The history, use, and pharmacology of spices

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Over the past few years, some who would like us to revise our eating habits have advocated a kind of simplistic asceticism. They argue that we should eat simply and functionally, eschewing wherever possible ingredients which are processed, or which do not perform a primarily nutritional role. They reserve for particular disdain those ingredients we use principally for their aesthetic value, such as colors and flavors. These they dismiss as "cosmetics," with the implication that they have no value. Few comments have been so insensitive to history, culture, and pharmacology.

This paper discusses a traditional category of those "cosmetics," the spices and herbs—broadly called "spices"—and some of their aspects.

We have used spices for millennia for their flavoring value, but they have always filled other roles as well.

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Their use must have preceded the development of writing, since many of our earliest written records refer to them as well-known and highly prized commodities. There are references in Mesopotamian and Egyptian writings to anise, indigenous to Egypt; cinnamon, which even in those days, had to come by boat from Ceylon; coriander, cumin, and dill. Undoubtedly, the Egyptians used others, but their identity is less certain.

The earliest Biblical reference to spices, in the twenty-third verse of the thirtieth chapter of Exodus, is a recipe for an anointing oil, including both cinnamon and cassia as well as something variously identified in different translations as sweet cane or calamus and the inevitable myrrh. This anointing oil was to be reserved for the priests and the sacred instruments in the Temple. Since burnt offerings, particularly of animal origin, were common in those days, one may reasonably guess that the use of the anointing oil was to mask the unpleasant odor of burning flesh. Indeed, cinnamon has been used much more recently in this way in Indian religious ceremonies. Proverbs 7:17 mentions the prostitute who sprinkled her clothes with cassia, indicating its use as a perfume. The word "perfume" incidentally comes to us from the Latin *per fumum*—"through smoke"—a reference to its use as an incense.

As communication improved in Greek and Roman times, the spice trade grew, and it became the source of the wealth of Alexandria. The middlemen there, to protect their sources, invented all kinds of wild tales about where spices grew and the conditions under which they were obtained—all in an effort to discourage those who would bypass the middleman.

This trade grew even after the fall of Rome, and the search for spices characterized much of our history as the Middle Ages moved into the Renaissance. Indeed, it was primarily the search for better routes to the source countries that led Prince Henry the Navigator to establish his famous school at Sagres. It was the impetus behind the exploratory voyages of Vasco da Gama. And it was the reason Columbus sailed east looking for the spice islands. His voyage remains to this day the best example, though a serendipitous one, of successful government-sponsored research.

It is worth asking why all this is so, and why there was this compelling need for such expensive merchandise. Why indeed should people risk life and limb and face terrible dangers, many of them no less terrible for being imaginary, simply for substances which we buy without much fuss at our local supermarket? To understand why requires reaching back into history and considering in some detail the varying roles of spices.

- Perfumes
- Offerings
- Medicines
- Preservatives

- Flavors
- Cultural Marks

We have already alluded to the use of spices as perfumes and offerings. But I doubt if any of us in the Western world today, with our refrigerated food, our daily shower, and our municipal sewerage systems—not to mention Ban, Clorets, and Lysol—can possibly imagine the value people placed only a few hundred years ago on anything that simply smelled *good*.

The next role on the list is that of medicine. Bear in mind that only 100 years ago, there were so few genuinely effective drugs—drugs that would meet today's standards of efficacy—that one can list them on the fingers of both hands: morphine and the other opium derivatives, belladonna, quinine, ether, smallpox vaccination, and a few others. Fortunately, much disease, however miserable, is self-limiting. Anything that offered relief for the patient often got the credit for the cure. There were no controlled experiments or extensive clinical trials in those days, no "Dear Doctor" letters, no FDA insisting on package inserts and patient follow-ups. The development of the more effective—and frequently more dangerous—agents in the last 50 years has coincided with the disappearance of traditional remedies, and with increasing reliance on more scientific procedures with which to evaluate efficacy. Thus, the traditional herbal remedies have dropped from use in most instances without extensive evidence either of their efficacy, or lack of it. Some are still used today in the Far East. The rationale for, and effect of such use, are extraordinarily difficult to analyze.[1]

Particularly during the Middle Ages and, indeed, until the beginning of this century, spices were esteemed as preservatives for food. Here, again, partial knowledge makes truth difficult to separate from fiction. There has been only spotty investigation of the value of traditional spices as antioxidants or bacteriostatic or fungistatic agents. We know that some, sage and rosemary, for example, have constituents, probably polyphenols, that are fairly potent antioxidants.[2,3] We know that in cloves and thyme, eugenol and thymol, respectively, have significant bactericidal effects.[4,5] The unresolved question is whether, at their high cost, they were ever used in sufficient quantity to have a truly preservative effect. They may have instead simply masked the spoilage that had already occurred.

