

Taking the spice route: Psychoactive properties of culinary spices

Intoxication and toxicity can mimic psychiatric symptoms

Many substances that are not typically thought of as “substances of abuse” possess—when adequately dosed—clinically meaningful psychoactive properties. In addition to the more familiar effects of alcohol, psychostimulants, opioids, *Cannabis*, and hallucinogens, you may encounter psychiatric phenomena resulting from abuse of more obscure substances, including culinary spices.

The clinician treating a patient in an apparent intoxicated state who has a negative drug screen might ask that patient if he (she) abuses spices. This might be particularly relevant when treating patients thought to have limited access to illicit substances or those with ready access to large amounts of spices, such as prisoners, young patients, and those working in the food service industry.

Abuse of spices can be a problematic diagnosis

Patients may misuse culinary spices to achieve euphoria, or a “natural high.” They may present with medical or psychiatric symptoms, including acute altered mental status, but the psychoactive substances are not identified on routine toxicology studies. In addition, patients may not attribute their use of spices for psychoactive effect to “drugs,” because these materials are legal and readily available. This may lead to misdiagnosis of a systemic medical disorder or a primary psychiatric illness to explain the patient’s symptoms and initiating a psychotropic agent and other psychiatric services when a substance abuse program might be a more appropriate clinical intervention.

Some spices contain psychoactive compounds that can alter CNS function (*Table, page 22¹⁻⁷*), might be abused for



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Abuse of spices

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Some spices contain psychoactive compounds that can alter CNS function, might be abused, and can be toxic



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Table

Classification of culinary spices with psychoactive effects

Botanical basis	Types	Active ingredients	Psychoactive effects
Dried fruit or seeds	Nutmeg	Myristicin, elemicin, safrole	Stimulant, sedative, hallucinogenic
	Vanilla	Vanillin, piperonal	Stimulant, sedative
	Fennel	Anethole	Stimulant, sedative
	Black pepper	Piperine	Stimulant
Dried flower buds	Cloves	Eugenol	Sedative
Arils	Mace	Myristicin	Stimulant, sedative
Barks	Cinnamon, ceylon/cassia	Eugenol, coumarin	Stimulant, sedative
Roots and rhizomes	Asarone	Calamus	Stimulant, sedative
	Ginger	Gingerols, shogaols	Stimulant, sedative
	Turmeric	Curcumin	Sedative
	Galangal	1,8-cineole, β -pinene	Stimulant, sedative, hallucinogenic
	Asafetida	Resin, gum, essential oil, propenyl-isobutylsulfide, umbelliferone, vanillin	Sedative
Stigmas	Saffron	Picrocrocin, safranal	Stimulant

Source: References 1-7

recreational purposes, and can be toxic in an excessive amount. Internet resources, including anonymous web-based communications, and anecdotal materials about non-traditional recreational drugs, are available to anyone with Internet access.⁸ However, little research has been conducted into the prevalence of abuse (Box)⁹ and spices' psychoactive properties. The lack of toxicology detection of spices in the medical setting presents a diagnostic challenge.

The psychoactive plants used in "natural high" products mainly are psychoactively inactive in their natural form, but extracts or alkaloids obtained from them might induce 1 or more of 3 classifications of psychoactivity:

- stimulant
- sedative
- hallucinogenic.

Many of these substances are considered to be aphrodisiac, and some may be abused to increase sexual function.

The following is a review of common spices that have been reported to possess potential psychoactive properties.

Nutmeg

Nutmeg (*Myristica fragrans*) is a common and easily accessible means of reaching euphoria in adults.¹⁰ The aromatic oil of

nutmeg contains myristicin, a psychoactive substance that is chemically similar to hallucinogenic compounds such as mescaline. Its psychoactive effects could be attributed to metabolic formation of amphetamine derivatives from its core ingredients, elemicin, myristicin, and safrole.^{11,12}

