Nervine Herbs for Treating Anxiety

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Nervine Herbs for Treating Anxiety

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Abstract

Anxiety is a common ailment in our society. However, the drugs available to treat mild-to-moderate anxiety, particularly benzodiazepines, are problematic because they can cause injury, produce side-effects, and create dependence. Nervine herbs have been widely used historically to treat mild-to-moderate cases of anxiety, and these herbs appear to be very safe, nonaddictive but their properties as anxiolytics have been poorly researched.

This article discusses the clinical uses of a number of nervines: oat seed (*Avena* spp.), hawthorn (*Crataegus* spp.), California poppy (*Eschscholzia californica*), lavender (*Lavandula* spp.), chamomile (*Matricaria recutita*), lemonbalm (*Melissa officinalis*), passionflower (*Passiflora* spp.), skullcap (*Scutellaria lateriflora*), and verbena (also called vervain; *Verbena* spp.).

Introduction

Botanical practitioners often prescribe nervine herbs to help their patients cope with stress, anxiety, insomnia, mild depression, and similar problems. These herbs have a long history of traditional use and appear to be safe and effective. Unfortunately, they have received little to no scientific attention.

A recent French clinical study pointed out the great need for serious research on the use of nervines. The authors explained that patients frequently consult their physicians about anxiety disorders, and estimated that 25 percent of adult French patients suffer from some type of anxiety disorder.[1] The statistics also show that anxiety disorders are common in American patients.[2] Typically, anxiolytics or hypnotics, most commonly benzodiazepines, are prescribed for these patients. However, the use of these drugs is problematic.

With short-term use, because of their sedative nature, they can cause loss of memory, may disturb balance in elderly patients, may produce degradation of sleep quality, and may diminish alertness in drivers, leading to accidents and injuries. These agents can also cause rebound insomnia and anxiety after discontinuation or paradoxical worsening of anxiety during use. With long-term use, the drugs can lead to dependence and withdrawal symptoms as well as such-side effects such as somnolence, fatigue, gastrointestinal (GI) upset, and vertigo.

If traditional wisdom and the current professional evaluation of nervines are correct, botanicals may provide a much better initial prescription for most of these patients, allowing practitioners to reserve the stronger pharmaceuticals for more difficult and persistent cases of anxiety. It follows that research to evaluate the clinical effectiveness and safety of these herbs in mild-to-moderate anxiety disorders should be made a much higher priority than at present.

In fact James A. Duke, Ph.D., the renowned botanist and ethnobotanist (formerly with the U.S. Department of Agriculture, and now at Green Farmacy, Fulton, Maryland) has proposed that all drug trials funded by the National Institutes of Health should be required to compare drugs not just to placebo but also to an herbal medicine (personal communication with Dr. Duke, June 2004).

In the meantime, this article explains how nervines are commonly used in practice and attempts to clarify some of their clinical distinctions. When relevant research is available, this is noted but, because such research is limited, the article mainly describes present clinical pictures.

A few botanicals—such as St. John's wort (*Hypericum* spp.) for mild-to-moderate depression, kava (*Piper methysticum*) for mild-to-moderate anxiety, and valerian (*Valeriana* spp.) for insomnia—have a substantial amount of research support and those uses are not discussed. Instead coverage includes some commonly used but less well-known nervines. Tables 1 and 2 provide additional information on most of the nervines in use, including some of their specific uses and dosages and include these three herbs.

Hawthorn and California Poppy

In the French study mentioned above, researchers administered a tablet combining 75 mg of dried hydroalcoholic extract of hawthorn flower (*Crataegus oxyacantha*, now known as *C. laevigata*), 25 mg of dried aqueous extract of California poppy flower and 75 mg of elemental magnesium. Patients took 2 tablets twice daily for 3 months. Two hundred and sixty-four (264) patients participated in this multicenter study, which measured a change in Hamilton anxiety scale, change in patient self-assessment, number of responsive subjects (defined as at least 50-percent reduction on the Hamilton or self-assessment scale), and the physician's clinical global impression. Only physicians specializing in the evaluation of drugs in mental disorders participated.