Again, we suffer from the poverty of our own imagination. If we consider for a moment those foods which are the result of "natural" spoilage, and which we still eat because we have come to like them, foods such as beer, limburger cheese, or sauerkraut, we have a faint idea of how much of the food supply of a few hundred years ago must have tasted. Even allowing for some adaptive tolerance to rancidity and putrefaction, effective masking agents must have been very valuable indeed.

The observation that regional use of spices is roughly proportional to average daily temperature, is consistent with their effectiveness in any or all of three roles: as preservatives, masking agents, or medicines, i.e., gastrointestinal antiseptics.

As a result of their past use, spices have been incorporated into our culture. They are now accepted on aesthetic, social, and historical grounds quite removed from whatever initial circumstances may have led to their use. No one has explored this more effectively than Rozin.[6]

Because we cannot possibly consider the history, use, and pharmacology of all spices and herbs, we will examine only a sample, those we might consume in a typical evening meal.

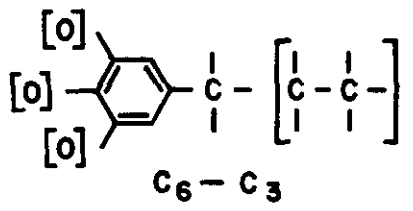
Let us begin with sesame seed chicken chunks as hors d'oeuvre. If you are a purist, sesame seed is not really a spice, since it has no volatile oil, the component which gives spices their distinctive aromas. In many other areas of the world, sesame is the principal source of vegetable oil, since it produces a high-quality oil, quite resistant to rancidity, even with the most primitive crushing and pressing equipment. The remaining seed is useful protein for humans or animals. There are few of us who have not enjoyed halvah in which crushed sesame seed is a major component. Today in the United States, we regard sesame as a spice which contributes its bland, nutty flavor to many products.

Sesame is indigenous to Indonesia and tropical Africa. It is perhaps the oldest condiment; it is probably the oldest source of vegetable oil, having been used in the Tigris and Euphrates areas about 1600 B.C. The Egyptians knew it, and called it "sesemt" or something like that. Our sesame today comes from many countries in the warm temperate zone tropics, among

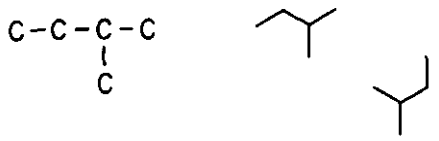
them Mexico and several Central American countries, Ethiopia, and Sudan. We even grow a little domestically, but only a little because of the high cost of labor. If one may speak teleologically, the purpose of sesame seed is to perpetuate the species, not to serve the needs of humans. To serve that earlier purpose, the seeds of the sesame plant are contained in a pod which pops open on maturity to scatter the seed—perhaps the origin of "open sesame." Humans circumvent this by hand harvesting and drying the stalks in shocks prior to maturity, thereby reducing the spillage and confining it to a smaller area. In other species, such as corn, the selection pressure of thousands of years of cultivation has totally transformed the plant from one which grew wild to one which now could not survive except under intensive cultivation. The sesame plant is more refractory; it has not yielded to this kind of pressure, although a few so-called "non-shattering" varieties have been developed and are the object of considerable current interest.

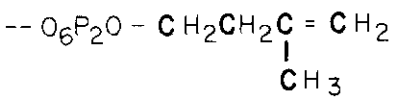
In discussing the biochemistry and pharmacology of spice constituents, it will be helpful to note certain recurrent structural features. One is a benzene ring to which at least one, and usually a chain of three, carbon atoms is attached. Opposite that side chain may be from zero to three oxygen atoms, each bearing either a hydrogen atom, a methyl group, or a methylene group (I).

Another common structural feature is the isoprene unit, a group of five carbon atoms. Two or more such units may combine in a myriad of ways (II).