Nutmeg and its active component, myristicin, produce central monoamine oxidase (MAO) inhibition as evidenced by the ability to lower the convulsive dose of IV tryptamine in mice and to increase brain 5-hydroxytryptamine concentrations.^{13,14} Although myristicin's potency is not comparable to that of the more potent MAO inhibitors such as tranylcypromine and iproniazid (which is not available in the United States), it seems adequate when compared with its low toxicity.¹⁴ Nutmeg extract is associated with a significant antidepressant effect in mice, which seemed to be mediated by interaction with the adrenergic, dopaminergic, and serotonergic systems.¹³ Nutmeg is associated with sustained increase in sexual activity in animal studies, with no evidence of adverse effects and toxicity, suggesting that nutmeg possesses clinically significant aphrodisiac activity.¹⁵

Psychoactive effects can be achieved by ingesting 5 to 15 g of nutmeg.¹¹ Acute nutmeg intoxication produces palpitations,

dizziness, anxiety, and hallucinations, mostly resolving within 24 hours, while effects of chronic abuse are reported to be similar to *Cannabis* use, including euphoria, giddiness, anxiety, fear, sense of impending doom, detachment, confabulation, and hallucinations.^{11,16} Urine drug screens are negative unless other psychoactive substances have been ingested.¹⁷

Suspected nutmeg intoxication or poisoning should be treated with supportive treatment. Use sedatives with caution because of alternating periods of delirium and obtundation during nutmeg intoxication.¹⁷

In case reports, myristicin poisoning induced CNS neuromodulatory signs that mimicked an anticholinergic hyperstimulation state.^{12,18} Fatal myristicin poisoning is rare; 2 cases have been reported, 1 in combination with flunitrazepam (not available in the United States).^{19,20} Nutmeg also has sedative properties and can cause GI symptoms when ingesting excessive amounts.^{1,20,21} Grover et al²¹ described no harmful effects on blood pressure and electrocardiogram; however, Shah et al²² reported palpitations and dry mouth.

Vanilla

Vanilla (species of the genus *Vanilla*) contains piperonal, also known as heliotropin.¹ Piperonal has aromatherapeutic qualities that might elevate mood and well-being. In the early 1990s, the Memorial Sloan-Kettering Cancer Center in New York City described heliotropin as a powerful aromatherapy tool. Patients who were undergoing an MRI in an environment scented with heliotropin demonstrated a 63% reduction in anxiety compared with those who were not exposed to fragrance.²³ The Smell and Taste Treatment and Research Foundation in Chicago found that vanilla can promote sexual arousal.²⁴

Short-term effects of vanillin—a major component of vanilla—include a feeling of relaxation and reduced stress; long-term use can produce an antidepressant effect.¹ There are no reports of vanilla abuse to achieve these effects; however, patients might abuse vanilla extract because of its alcohol content (up to 35% ethanol).²⁵

Box

Abuse of spices: Prevalence unknown

Epidemiology of the prevalence of abuse of culinary spices has been limited to case reports, case series, and estimates of population use based on registry-type data (eg, 17 cases of nutmeg intoxication were reported to a Texas poison control registry between 1998 and 2004).⁹ Because abuse of culinary spices does not have DSM-5 nomenclature—other than substance abuse not otherwise classified—population-based and clinical studies on prevalence are not available. However, because individual cases may present—often in acute care setting—for clinical attention, psychiatrists and other medical specialists, such as emergency physicians, should consider the possibility of culinary spice abuse in cases of intoxication that otherwise escape diagnostic classification.

Standard treatment for alcohol intoxication and withdrawal is indicated in cases of suspected vanilla abuse.

Fennel

The essential oil of fennel (*Foeniculum vulgare*) can be neurotoxic and epileptogenic. Skalli and colleagues recently reported a case of seizure induction in a young woman after ingesting cakes containing fennel oil.²⁶ Fennel oil also has been reported to have significant interaction with the fluoroquinolone-type antibiotics. Be aware of adverse effects associated with fennel ingestion; question patients if atypical seizures or reactions to antibiotics occur.²⁷

Spices such as fennel, dill, cinnamon, saffron, and anise also contain psychoactive substances that are chemically similar to myristicin, which can induce sedation, stimulation, or hallucinations.⁷

Black pepper

Piperine, which gives black pepper (*Piper nigrum*) its spiciness, enhances thermogenesis of lipid metabolism, accelerates energy metabolism, and increases serotonin and endorphin production in the brain.²⁸ Black pepper is reported to potentiate γ -aminobutyric acid A receptor subtypes,²⁹ and could present

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Treat suspected nutmeg intoxication or poisoning with supportive measures; use sedatives with caution



Abuse of spices

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Compounds found in ginger may interact with the serotonin 5-HT1A receptor, suggesting a possible mechanism for reducing anxiety

possible applications for treating insomnia, epilepsy, and anxiety disorders.

