Vanillin: One Drug, Many Cures*

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Chemically, 'vanillin' belongs to the class of benzaldehydes, its structural formula being 4-hydroxy-3-methoxybenzaldehyde. It is one of the key constituents of vanilla pods, primarily from the species of *Vanilla planifolia*. However, since it is uneconomical to grow vanilla on a large scale, it is prepared synthetically to meet the diverse demands of growing food and pharmaceutical industries. Recently, vanillin has warranted the attention of the scientific community because of its versatility and utility. From the medicine cabinet to your savory platter, its ubiquitous presence is what makes one wonder, "is this the next-gen supermolecule we had been waiting for?"

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Introduction

The term 'vanillin' has been derived from *vanilla*, its origin being the Spanish word *vainilla*, a diminutive form of *vaina* or *sheath* [1]. Vanillin, an aromatic compound, is known to occur naturally as a glycoside bound to sugar (such as glucovanillin in vanilla pods) or as a precursor bound to the large lignin molecules in wood. It has a white crystalline structure and a characteristic pleasant flavor. Researchers have identified it as a phytochemical—glucoumarin—amongst 171 aromatic compounds found in vanilla bean [2]. Vanilla pods consist of vanillic acid, p-hydroxybenzaldehyde, p-hydroxybenzoic acid, sugars, lipids, minerals, water, and cellulose besides vanillin [3]. Chemically, vanillin is a methylester of 4-hydroxybenzoic acid—a ring compound that contains a carboxyl group and a hydroxyl group (4-hydroxy-3-methoxybenzaldehyde) (*Figure* 1).

Keywords
Vanillin, vanilla, food, flavoring, preservative, drug, antimicrobial.

Vanillin imparts its typical delicate and mellow flavor to a wide

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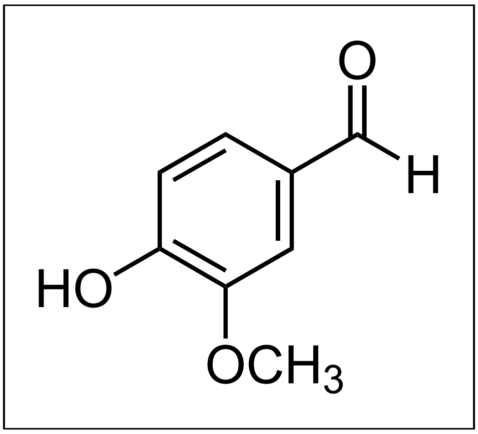

Figure 1. Chemical structure of vanillin.
(Image Credit: *Wikimedia Commons)*

The chemical structure of Vanillin was worked out by Tiemann and Haarmann in 1874, who reported it to be 3-methoxy-4-hydroxybenzaldehyde.

range of raw and processed foods such as lychee, raspberry, potatoes, olive oil, coffee, maple syrups, oatmeal, Peru balsam, and clove oil. Nicolas Theodore Gobley first isolated it from the seed pods of *Vanilla planifolia* in 1858 by evaporating the vanilla extract to dryness and further re-crystallizing the resulting solids from hot water (hence, the name vanillin). Its chemical nature was worked out in 1874, and it was synthesized from coniferin present in the tree sap during the same year. Since then, a plethora of alternative sources like sawdust, waste residues of rice bran, maize bran, etc., have been explored with the help of different biotechnological approaches. Only 1–2% of the total world market for vanillin is met by the extraction of vanilla beans, while the remaining share comes from precursors like guaiacol, lignin wastes, eugenol, ferulic acid, etc., (*Figure* 2).

Isolating vanillin from the vanilla pods is a costly and a laborious process. Scientific evidence shows that approximately 500 kg of vanilla pods are required to produce 1 kg of vanillin. The cost of natural vanillin, therefore, is high and fluctuates with the availability of vanilla pods!