I

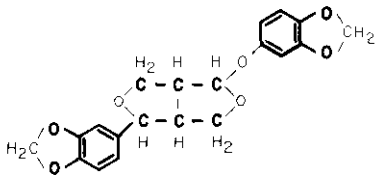
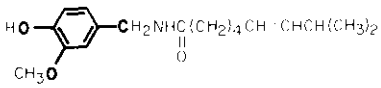
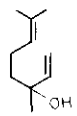
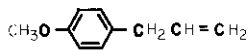
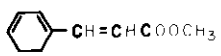




II

Sesame oil contains several constituents other than the triglycerides of which most vegetable oils, including sesame, are composed. These unusual constituents are sesamolin (III), sesamin, and sesamol. Note the benzene ring/three carbon feature we just mentioned.

Stuffed mushrooms contain nutmeg, about which more later, and a trace of red pepper and paprika. Both of them, as well as the sweet, or Bell pepper, and the hottest cayenne are known as capsicums, and

Spice	Botanical Name (and Family)	Significant Constituent(s)	Structural Formula	Structure Number
Sesame	Sesamum indicum L. (Pedaliaceae)	Sesamolin		III
Red and Bell Peppers Paprika	Capsicum annuum L., C. frutescens L. (Solanaceae)	Capsaicin		IV
Basil	Ocimum basilicum L. Labiatae)	Linalool		V
		Estragole		VI
		Methyl cinnamate		VII

come from the family *Solanaceae*, the potato family. The red pepper family, allspice, and vanilla are the three major spice contributions of the Western Hemisphere.

Columbus found the American Indians in the West Indies growing red pepper, and he took specimens with him back to Spain. The Mayans in Guatemala called it "ic," and used it not only as a seasoning, but as a medicine for cramps and diarrhea.[7] It survives today in eastern and western herbal medicine as a drug for external applications, a counterirritant in liniments,[8] and a preparation for atonic dyspepsia and flatulence.[9a]

Because red pepper grows well in many areas of the world, from fairly moist to quite dry, and the milder varieties are quite tolerant of colder weather, the plant has become widely distributed throughout the world. Thus, as Rozin has pointed out, combined with vinegar and sugar, and added to other ingredients, it becomes the sweet-sour-hot principle of Szechuan cooking.[6] It plays a fundamental role in several types of Mexican cuisine, while paprika and sour cream are typically Hungarian.

The heat or pungency of red pepper is due to "capsaicin," and to some of its close chemical relatives. So far as is known, only the capsicums appear to contain capsaicin, but its structure (IV) contains the basic framework we found only a moment ago in the wholly unrelated plant, sesame. Note also the amide group, which in capsaicin as well as in piperine to be discussed later, seems connected with the pungency.

However much one may like spinach and mushrooms, they certainly have their interest heightened by a well-balanced vinaigrette dressing. This dressing uses both basil and tarragon. Basil is a member of the *Labiatae* family, often called the mint family, although it contains many other plants of interest from hyssop and lavender to sage and catnip. It was called *tulsi* in Sanskrit, and was sacred to Vishnu. It was once believed to be an antidote to the poison of the basilisk, that mythical lizard which could kill with a glance, although it is not clear whether the name came from the antidote or the antidote from the name. It has long been thought to have preservative properties. You may recall that Salome put the head of John the Baptist in a pot of basil in order to preserve it. Dioscorides thought it was good for the eyes.[10] Basil is often called the tomato herb, but it complements a wide variety of foods, not just those in which tomatoes are used.

The principal constituents of oil of basil are linalool (V), estragole (VI), and methyl cinnamate (VII).

Fashions change in science. We no longer attribute to basil the ability to counteract the basilisk or to protect the eyesight. Today we note that estragole in high doses has been shown to cause tumors when administered to newborn mice. (Nevertheless, I finish my spinach and mushroom salad, including the dressing.)

Tarragon is from the *Compositae* family, sometimes called the sunflower family, to which, incidentally, lettuce, chrysanthemums, dandelions, and the sneezer's bane, goldenrod, also belong. It originated in Southern Russia and Western Asia, but now comes to us from France, Yugoslavia, and other European nations. Substantial quantities are also grown in the Southwestern United States. Tarragon was probably unknown to the Greeks and Romans. It is rarely mentioned in medieval works, but it was well known by the sixteenth century. Gerard, in his 1597 Herbal, warned that "it was not to be eaten alone in sallades, but joyned with other herbes as lettuce, pursalin, and such like. . . , neither doe we know what other use this herbe hath."[11] Apparently it had not been around long enough to accumulate any folklore. Tarragon's somewhat anise-like note is the distinctive flavor in Béarnaise sauce, and it is a common component of dressings, sauces, marinades, and salads. Its subtle use is part of the French wine-herb style of cooking.

