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Natural Vanilla: A Potential Pharmaceutical Flavorant

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This paper discusses numerous natural flavouring agents,which can effectively mask the objectionable odour of drugs, but it requires skillful application, which does not affect the bioavailability of drug formulations. Vanilla flavour in pharmaceutical formulations helps in attaining a product having a rich mellow aroma with sweet, spicy, woody and balsamic note. Natural vanilla flavour extract has the added advantage of several chemical constituents along with the major constituents (vanillin, *p*-hydroxybenzaldehyde and others), which help in improving the product preference in general and gaining patient compliance in particular.

INTRODUCTION

Natural vanilla flavour is extracted from the cured beans of *Vanilla fragrans*. Among the many volatile aromatic compounds of vanilla extract, vanillin is the single most flavour impact constituent along with other non-volatile compounds, which contribute to the overall flavour quality of the essence of vanilla. The fragrance and flavour of vanilla beans is due to aromatic compounds produced during the curing operation.

Curing of vanilla beans

Green vanilla pods are almost odourless and the characteristic flavour of vanilla develops only upon curing[1]. A number of procedures have been evolved for curing of vanilla, but they all are characterized by four phases in order to be transformed into a commercially desirable product. The four phases are killing, sweating, drying and conditioning, which are listed in Table-1 along with the methodology and objective of each phase. Drying, curing and subsequent conditioning of pods or beans is the most important process, and the value of the product depends more on the process than on cultivation[2].

Chemical composition of cured vanilla beans

Vanilla beans are a treasure-house of various volatile and non-volatile chemical constituents. The characteristic fragrance, associated with the cured beans, is developed during the process of curing. Three glycosides, *viz.*, glucovanillic alcohol, glucovanillin and an unidentified one together with two enzymes appear to be present in the fresh pods. During curing, glucovanillic alcohol and glucovanillin undergo enzymatic hydrolysis to yield vanillin, the chief odorous constituent of the cured beans. The hydrolytic product of the third glycoside is an ester with a strong and pleasant odour[3].

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TABLE-1
STAGES INVOLVED IN CURING OF VANILLA BEANS

Phases	Methodology	Objective
Killing	Done by dipping in hot water at 65°C for 2–3 min.	Abolishing tissue and cellular activity by this treatment.
Sweating	Achieved by folding the beans in blankets, carried for about 7–10 days.	Colour development due to oxidation of polyphenolic compounds and flavor development due to breakdown of glycoside called glucovanillin to vanillin.
Drying	Carried under sunlight for 7–10 days, 2–3 h a day.	Reducing the microbial spoilage and favouring beneficial chemical changes to take place.
Conditi oning	Done by storing the beans in closed boxes, carried for several months.	Various chemical and biochemical reactions such as etherification, esterification, oxidative degradation etc. which produce various volatile aroma constituents.

The major volatile constituents of vanilla responsible for aroma and flavour, such as carbonyls, aromatic alcohols, aromatic acids, aromatic esters, phenols, aliphatic alcohols, acids, lactones, aromatic and aliphatic hydrocarbons, terpenoids, heterolcyclics are present in general, whereas *p*-hydroxybenzoic acid, *p*-hydorxy benzyl methyl ether and acetic acid are present in particular[4, 5] (Table-2).

TABLE-2
VOLATILES IDENTIFIED IN THE CURED VANILLA BEANS

Aromatic constituents	**Lactones**	**Heterocyclics**	**Aliphatic constituents**
Benzaldehyde	Butyralactone	Furfural	Methyl valerate
Salicylic aldehyde	**Terpenoids**	Thiophene	Nonane
p-Hydroxybenzaldehyde	Limonene	*cis*-Vitispirane	Undecane
p-Hydroxybenzoicacid	*p*-cymene	*trans*-Vitispirane	Tetradecane
p-Hydroxybenzylalcohol	Geraniol	2-Pentyl furan	Dodecane (two isomers)
Vanillin	Myrcene	Furfuryl alcohol	Heptadecane
Vanillyl alcohol	Nerol	2-Acetylpyrrole	Eicosane
Phenolics	Linalool		Ethyl levulinate
Phenol			Octanoic acid
Guaiacol			Acetic acid
p-Ethylgauiacol			Butyric acid
Anisole			Isovaleric acid
Vanillyl methyl ether			Glycolic acid
			Lauric acid

The non-volatile constituents that impart characteristic vanilla flavour are polyphenols, resins and free amino acids. All these constituents together impart delicate, rich and mellow aroma with sweet, spicy, woody and balsamic note. The fat content of vanilla beans ranges from 4.5 to 15% and major fatty acids are oleic and palmitic acids.

Medicinal uses of vanilla

They are most commonly used in the form of extracts of the beans with various solvents and in various concentrations: (a) As stomach sedative, helps in calming an agitated stomach. (b) As natural calmative, to calm down patients undergoing

magnetic resonance imaging (MRI) and computerised axial tomography (CAT) scans. (c) It is said to exhilarate the brain, prevent sleep, increases muscular energy and stimulates the sexual propensities. (d) Also found useful in respiratory pain and congestion, deep coughs, stomach ailments and even made into a salve to treat syphilis. (e) Used in the treatment of hysteria and nervousness. (f) Also used as an aromatic stimulant, to treat rheumatism and low forms of fever. (g) Weight loss of overweight people was seen when they were given vanilla-scented skin patches and it was found that their sweet food intake was significantly reduced, leading to greater weight loss than those given dietary advice alone[6, 7]. (h) Recent research has strengthened the possibility that a form of vanilla may become a drug to treat sickle cell disease[8].