As in most anxiety studies, the placebo response was high (40 percent). However, the decrease in Hamilton anxiety scale results and the self-assessment of anxiety results were both significantly

greater in the herb group than in the placebo group. The physicians rated the combination formula, with 90 percent in favor of the study drug as opposed to 80 percent for placebo. The researchers elected not to include a benzodiazepine arm as they were looking for a clinical solution to mild-to-moderate anxiety rather than a substitute for those drugs. The researchers concluded that the combination formula was an effective and safe alternative, symptomatic treatment for mild-to-moderate anxiety states in clinical practice.

Interestingly, hawthorn is not typically considered a nervine. Instead, this herb is primarily viewed as a heart medicine and is fairly well-researched as such. However, many herbal practitioners have noted that hawthorn has a calming effect and that it can also help alleviate cardiac symptoms of anxiety such as palpitations and increased blood pressure.

Unlike hawthorn, the lovely California poppy is primarily used as a nervine. The California and the opium poppy (*Papaver somniferum*) are in the Papaveraceae family although only opium is narcotic. California poppy will not produce a high and helps to normalize psychologic function. This herb has mild analgesic effects and is a lighthearted calmer.

Surprisingly, low-dose opium appears to have similar effects to California poppy, being described as an antidepressant and hypnotic in older herbals.[3] Only at high doses or as purified heroin or morphine, does opium dull consciousness, cause euphoria, and induce sleep.

There are anecdotal reports that California poppy used alone has helped individuals overcome their fear of flying or of public speaking. Nonetheless, most clinicians seldom use California poppy alone, instead using it to harmonize and boost the actions of other nervines. In a lower dose in a mood formula, California poppy makes life seem a little better, a little more manageable, to patients. In a higher dose in a sleep formula, the herb makes the patient more ready to fall asleep. Mixed with valerian or other herbs, California poppy creates a sleep mixture that works if pain, say from a sprained ankle, is interfering with sleep.

Studies show that California poppy tea reduces anxiety, acts as a mild analgesic, and helps prevent drug-induced memory loss in mice.[4] Animal studies confirm that an aqueous–alcoholic extract of California poppy has sedative effects at higher doses and anxiolytic effects at lower doses.[4] California poppy contains protopine, a com-

Table 1. Other Common Clinical Uses for Nervines[a]

Herb Common name (Latin binomial)	Easily fatigued; mildly depressed	Anger issues	Trouble with concentrating	Sleep problems (Nonorganic)	Heart palpitations	Panic	Other major indications
California poppy (*Eschscholzia californica*)				X		X	Pain
Chamomile (*Matricaria recuita*)		X	X	X			Indigestion; inflammation
Hawthorn (*Crataegus* spp.)					X		Cardiovascular disease
Kava (*Piper methysticum*)			X	X		X	Pain; addiction
Lavender (*Lavandula* spp.)	X			X			Infections
Lemonbalm (*Melissa officinalis*)	X		X			X	Viral infections
Linden (*Tilia* spp.)				X	X		Viral infections
Motherwort (*Leonuris cardiaca*)			X	X	X		Uterine weakness
Oats (*Avena* spp.)	X	X	X			X	Addiction
Passionflower (*Passiflora incarnata*)			X	X	X	X	Pain
Skullcap (*Scutellaria lateriflora*)		X					Pain
St. John's wort (*Hypericum* spp.)	X		X				Neuropathy; viral infections
Valerian (*Valeriana* spp.)				X		X	Pain
Verbena (*Verbena* spp.)		X					Hormonal imbalance; indigestion

[a]Notes: X = Indication for use; each herb is used as a nervine to address general anxiety and irritability.

pound that is suggested to have both antiacetylcholinesterase and antiamnesic properties.[5] The extracts injected i.p. did not induce any acute toxic effects and its LD_{50} was more than 5000 mg/kg.