The main constituents of tarragon that have been identified are our weakly carcinogenic friend, estragole and *p*-methoxycinnamaldehyde (VIII).

With roast rib of beef, we might have horseradish sauce. Horseradish is one of the *Cruciferae*, the mustard or cabbage, family. It appears to have originated in temperate Eastern Europe. It was not mentioned by that Roman gourmet, Apicius, perhaps the first of the food editors, nor did it appear to be known to ancient Oriental civilizations. It moved to Western Europe during the Middle Ages, and was taken to North America by the early colonists. We use it primarily as a source of pungency. Thus, it finds a role in many condiments and hot sauces.

In countries where folk medicine is still popular, such as India, it enjoys some use as an external counterirritant and taken internally, as a digestive stimulant. It is also a diaphoretic, i.e., it induces sweating, and a diuretic.[9b]

Its characterizing constituent, that gives it its "bite," is allyl isothiocyanate (IX), which, in the intact plant, is bound to a sugar residue. When the root is ground, however, the allyl isothiocyanate is released through the action of an enzyme in the plant tissues called sinigrin, or myrosinase.

Carrots may be flavored with, among other things, ginger. Ginger, in the Latin form, gave its name to the family, *Zingiberaceae*. It originated in Southern Asia, but spread in medieval and later times throughout the tropics of both hemispheres. It was mentioned by Confucius in his *Analects*. The Greeks and the Romans got it from Arab traders. It was known in England before the Norman Conquest. Since it was delivered to Europe even in the Middle Ages from the Far East as living rhizomes, it thus was easily transplanted to the West Indies early in the sixteenth century. Jamaica was exporting it in 1547.[7]

Ginger is an extremely versatile spice, though it should be classified as one of the "sweet spices," i.e., those that tend to be used with foods with a significant sweet note in them. It blends well with other

spices in a variety of baked foods, fruits, vegetables, and meats. With soy sauce and sherry, it is one of the basic principles of Chinese cooking.

One of ginger's non-volatile "bite" constituents is gingerol (X). But the volatile oil contains other substances, including a number of sesquiterpene hydrocarbons, such as α-curcumene (XI).

There are many sources of pungency that are used in our food—far more than we can discuss here. It is interesting to speculate on why an objectively painful stimulus should be so highly prized—a question worth pursuit.

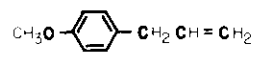
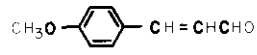
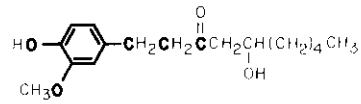
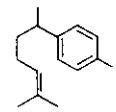
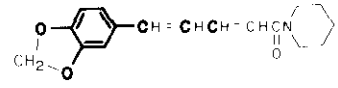
Some of you may use the pepper shaker on occasion. Pepper, one of the *Piperaceae* family, is indigenous to the Malabar Coast of Southwest India. Commercial sources today, however, include not only that area, but Indonesia, Malaysia, and Brazil, where the Japanese have established extensive plantations. White pepper and black pepper come from the same plant, *Piper nigrum*. Black pepper is picked when it is immature and green in color. On curing and drying the whole berry turns black. White pepper is picked at or near maturity when it is yellow to red. The ripe berries are steeped in water, the outer thin layer of pulp is washed away, and the kernel that remains is white pepper.

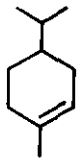
Pepper has a long history. Sanskrit medical references to it are over 3,000 years old. Theophrastus in the fourth century B.C. described it and a relative, long pepper. Pliny quoted prices. In the Middle Ages rents, dowries, and taxes were often paid in pepper, and when Alaric sacked Rome, he was paid off by the Romans in pepper. It was the need for spices, especially pepper, that drove Vasco da Gama to the Malabar Coast in 1498.

Pepper has enjoyed a substantial use in medicine. The Merck Index of 1907 mentioned its use in flatulence, dyspepsia, the ague, and wherever a stimulant, febrificient, rubefacient, a tonic, an irritant, or an antipyretic was called for.[12] Today, of course, all of that is over, and it is simply the most popular of the table spices. It goes well in any dish, except sweets, particularly with meats, fish, soups, sauces, and stews.

