, Mint, Walnut, Chocolate, Anise	Bitter flavor (Flavoring agents with free bases, including amides and alkaloids like amphetamines, provide a harsh taste. High molecular weight salts, halogenated chemicals, aliphatic thio-compounds, and polyhydroxy compounds with molecular weights greater than 300 may taste harsh.)
Licorice, Raspberry, Citrus flavor,	The sour taste corresponds to the amount of hydrogen ion concentration and is brought about by hydrogen ions.

Selection of flavorings based on the intended flavor of the medication formulation: [3,13]

Table 4: Selection of flavorings on the basis of the taste of drug to be formulated

Types of Drugs	Preferred flavoring Agents
Vitamin C	Orange, Lemon Flavor
Analgesic	Cherry, Raspberry
Barbiturates	Banana-Pineapple, Orange,Strawberry, Cinnamon-Peppermint, Peach-Orange, Banana-Vanilla.
Anathematic	Mango, Chocolate, Vanilla
Electrolyte-solutions geriatrics	Cherry, Mango, Lemon, Raspberry, Wild Cherry, Mixed Fruit, Wild Strawberry Flavor, Grape
Antihistamines	Grape, Cherry, Honey, Raspberry, Wild Cherry, Peach-Orange, Cinnamon, Apricot.
Multi-vitamin	Fruity Flavor, Mango
Antacid, H2 receptor blockers	Peppermint, Mint, Anise
Expectorants	Anise, Apricot, Clove, Cherry, Strawberry-Lemon, Fennel, Coriander, Pineapple, Orange-Lemon, Clove, Custard-Mint-Strawberry
Antibiotics	Maple, Fruit-Cinnamon, Pineapple, Banana-Vanilla, Strawberry, Raspberry, Vanilla, Butterscotch, Orange, Cherry.

Fig. 7: Liquid flavouring agents

reduce flatulence) make it profitable in this form of preparation, are a couple of examples of flavoring syrups. Additionally, ginger syrup has an appealing smell and flavor which make it a good complement to rhubarb-based laxative mixes. [2,13]

3. Aromatic oils, such as those from peppermint, lemon, orange, caraway, clove, and dill [2,13]
4. For the purpose of creating synthetic flavors, various compounds such as vanillin, benzaldehyde, chloroform, artificial sweeteners (sugar substitutes), and others are combined with or rather than essential oils. The alcoholic beverages, aldehydes, ester compounds, ketone bodies, fatty acids, and the lactones are only a few of the different organic molecules that are exploited. [2,13]

Most popular flavors: [1,7,13,14]

4. Inventive Flavoring Agents: [7]

1. Sodium gluconate, which has a high purity of more than 99.5% and the best pricing.
2. L-Theanine
3. Methylene chloride

4.1. Choosing flavoring ingredients

The choice of appropriate flavoring agents for a pharmaceutical product relies on the composition of the effective medicinal ingredient in order to reduce the unpleasant taste and odor of drug products and promote taste and texture. The sense of smell is more acute than the sense of taste. Therefore, flavoring compounds are chosen based on their flavor and aroma as well as the medicine that will be created. Use flavoring ingredients with great strength to cover up the API's offensive and highly concentrated odor.[1] Making ingredient choices according to flavour (never use a flavoring agent that has a bitter taste to mask a drug that has a bitter flavor):

5. Conclusion

In some pharmaceutical formulations, flavoring compounds are one of the excipients. Additionally, flavorings or flavorants are other names for flavoring compounds. Aroma and taste, which are both essential elements, are both included in flavoring agents. Depending on their source, flavoring agents are categorized as natural, artificial, or N&A. N&A are the most often utilized of these because they offer a wide range of flavors and a very little modification in the ingredient chain length can have a significant impact on the type of flavor.Flavoring agents are also classified on the basis of their physical form as solid flavoring agents and liquid flavoring agents. There are also types of flavoring agent used in the preparation are like sweeting agents, aromatic oils, flavored syrup, synthetic flavors. For enhancing accessibility by masking the disagreeable taste and odor of drug products, the choice of suitable flavoring compounds for a drug product relies on the nature of the active medicinal components. The flavor of the medicine being developed is taken into consideration while choosing flavorings.

6. Source of Funding

None.

7. Conflict of Interest

Authors Declares no Conflict of Interest.

References

1. Sharma AV, Sharma PV. Flavoring Agents in Pharmaceutical Formulation. *Ancient Sci Life*. 2023;8(1):38–40.
2. Sharma AV. Flavoring Agents in Pharmaceutical Formulations. *Ancient Sc Life*. 1988;8(1):38–40.
3. Somil D. Review of Flavoring agents used in Pharmaceutics. *World J Pharm Med Res*. 2019;5(4):116–7.
4. Flavoringfrom Wikipedia. Available from: encyclopediahttps://en.wikipedia.org/wiki/Flavoring#cite_ref-fda-title21-2022_5-2.
5. Small DM, Green BG. A Proposed Model of a Flavor Modality Archived 19 September 2021 at the Wayback Machine. *Neural Bases Multisensory Processes*. 2012;p. 36.
6. Jeremy W, Kluender. Sensation & perception. 3rd ed. and others, editor. Sinauer Associates.; 2012. p. 1–7.
7. Available from: https://www.thepharmaeducation.com/2020/07/flavoring-agents-in-pharmaceutical-formulations.html?m=1.
8. Food and Drug Administration; 2022. Available from: https://foodsafetyhelpline.com/what-are-flavouring-agents-what-do-fssai-regulations-say/.
9. Flavourings and Flavour Enhancers - User Guide. *The Australia and New Zealand Food Standards Code*. 2002;.
10. Food Helpline Research. Available from: https://foodsafetyhelpline.com/what-are-flavouring-agents-what-do-fssai-regulations-say/.
11. Saffarionpour S, Ottens M. Recent Advances in Techniques for Flavor Recovery in Liquid Food Processing. *Food Eng Rev*. 2018;10(2):81–94.
12. Lachman L. Theory and practice of Industrial Pharmacy. *Chapter*. 2021;12:365–74.
13. Gunn C, Carter SJ. Cooper and Gunn's Dispensing for pharmaceutical Students. 12th ed. Bombay: Kothari Book Depot; 1973. p. 250.
14. Remington. Practice of Pharmacy. 16th ed. Easton Penn, U.S.A.: Mack Publishing Co; 1980.

Author biography

Apurva A. Salunkhe, PG Student

Firoj A. Tamboli, Head

Manasi S. Zade, PG Student

Yash R. Ghadge, PG Student

Monali D. Kore, PG Student

Amruta D. More, PG Student

Cite this article: Salunkhe AA, Tamboli FA, Zade MS, Ghadge YR, Kore MD, More AD. Natural flavoring agents used in pharmaceutical industry. *Int J Pharm Chem Anal* 2023;10(3):150-155.