Cloves

Non-culinary uses of clove (*Syzygium aromaticum*, a tree in the myrtle family) include flavored cigarettes. However, in 2009 clove cigarettes were banned in the United States as part of a public policy to reduce the number of children who start smoking.³⁰ Eugenol, which constitutes as much as 90% of the essential oil extracted from cloves (and is responsible for the aroma), can cause hepatotoxicity³¹ and palpitations³²; it can be toxic in quantities as low as 5 mL.³³ Eugenol is present in other spices, such as nutmeg and cinnamon, and has been reported to have sedative properties.¹

Mace

Mace is made from the covering of nutmeg (*Myristica fragrans*) seeds. It has a strong aroma resembling that of nutmeg. Whole mace contains 4% to 14% of a volatile oil similar to that found in nutmeg. Because mace contains the same oils that make nutmeg psychoactive¹ in excessive amounts—although nutmeg seeds are more potent—be aware of the psychoactive potential of mace.

Cinnamon

Cassia cinnamon (*Cinnamomum aromaticum*) is spicier and tarter than Ceylon cinnamon (*Cinnamomum zeylanicum*), which has a more flowery aroma. The 2 types of cinnamon can be distinguished by their different chemical composition. Ceylon cinnamon contains eugenol and benzyl benzoate; cassia cinnamon contains coumarin.³ Eugenol is reported to have sedative effects.¹ Coumarin is a precursor molecule in the synthesis of a number of synthetic anticoagulant pharmaceuticals, including coumadin. Because of the toxic component of coumarin, European health

agencies have warned against consuming high amounts of cassia.³⁴ There are no reports of side effects arising from the occasional use of cinnamon as a spice.

In a study by Frydman-Marom et al,³⁵ cinnamon extract (CEppt) was found to act on the CNS by inhibiting development of Alzheimer's disease in animal models.

Asarone

Asarone is found in the *Asarum* family of spices that includes *Acorus calamus*. Asarone is chemically similar to mescaline. Although anecdotal reports indicate that *A. calamus* is a hallucinogen, research shows no evidence that it contains hallucinogenic substances.³⁶ Han et al³⁷ reported an antidepressant effect with the essential oil and asarones for the rhizomes of *Acorus tatarinowii*. In animal studies, asarone was found to reduce spontaneous motor activity, and even in low doses, reduced anxiety without decreasing acuity of perception.³⁸

Ginger

Ginger (*Zingiber officinale*) is regarded as a sedative, general stimulant, and aphrodisiac.^{1,4,5} Its main constituents are phenolic compounds such as gingerols and shogaols, and sesquiterpenes such as zingiberene.⁴ Ginger is an inhibitor of thromboxane synthetase, a property shared by tricyclic antidepressants.³⁹

Research indicates that 9 compounds found in ginger may interact with the serotonin 5-HT1A receptor, suggesting a possible mechanism for reducing anxiety.⁴⁰ A study by Nievergelt et al⁴¹ indicates that by binding to human serotonin receptors, ginger might influence GI function. Ginger extract contains a cholinergic and spasmogenic component, which provides a mechanistic insight for the prokinetic action of ginger.⁴⁰

Turmeric

Turmeric (*Curcuma longa*) has been investigated for possible benefit in Alzheimer's disease⁴²; research into curcumin, the active substance of turmeric, is increasing. Although the original report was retracted after publication, curcumin was reported to selectively bind to hu-

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Physicians practicing in an environment where street drugs are difficult to obtain (eg, prisons) should consider monitoring for abuse of spices

man cannabinoid receptors type 1 (CB1) with nanomolar affinities and to function as an antagonist/inverse agonist.⁴³ However, Gertsch et al⁴⁴ found that curcumin did not interact functionally with the CB1 receptor, although this compound appears to share the ability of the CB1 receptor inverse agonist.