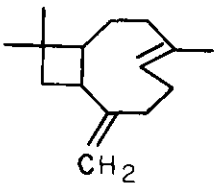
Its bite is due to piperine (XII) and some closely allied substances such as piperettine. The aroma is harder to explain. The principal constituents of the oil are a group of terpenes: limonene (XIII), β-caryophyllene (XIV), α-pinene (XV), and β-pinene (XVI). While these contribute to the odor, they are by no means its characterizing components.

For dessert let's have chocolate mousse pie accompanied by a spiced whipped cream which contains

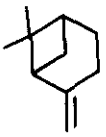
Spice	Botanical Name (and Family)	Significant Constituent(s)	Structural Formula	Structure Number
Tarragon	*Artemesia dracunculus* L. (Compositae)	Estragole		VI
		p-Methoxycinnamaldehyde		VIII
Horseradish	*Armoracia rusticana* L. (Cruciferae)	Allyl isothiocyanate	$CH_2=CHCH_2NCS$	IX
Ginger	*Zingiber officinale* Rosc. (Zingiberaceae)	Gingerol		X
		alpha-Curcumene		XI
Black Pepper	*Piper nigrum* L. (Piperaceae)	Piperine		XII



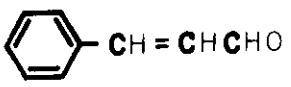
XIII



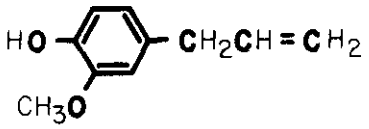
XIV



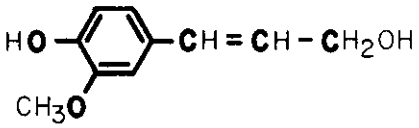
XVI



XVII



XVIII



XXIV

cinnamon, nutmeg, mace, and vanilla.

Cinnamon, you recall, is the first spice mentioned in the Bible, along with cassia. The children of Israel were aware of a distinction we in this country disregard—the difference between cinnamon and cassia. Both are members of the Laurel family, but cinnamon, properly speaking, comes mostly from Ceylon and is the species *Cinnamomum zeylanicum*, whereas several species of cassia come from Southeast Asia and China. Both are the bark. These continue to be, even today, the principal commercial sources.

The Bible mentions cinnamon elsewhere. The book of Revelations predicts the merchants will not buy Babylon's i.e., Rome's, cinnamon. Rome certainly must have had a fair amount of it in those days; Nero burned a year's supply of cinnamon at the funeral of his wife Poppaea in 66 A.D. His expensive remorse may have been because she died after he kicked her.

Cinnamon once enjoyed enormous importance as a medicine. Seventy-three years ago, The Merck Index reported that it was a laxative, a cathartic, a stomachic, a carminative, an astringent, and a stimulant.[12] Some of these uses are approved today in Eastern folk medicine. A pharmacology team visiting the People's Republic of China in the mid-1970s found it used for stomach ache, for amenorrhea and dismenorrhea, and, in common with other herbal remedies, for dysuria, the common cold, headache, and fever.[1] The volatile oil in the bark has shown antiviral, hypotensive, and cardiovascular effects.[13] Related to these may be its sedative and hypothermic action in mice. Of all these past uses, in 1980 the U.S.P. listed only its carminative—its gas-expelling—action, and Digel seeks to replace that.

The oil of both cinnamon and cassia is largely cinnamaldehyde (XVII), while that of cinnamon also contains a small amount of eugenol (XVIII).

Cinnamon and cassia are sweet spices, used particularly with baked goods and fruit dishes.

Nutmeg and mace have the unusual distinction of being spices from the same plant. The nutmeg tree is one of the *Myristicaceae*. These originated in the Moluccas and other East Indian islands, which are also today commercial sources, along with Grenada and Ceylon.

Mace is a scarlet membrane, the aril, which is wrapped around the hard seed coat which encloses the nutmeg. All of this is encased in a pulpy fruit about the size of an apricot, which on maturity, splits open to reveal the scarlet mace.

It, like other spices, was imported by Arab traders from at least Roman times onward. By the end of the twelfth century, both nutmeg and mace were well known in Europe. The supply was apparently sufficient so that in 1191 the streets of Rome were fumigated with nutmeg and other spices for the coronation of Henry VI.