Natural vanillin is obtained from vanilla pods through four successive steps namely, kilning, sweating, drying, and conditioning. Madagascar is presently the largest producer of natural vanillin. Only cured vanilla pods, also known as 'fine vanilla', display the characteristic flavor property on account of the hydrolysis of β-D-glucosides or glucovanillin into glucose and vanillin by β-D-glucosidases enzyme during fermentation. The vanillin content of the cured pods is usually 2–2.5% depending upon the origin (Mexico 1.75%, Sri Lanka 1.50%, and Indonesia 2.75%) [4]. Vanillin production accounts for about 410 million dollars per an-

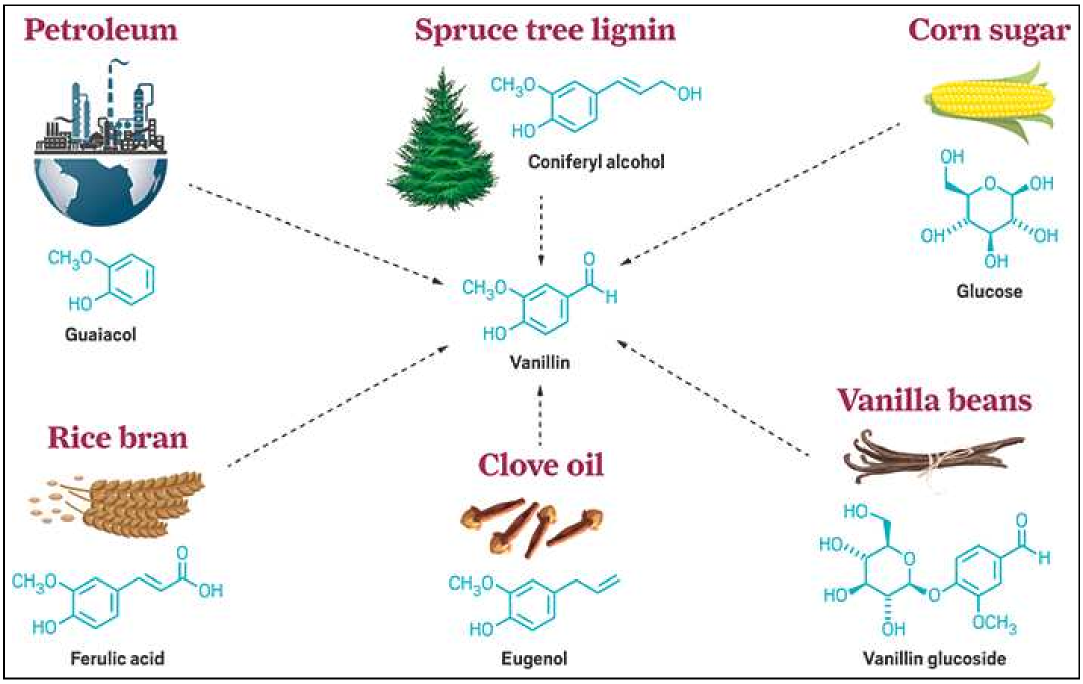

Figure 2. Different sources of vanillin. (Image Credit: cen.acs.org.)

num globally. Over the past several years, there has been a steady growth in global demand for vanillin (about 3–4%).

Nutraceutical Uses of Vanillin

Several studies on vanillin have shown that it exhibits anticarcinogenic and anticlastogenic properties, which if properly utilized, might give way to the next 'wonder drug' from vanillin or its derivatives [5, 6]. However, its effectiveness should be well-studied before any anticarcinogenic drug is marketed through labeling it as one of the key ingredients. Its efficacy as a drug may be enhanced with the help of nanotechnology (i.e. labeled radioisotopes, nanocarrier molecules acting as nano-robots for identifying the carcinogenic sites and ravaging the tissues with the chemical).

Researchers have successfully proven that vanillin can arrest the cell cycle in human colorectal cancer cells. Besides, it is also involved in DNA repair and is considered as an anti-mutagenic compound.