Native Americans claimed that even the scent of California poppy was poisonous to pregnant women, and it is contraindicated in pregnancy because its constituent allocryptopine (and possibly other alkaloids) have an oxytocic effect.[6] There are no other known adverse effects, contraindications, or interactions.

Immature Oat Seed

One of the safest and most popular nervines is the immature seed of oats. It is prescribed for acute and chronic anxiety, stress and excitation, neurasthenic and pseudoneurasthenic syndromes, skin diseases, connective tissue deficiencies, weakness of the bladder, and as a tonic and roborant. The German Commission E, however, concluded that its effectiveness for these conditions had not been established.[7]

The Eclectics considered tincture of oat seed to be a mild stimulant and nerve tonic and many Eclectics considered it to be of some importance for treating nervous debility and afflictions bordering closely upon nervous prostration. The herb was deemed useful for treating headaches resulting from exhaustion or overwork or the nervous headache sometimes associated with menstruation. But the Commission cautioned that oat seed was not a remedy of great power and would not always be useful. The Eclectics did not consider this herb's use for addressing morphine addiction to be substantiated.[8]

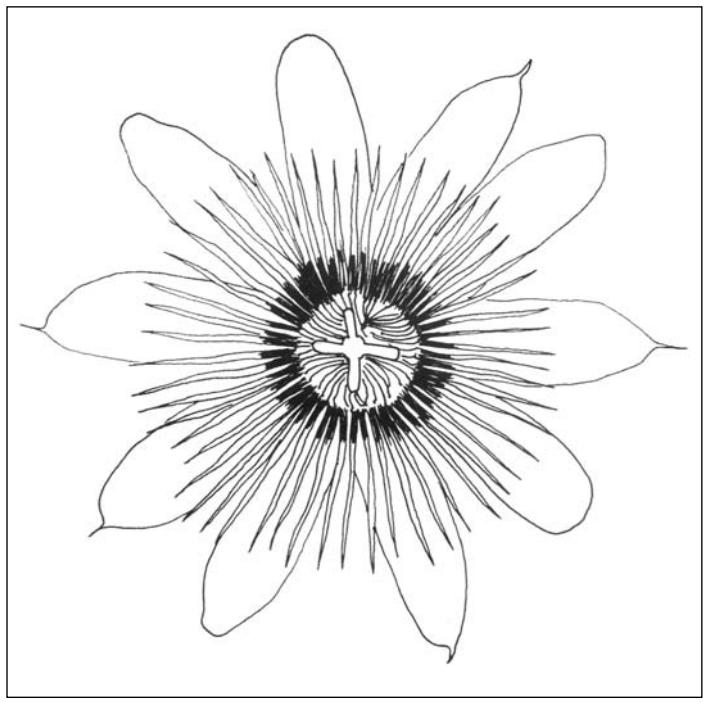
Many Western herbalists prefer to use oat seed tincture as a simple to quiet temporary, mild anxiety or to take the edge off moods that might otherwise be expressed as angry outbursts or losses of self-control. We have also used it for dogs to calm them and avert seizures.

Oat seed tincture is frequently included as an ingredient in formulas intended to help patients quit smoking. This aspect of oats has been the subject of some research, mostly with negative results.[9,10]

These results mirror the conclusion of the Eclectics: Oat seed is not strong enough to have a substantial effect on serious addictions such as cigarette smoking, although the herb's calming effect may be somewhat helpful as a component of a treatment for these addictions. Oat seed is, however, safe for use in essentially anyone, with no known contraindications, adverse effects, or interactions.

Passionflower

Passionflower leaf may be more useful in formulas for treating addiction. The herb is frequently used in herbal sleep formulas as well as in calming formulas for treating anxiety. The German Commission E has approved the use of passionflower for addressing nervous restlessness.[7] According to the Eclectics, passionflower was specifically indicated for irritations of the brain and nervous system with atony, insomnia from worry or overwork or from febrile excitement, sleeplessness of young or aging patients, convulsive movements, hysteria, infantile nervous irritability, dyspnea, or heart palpitations from excitement or shock.[8] Passionflower was considered to be a very effective remedy for whooping cough and spasmodic asthma.