Following the voyages of da Gama, Portugal found in 1512, the East Indian island of Banda, then and now a principal source of nutmeg, and, for a century thereafter, dominated the spice industry. Lisbon became the richest port in Europe. The Dutch drove the Portuguese out in 1602 and for more than a century, created a monopoly, destroying and forbidding the cultivation of nutmeg in other islands. They were finally thwarted by fruit pigeons which ate the fruits and scattered the seed wherever they chose, and by the French, who smuggled the tree to Mauritius. From there it was transplanted to St. Vincent in the British West Indies, to Trinidad, and finally to Grenada, now the principal West Indian source.

Nutmeg is another of the sweet spices, and it also enhances the flavor of meats and vegetables. It is widely used in baking, and goes particularly well with some vegetables such as spinach.

Nutmeg has enjoyed a considerable role in medicine. In India it is regarded as a stimulant, a carminative, an astringent, and an aphrodisiac. It is used "in tonics and electuaries, and forms a constituent of preparations prescribed for dysentery, stomach ache, flatulence, nausea, vomiting, malaria, rheumatism, sciatics, and the early stages of leprosy."[9c] A versatile remedy, indeed! The encyclopedia goes on to warn of its narcotic action, but adds that it is used for inflammations of the bladder and urinary tract.

Its main constituents are α-pinene (XV) and camphene (XIX). The ingenious Yankee who made Connecticut the "Nutmeg State," selling wooden nutmegs, had a good nose. A major constituent of the pine knots from which they carved these is the same α-pinene. Nutmeg also contains a substance, myristicin (XX), which is a narcotic and hallucinogen, along with a number of other closely related substances, including elemicin (XXI) and methyl eugenol (XXII).

Last on our list as an ingredient of whipped cream is vanilla. It is a member of the orchid family and native to tropical America and the West Indies. The plant is a non-woody climbing vine which grows readily from cuttings. It is occasionally pollinated in the wild by hummingbirds or perhaps some insects. But every vanilla bean of commerce is produced by hand pollinating a flower. The characteristic flavor is not present in the green bean, but develops when it is cured. The curing process begins at or shortly after maturity. It will occur naturally if the bean is left on the vine, when it begins to split at the blossom end. Scalding, freezing, or physical damage will also start the process, and these are employed commercially.

The Spanish conquistadors found vanilla already in use by the Aztecs. Bernal Diaz, with Cortez in 1520, saw Montezuma drinking *chocolatl*, a drink of roasted chocolate beans, ground corn, and honey flavored with vanilla, called by the Aztecs *tlilxochitl*. Its use spread rapidly to Europe, and by 1700 it was used in France for flavoring chocolate and tobacco—uses not different from those today.[7]

The Merck Index of 1907 reported its use as an emmenagogue, an aphrodisiac, an antihysteric, and an antirheumatic. Those have long since disappeared. We take it mostly in ice cream.

The major single characterizing component of vanilla is vanillin (XXIII), which also occurs in many aromatic resins, and in dahlia rhizomes. Vanilla contains a number of closely related substances, but these are not major flavor contributors. Much of the flavors comes from quite minor ingredients.

Even this limited review of spices permits us some generalizations. First is that their continued use as flavors necessarily involves at least one kind of pharmacological effect, that of flavor perception. Several possess other, well-established effects. Who is there who has not perspired from eating food heavily laced with red pepper? The central nervous system effects of myristicin are well known, and the side effects of abuse sufficient to discourage reuse. The antimicrobial activity of some essential oil constituents is well known, though its utility in a modern context is not well explored. That, too, implies some possible degree of activity on more complex organisms. The antioxidant activity of ingredients, such as sesamolin and sesamin, is associated with a synergistic effect

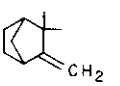
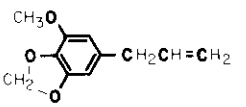
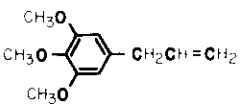
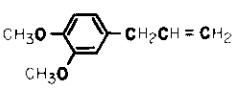
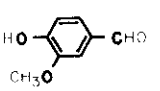
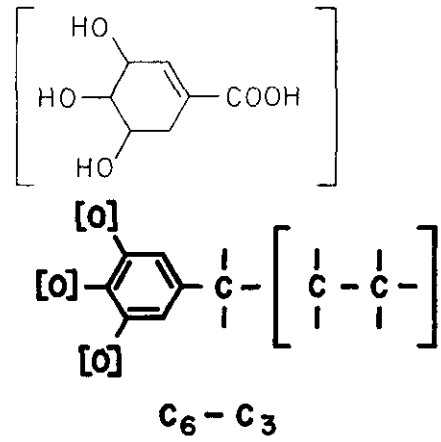
Spice	Botanical Name (and Family)	Significant Constituent(s)	Structural Formula	Structure Number
Nutmeg Mace	*Myristica fragrans* Houtt. (Myristicaceae)	alpha-Pinene		XV
		Camphene		XIX
		Myristicin		XX
		Elemicin		XXI
		Methyl eugenol		XXII
Vanilla	*Vanilla planifolia* Andrews *V. tahitensis* Moore (Orchidaceae)	Vanillin		XXIII