Vanilla in pharmaceuticals

Vanilla is used extensively to flavour tinctures and syrups. A sweet tincture was made to treat stomach disorders and its medicinal value was listed in the *American Pharmacopoeia* until 1916. It is used to perfume medicinal ointments, a practice that continues even today[6]. The chief constituent of vanilla, vanillin, is used for the synthesis of various active pharmaceutical ingredients (APIs) such as papaverine, L-dopa, L-methyl dopa and the antimicrobial agent trimethoprim[9].

It is used as a flavouring agent in herbal toothpaste, *e.g.*, vanilla and rose geranium toothpaste[10]. Also in the preparation of compound benzaldehyde elixir, as a vehicle for administering bromides and other salts[11].

Vanilla in food

Natural vanilla extract is gaining ground in chocolate, biscuit, ice cream, sweet dishes, cakes, puddings, soft drinks, tobacco, liquors, etc. and in confectionary as a flavouring agent. Beverage line extensions like flavoured coffee are in many cases being centred on a vanilla profile. It enhances the flavour of caramel, coffee, fruit nut and some dairy products. It is also used in spice oleoresin formulations, sausages, seasonings, etc. In all those formulations containing vanillin, vanilla flavour gives a natural rounded-off flavour[12, 13].

Natural vanilla *vs.* synthetic vanilla

Vanilla has largely been replaced by synthetic vanillin, which is much cheaper than the natural product. Synthetic vanillin, however, does not match the delicate, natural flavour of vanilla extract since it lacks the resinous and other aromatic constituents of the latter; also, the synthetic product has a less pleasant after-taste. Therefore, natural vanilla continues to find a ready market and is preferred in perfumery[3].

Handling of vanilla beans

Persons employed in handling vanilla occasionally suffer from vanillism, characterized by headache, gastric trouble and rash, the latter probably due to crystals of calcium oxalate found in the plant, and due to insect bite of grain mite of genus *Acarus* (*A.siro*) which commonly infests the vanilla pods. In addition, it was found that violent dermatitis occurred in workmen handling vanilla beans. This was found to be due to the oily exudates from the vanilla pods[15, 16].

Regulatory considerations on vanilla extract

USFDA as per title-21 Code of Federal Regulations (CFR) paragraph 169.175 states that vanilla extract is the aqueous ethyl alcohol of the sapid and odorous

principles extractable from vanilla beans. In vanilla extract, the content of ethyl alcohol should not be less than 35% by volume and the content of vanilla constituent not less than one unit per gallon. Vanilla extract may contain one or more of the following optimal ingredients: glycerin, propylene glycol, sugar (including invert sugar), dextrose and corn syrup (including dried corn syrup)[17,18].

Stability of natural vanilla flavour

Flavour and aroma changes may be due to simple viscosity increase, adsorption of the flavour compounds and changes in diffusion rate. Deterioration of vanilla flavoured formulations during storage is a direct measure of vanillin instability. Vanillin, the main flavouring component of vanilla extract, may undergo the following types of reactions leading to its organoleptic loss. It includes enzymatic oxidation, Schiff base formation and physical interactions with hydrocolloids[19]. Vanillin is stable under normal temperatures and pressures, provided if it is not in contact with incompatible materials like strong oxidizing agents, strong bases, strong reducing agents, chemicals like bromine, perchloric acid, potassium *t*-butoxide, *t*-chlorobenzene and sodium hydroxide, formic acid and thallium nitrate in particular[19].

REFERENCES

1. A.S. Ranadive, Spices, Herbs and Edible Fungi, in: G. Charlambous (Ed.), Developments in Food Science, Elsevier, New York, pp. 517–577 (1994).
2. F.E. Arana, *Puerto Rico Agr. Expt. Sta. Rpt.*, 2, 1939 (1940).
3. Wealth of India: A Dictionary of Indian Raw Materials and Industrial Products, Vol. 10: Raw Materials, pp. 432–436 (1976).
4. I. Klimes and D. Lamparsky, *Int. Flavors Food Addit.*,272 (1976).
5. A. Ranadive, *J. Agric. Food Chem.*, **40**, 1922 (1992).
6. www.vanilla.com.
7. www.ibiblio.org.
8. C. Zhang, L. Xiang, L. Lian, Q. Chen, O. Abdulmalik, V. Vassilev, C.S. Lai and T. Asakura, *Brit. J. Haematol.*, 788 (June 2004).
9. J.W. Nicholas, J.M. Melinda and N. Arjan, *Phytochemistry*, **63**, 505 (2003).
10. www.organicformulations.com.
11. Remington's Pharmaceutical Sciences, 16th Edn., Mack Publishing Company, Easton, Pennsylvania, p. 1232 (1980).
12. Anon, *Food Sci. Tech. Ab.*, **26**, 29 (1994).
13. J.W. Purseglove, E.G. Brown, C.L. Green and Robinson, Spices, Longman, London, Vol. 2, pp. 644–735 (1981).
14. www.fasthealth.com.
15. www.herbdatanz.com.
16. D.A. De Rovira (Sr.), The Dictionary of Flavors, pp. 527–529 (1996).
17. Title-21, Code of Federal Regulations, Part 169.175, U.S. Government Printing Office (Revised as of April 1, 2005).
18. Mc.G.J. Robert and V.L. Jane, Flavor-Food Interactions, pp. 24–35 (1996).
19. www.avogadro.chem.

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