Passionflower (*Passiflora* spp.). Drawing ©2004. Kathy Abascal, B.S., J.D., R.H. (AHG).

In patients who are addicted to heroin, passionflower significantly enhanced the effect of clonidine for reducing withdrawal symptoms.[11] In this study, 65 patients who were addicted to an opiate were randomly assigned to take either clonidine and 60 drops of passionflower extract (further details were not provided) or clonidine and 60 drops of placebo liquid, 3 times daily, for 14 days. The Short Opiate Withdrawal Scale was used to assess the benefit of adding passionflower to the regimen.

Passionflower was as effective as oxazepam in the treatment of 36 patients with generalized anxiety disorder and was preferred over the drug by the researchers because the herb did not impair job performance.[12] The patients (20 women and 16 men) who met the *Diagnostic and Statistical Manual of Mental Disorders IV* criteria for a diagnosis of generalized anxiety disorder with a duration of at least 6 months participated in this 4-week-long trial. A proprietary liquid extract of *P. incarnata* (45 drops/day) was used in the study, and a psychiatrist assessed the patients, using the Hamilton Anxiety Scale (HAM-A) on 6 occasions during the study.

A passionflower constituent (a trisubstituted benzoflavone moiety) reversed tolerance and dependence on several psychotropic drugs in rats, including morphine, nicotine, ethanol, diazepam, and delta-9-tetrahydrocannabinol.[13] The herb enhanced libido and reduced the libido-depressing action of the psychotropic drugs in animals.[13,14] The herb had an anxiolytic effect in mice at doses of 50–150 mg/kg.[15]

Passionflower had a synergistic effect when administered with kava to mice.[16] Kava had a more pronounced effect on reducing amphetamine-induced hypermotility while passionflower prolonged barbiturate-sleeping time more than kava did. However, another study revealed that passionflower reduced the hexobarbital sleeping time of mice.

One pharmacologic study failed to show that passionflower bound to benzodiazepine, dopaminergic, or histaminergic receptors in vitro.[17]

Numerous species of *Passiflora* have been considered for use as medicine, primarily *P. incarnata* and *P. edulis*. One animal study found that while *P. incarnata* was active as an anxiolytic, *P. edulis* was devoid of any activity.[18] *P. incarnata* is also the species most commonly referenced by older herbals. Therefore, until and unless *P. edulis* is shown to be as or more effective than *P. incarnata*, *P. incarnata* should be used preferentially.

There are reports of passionflower causing tachycardia but the herb's overall safety profile is very high and passionflower can be used in pregnancy.[19] There are lingering concerns that aqueous passionflower extracts can increase serum amylase levels, presumably because of pancreatic damage, as has been observed in clinical trials.[20] Actual pancreatitis has only been reported very rarely so these laboratory changes are of unknown importance.

Lemonbalm

Lemonbalm leaves have a long history of use as anxiolytics and memory support. The German Commission E has approved the use of lemonbalm for addressing nervous sleeping disorders and functional GI complaints. Clinicians often prescribe lemonbalm as a mild mood elevator and calming herb for patients who have anxiety.

Table 2. Doses for Nervines and Possible Safety Considerations[a]