Table I. Total Medicinal Uses of Spices and Herbs Cited in the National Formulary

1906	125
1916	112
1936	61
1942	48
1950	25
1965	7*
1980	4*

* Used only as flavors



Shikimic Acid Pathway

when these are used together with the pyrethrin insecticides. The repeated references to the use of spices as stimulants, carminatives, stomachics, and digestives suggest that these traditionally imputed benefits certainly related to their flavor characteristics bear reinvestigation by modern methodology. All of these have implications for pharmacological effects. But it is difficult to separate folklore from reality. As mentioned earlier, we began to use more rigorous methods of assaying for pharmacological and therapeutic effects only after, as shown in Table I,[14] we had already gone long toward replacing these substances with more active synthetics.

The second generalization is that our concept of the composition of plant constituents is gradually shifting. Once we thought each essential oil had a quite different composition based on characteristic constituents, with only some overlap—an unspoken principle clearly assumed in such classical reference works as Guenther's The Essential Oils.[15] But that was before the days of gas chromatography, mass spectrometry, liquid chromatography, and our ability to isolate and identify exceedingly small amounts of substances.

There are substances which apparently are unique to a certain species or genus. Examples are sesamin and sesamolin in sesame, capsaicin in the *Capsicum* species, and piperine in the *Piperaceae*. But I have called attention earlier to the close similarities in structure between these and many of the other constituents we have discussed. It is apparent that most of them are variations on a basic structure, variations which produce remarkably different effects in flavor and pharmacological action in view of what seem to be relatively minor modifications in structure. Indeed most of the characterizing components we have discussed—gingerol, the bite ingredient of ginger, capsaicin in red pepper, estragole in tarragon and basil, piperine in black pepper, eugenol in cloves and cinnamon—are variations on the basic unit of coniferyl alcohol (XXIV), which is thought to be the fundamental building block of lignin, the skeleton of most higher plants. This structure, to which we called attention earlier and which is enclosed in the dashed line boxes in the structural formulas, is a product of one of the major routes of biosynthesis in plants, the shikimic acid pathway. Thus, not only are these substances with very different effects related to a single source, but a number of them occur very widely even through the limited number of spices discussed here. Eugenol, the major constituent of oil of cloves and the second component of cinnamon, occurs also in basil, nutmeg, pepper, and vanilla. Methyl cinnamate, the third most important component of basil, occurs also in cinnamon and vanilla.

It goes beyond this, however. The second major group of essential oil components at which we have looked are the terpene derivatives—those built up from two or more isoprene units. Here the pattern, found in structures V, XI, XIII, XIV, XV, XVI, and XIX, is even more apparent. Linalool, the major component of basil, occurs in virtually every other spice we reviewed excepting only horseradish, sesame, and tarragon, and it probably occurs in tarragon had we looked with sufficient care. α-Pinene, of real and Connecticut nutmeg fame, is the major constituent of nutmeg, and a significant component of pepper, but it also occurs in basil, in cinnamon, in ginger, and in vanilla.

Thus, we see a rather different pattern evolving as our knowledge grows. Some essential oils clearly contain one or a few constituents which themselves, or with close relatives, are characteristic of a particular genus or species. But most of the components of essential oils, including many of the most important constituents, appear to occur widely throughout nature in most of the plants examined. Thus, it is not their singular occurrence, but rather the pattern of their occurrence which gives character to the oil. This is a subtly different view of the composition of natural products from that which we first learned, but it reflects the more refined analytical knowledge of recent years. I suspect that we will continue to see it evolve.

This confirms the essential unity of nature, and provides a remarkable example of the diversity of effect which can be achieved with a remarkable economy of source and structure. Therein lies a lesson we can learn from the plant world.

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