Vanillin, which is widely used as a flavoring agent has a great antimicrobial potential which widens its prospects of being used as an effective preservative in foodstuffs. Vanillin, one of the con-

Vanillin acts as a potent preservative in minimally processed apple products such as apple puree at the concentration of approximately 13 mM. It is effective in liquid media (such as fruit juices and soft drinks) since these are free lipids and proteins that hinder its ability to kill bacteria!

stituents of the essential oil fraction of the vanilla bean, exhibits a structure similar to the eugenol [2-methoxy-4-(2-propenyl) phenol] from cloves and harbors antimycotic and bacteriostatic properties [7, 8]. Its preservative effect has been studied by researchers in fruit purees where it inhibited inoculated yeast, mold, and bacteria at 2000–3000 ppm. Its effectiveness against the panoply of yeasts and moulds is well-documented and hence, it could act as a broad-action preserving agent in the future fruit drink industry [9]. However, the synergistic effects of vanillin with other natural preservatives have not been studied until now [10]. It can be used as an essential ingredient in some food items such as flavored milk and other milk products, baked goods, and confections where it will not only serve as a flavoring agent but also as an excellent preservative. Since it is effective against gram-positive and gram-negative bacteria like *Enterobacter aerogenes*, *Escherichia coli*, *Lactobacillus casei*, *Pseudomonas aeroginosa*, *Salmonella enterica* subsp. *Enterica serovar*, etc., its role in preventing the occurrence of epidemic outbreaks and foodborne diseases needs to be further investigated [11, 12]. Also, its potential as a broad-spectrum antibiotic and an antifungal agent can be exploited for the abatement of many diseases. Further, it can find extensive application in the packaging industry as an active antimicrobial constituent of the packaging material [13].

Vanillin prodrug has been successfully created and tested on rats with sickle cell mutation for combating sickle cell anemia. Vanillin forms a covalent bond with the sickle hemoglobin and inhibits the sickling of cells. Since vanillin degrades upon oral administration, a prodrug MX-1520 was developed by the researchers that enhanced the bioavailability of vanillin (about 30 times higher) [14].

Vanillin displays a mild antioxidant potential towards polyunsaturated fatty acids (PUFA) rich foods, thereby opening up new possibilities of its novel use in the food industry: as a preservative in fruit creams, clarified butter, butter, chips, biscuits, etc., [9]. Vanillin also acts as an anti-inflammatory agent and can be used in the synthesis of drugs for combating arthritis, allergies, and gout.

Other Uses of Vanillin

The majority of industrial sectors use vanillin in a variety of ways. It is omnipresent—from your anti-hypertension prescriptions to your savory platter, from your kitchen to your medicine cabinet. Its consumption in foods and beverages has been estimated to be 60% while in flavors, fragrances, and pharmaceutical intermediates, it is limited to 25%. An interesting application of vanillin can be in radiocarbon dating, for instance, in determining the age of historically important 'lignin' artifacts. A careful examination of levels of vanillin in an artifact may help reveal its age, e.g., in much debated 'shroud of Turin' that dates back to 1260–1390 A.D. [15].

Vanillin has acquired GRAS (Generally Recognized as Safe) status and is utilized in a wide variety of applications such as food flavoring, perfumery, animal feed, pharmaceutical, agrochemical, and industrial products!

Vanillin, as a flavoring, dominates the ice cream and chocolate industry (with a market share of 75%); smaller amounts being used in confections and baked goods. It is used as an odor agent in perfumery and as a reagent in analytical chemistry. Not only is it the 'dark horse' of the food industry, but it is also taking a rise in the pharmaceutical industry. 40% of vanillin is used in drugs such as Aldomet (antihypertensive formulation), L-dopa (treatment of Parkinson's disease), and Trimethoprim (treatment of upper respiratory tract infections and some forms of venereal diseases). Other sectors that have utilized vanillin's potential are the perfume and the metal plating industries. Besides, other miscellaneous uses are—as an anti-foaming agent in lubricants, as a brightener in zinc coating baths, as an antioxidant in linseed oil, as an attractant in insecticides, as an agent counteracting tobacco-induced dryness in the mouth, as a catalyst to polymerize methyl methacrylate, as a solubilizing agent for riboflavin, in the general-purpose stain for developing TLC plates, and in examining the localization of tannins in cells [16].

However, when used as a flavoring agent in cigarettes in concentration as low as 0.05%, it poses the risk of cancer and serious addiction. So, next time if you curse the manufacturer for spoiling your lungs, remember that it is vanillin, the sneakiest culprit hidden underneath the glamorous folds of a cigarette.

Suggested Reading

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