Herb Common name (Latin binomial)	Adult dose, tincture	Negative drug interactions	Safety concerns
California poppy` (*Eschscholzia californica*)	0.5–1 mL qid	Theoretical concern that it may potentiate monoamine oxidase–inhibitors	None known; Considered safe in pregnancy
Chamomile (*Matricaria recuita*)	4–6 mL tid	—	None known; Considered safe in pregnancy
Hawthorn (*Crataegus* spp.)	4–5 mL tid	—	None known; considered safe in pregnancy
Kava (*Piper methysticum*)	3–5 mL tid	Theoretical concern that it may increase toxicity of hepatotoxic drugs	Not safe in pregnancy; not for use in patients with liver ailments, patients on drugs that tax the liver, or patients who frequently consume alcohol; not for long-term use.
Lavender (*Lavandula* spp.)	1–2 mL tid	—	None known; considered safe in pregnancy
Lemonbalm (*Melissa officinalis*)	2–5 mL tid	—	None known; considered safe in pregnancy
Linden (*Tilia* spp.)	3–5 mL tid	—	None known; considered safe in pregnancy
Motherwort (*Leonuris cardiaca*)	1–2 mL qid	—	None known; considered safe in pregnancy
Oats (*Avena* spp.)	Tincture 1–5 mL qid	—	None known; considered safe in pregnancy
Passionflower (*Passiflora incarnata*)	3–5 mL tid	—	None known; considered safe in pregnancy; isolated reports of tachycardia and pancreatitis
Skullcap (*Scutellaria lateriflora*)	3–5 mL tid	—	None known; considered safe in pregnancy
St. John's wort (*Hypericum* spp.)	Tincture 2–5 mL qid	Can decrease blood levels of many prescription medications, including birth control pills, protease inhibitors, warfarin, and digoxin	Possible photosensitization but likely to be rare; otherwise none known; considered safe in pregnancy
Valeriana spp. (valerian)	4–8 mL qd–tid	—	None known; considered safe in pregnancy
Verbena (*Verbena* spp.)	1–3 mL tid	—	None known; not safe in pregnancy

[a]Note: Most nervines are poorly studied and their possible interactions with drugs are not fully known.

In a randomized, placebo-controlled, double-blinded crossover trial of 20 healthy volunteers, lemonbalm produced a sustained improvement in accuracy of attention and calmness at the lowest dose (300 mg/day) and a reduction of alertness and memory decrements at the highest dose (900 mg/day).[21] The study failed to confirm a significant effect on cholinergic binding.

The researchers noted that the lowest dose of lemonbalm appeared to be most efficacious and also noted that the low cholinergic-binding properties might have been a result of the loss of volatile components in the product used. We, and many other practitioners, prefer to use only products made from fresh lemonbalm to preserve these vital components.

Lemonbalm essential oil had a calming effect on patients with Alzheimer's disease.

In a double-blinded, randomized, placebo-controlled trial, 42 patients with mild-to-moderate Alzheimer's disease were given a daily dose of 60 drops of lemonbalm tincture over a 4-month period.[22] Lemonbalm significantly improved cognitive function compared to placebo, with significant improvement in cognition seen after 16 weeks of treatment. In addition, agitation was more frequent in the placebo group. This correlated with another clinical trial that indicated that lemonbalm essential oil had a calming effect on patients with Alzheimer's disease.[23]

At low doses, lemonbalm was said to have a sedative effect on mice (it increased their comfort with being in open spaces, which is interpreted as an anxiolytic effect); at higher doses, the extract had a peripheral analgesic effect and potentiated the sedative effect of pentobarbital.[24]

Lemonbalm does have a thyroid-inhibiting action (by acting both on thyroid-stimulating hormone [TSH] and on the cellular TSH receptor) in vitro.[25] Today, lemonbalm is sometimes used clinically to treat hyperthyroidism based on these in vitro studies. Yet, the general practitioner consensus is that the herb can be used safely in patients with low thyroid function. It may be that other constituents in the plant offset the effects of the isolated constituent in vitro.

Lemonbalm is also useful for treating herpes and other viral infections, and its pleasant lemony flavor often makes it useful as a taste enhancer in formulations.