Galangal

Major constituents identified in the galangal (or galanga) rhizome and leaf oil were 1,8-cineole, and β -pinene and camphor.⁶ Galangal, a member of the ginger (*Zingiberaceae*) family, interacts with MAO inhibitors, H2 receptor antagonists, and proton-pump inhibitors.¹ Anxiolytic, hallucinogenic, and stimulant properties have been reported.¹ An excessive amount can induce diarrhea, dizziness, nausea, and vomiting.¹

Saffron

Stigma of saffron (a member of the family *Iridaceae*) was found to be significantly more effective than placebo and equally as efficacious as fluoxetine and imipramine in treating depression. Saffron petal was found to be significantly more effective than placebo and as effective as fluoxetine and saffron stigma in a recent systematic review.⁴⁵⁻⁴⁸

Asafetida

Asafetida (*Ferula assa-foetida*), when combined with valerian root, is used as a sedative to treat hyperactivity.² The active ingredients of asafetida are the resin, endogenous gum, essential oil, propenyl-isobutylsulfide, umbelliferone, and vanillin. Several of the volatile constituents produce a sedative effect.² Additive effects can occur between the hypotensive property of asafetida and dopamine receptor agonists such as bromocriptine mesylate. Use caution when combining asafetida in conjunction with a CNS depressant or a stimulant.²

Recommendations for treating spice-abusers

Patients may present to psychiatry services with psychological and physiological evidence of intoxication with culinary

spices that may mimic 1) abuse of other substances, 2) primary psychiatric illness, and 3) primary medical illness. When you encounter a patient with a new psychiatric symptom, consider inquiring about the abuse of spices.

Patients might abuse more than 1 spice; a comprehensive screening approach might therefore be useful. Caution patients that ingesting these substance to excess can have harmful effects. Consider appropriate psychopharmacotherapy for underlying psychiatric symptoms to help patients who use spices maladaptively to self-medicate psychiatric symptoms.

Consider abuse of culinary spices in clinical presentations of psychiatric symptoms that do not seem adequate for a diagnosis of a primary anxiety, mood, or psychotic disorder, or in cases atypical psychiatric presentations that are—perhaps to your surprise—associated with negative toxicology studies for common, more familiar substances of abuse.

Physicians practicing in an environment where street drugs are difficult to obtain (eg, prisons) should consider monitoring for possible abuse of spices. Based on the available, albeit limited, literature, it appears that most culinary spice-associated intoxication can be managed:

- with an elevated level of clinical suspicion
- by ruling out other causes of intoxication
- using targeted, empirical psychopharmacotherapy to manage symptoms
- with supportive care that includes close psychiatric follow-up.

Consider comorbid abuse of other, more familiar substances of abuse in patients who misuse spices. As with inhalant abuse, the concept of “substance abuse” in clinical practice may need to be further expanded to include patients who abuse culinary spices. Patients could be screened for psychiatric illnesses known to increase the risk of substance abuse. These might include—but are not limited to:

- comorbid psychotic disorders
- mood disorders, particularly bipolar disorders
- trauma- and stressor-related disorders, particularly posttraumatic stress disorder

- personality disorders, particularly anti-social, borderline, and narcissistic personality disorders.

Pending the availability of population-based studies on abuse of culinary spices, the usual cautions regarding substance abuse seem to be appropriate when caring for these patients. Assessment for and management of comorbid psychiatric conditions is essential in the comprehensive psychiatric care of patients who abuse substances.

Last, general consideration of a 12-step recovery program appears warranted for these patients; the self-reflection and group support of such programs can be useful in helping patients control their use of these substances.

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Drug Brand Names

Bromocriptine mesylate • Parlodel	Imipramine • Tofranil Iproniazid • Marsilid
Flunitrazepam • Rohypnol	Tranylcypromine • Parnate
Fluoxetine • Prozac	

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continued

Clinical Point

Consider comorbid abuse of other, more familiar substances of abuse in patients who misuse spices

Bottom Line

Presentation of culinary spice intoxication can parallel that of other medical or psychiatric illnesses, or other drugs of abuse. Consideration and questioning for abuse of spices is necessary to ascertain the psychoactive effects of these substances when used surreptitiously. Management should follow substance abuse treatment protocols: inquiry into patterns of problematic use and readiness to change, assessment and management of psychiatric comorbidity, and referral to a recovery program.



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The self-reflection and group support of 12-step programs can be useful in helping patients control their misuse of culinary spices

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