Lemonbalm is exceedingly safe and is often used in children. There are no known drug interactions or contraindications. A typical adult dose of the fresh herb tincture is 2–5 mL, 3 times daily.[26]

Vervain

Verbena (or vervain) has a widespread and very long history of use. The Druids considered this herb to be sacred and used it in ceremonies and religious rites. The name "vervain" comes from the Celtic *ferfaen*, which meant "to drive away a stone," referring to a traditional use of verbena for treating bladder problems and urinary stones. The physicians of Myddfai in thirteenth-century Wales recommended verbena for addressing all diseases but especially those of the liver, lungs, and kidneys.[27] It was widely used in various traditions for treating colds, dyspepsia, weak nerves, and liver disorders. In South America, the herb continues to be used to stimulate milk production, especially in overstressed new mothers.[28]

As a nervine, the leaves and flowers of *Verbena* species are often used when there is a component of anger or agitation present in the patient. Herbalist Michael Moore, director of the Southwest School of Botanical Medicine, Bisbee, Arizona, gives the following clinical picture of a patient who is likely to benefit from the use of verbena:

> Verbena is useful in a flushed, red faced or angry person, it is a menopausal nervine that chills and calms, allowing sleep; it also quiets those sudden angry outbursts that frequently occur in perimenopause. It will have the same effect on younger women with outbursts related to premenstrual syndrome.

Dr. Moore also considers verbena to be a great occasional herb to use for children who are worked up, red in the face, overexcited, and unable to calm down (personal communication with Dr. Moore).

The German Commission E concluded that there was not enough evidence to establish the effectiveness of verbena for treating ailments of the oral and pharyngeal mucosa (angina, sore throats), of the respiratory tract (coughs, asthma, whooping cough), pain, spasms, exhaustion, nervous conditions, digestive disorders, liver and gallbladder diseases, jaundice, diseases and ailments of the kidneys and lower urinary tract, menopausal complaints, irregular menstruation, or lactation.[7] The Commission does consider verbena to be secretolytic.

Verbena's use as a nervine has not been researched. Several constituents in *V. littoralis* H.B.K. enhanced the activity of nerve growth factor–mediated neurite outgrowth in vitro.[29–31] The various verbena species are considered to be largely interchangeable in clinical practice.[32]

Verbena, in vitro, displayed a higher degree of binding to progesterone receptors and increased the progestin activity of saliva to a greater degree than did 150 other herbs and spices. Information on whether this activity constituted a significant effect was not available.[33]

In an abstract, it was reported that verbena combined with many other herbs (black cohosh [*Acatea racemosa*], red clover [*Trifolium* spp.], wild yam [*Dioscorea villosa*], sage [*Salvia spp.*], chasteberry [*Vitex agnus-castus*], astragalus [*Astragalus membranaceus*], motherwort [*Leonurus cardiaca*]) and soy isoflavones in an open-labeled study dramatically decreased menopausal symptoms of tiredness, absent-mindedness, and lack of energy as well as the typical menopausal symptoms of hot flashes, heart palpitations, and night sweats.[34]

Lavender (*Lavandula* spp.).

Lavender and Linden

Lavender leaf and linden (*Tilia spp.*) flower are two nervines with more pronounced sedative effects. Lavender is a mint native to the Mediterranean region while linden, sometimes slightly confusingly called lime flower, is in the Tiliaceae family and is not in any way related to true lime.

The German Commission E has approved the use of lavender flowers for addressing mood disturbances, such as restlessness or insomnia, functional abdominal complaints (nervous stomach irritations, intestinal gas), and nervous intestinal discomfort.[7]

The Eclectics considered lavender to be an agreeable and soothing lotion for treating headaches related to debility and fevers.[8] The herb was an ingredient in a soothing syrup prescribed for nervous irritability in children.

Practitioners today often add lavender as a component in a nervine formula, and consider the herb to be helpful but tend not to use it as a stand-alone treatment. The essential oil is commonly used as a calmative, to relieve mild headaches, as an antimicrobial, and to treat minor burns.

Historically, linden flowers were used in many parts of the world as sedatives, tranquilizers, and diuretics. Today, the flowers' primary use is as a treatment for colds and flu. Herbalists and other natural medicine practitioners also use linden flowers to relax blood vessels, and the herb is often used in small doses to calm older, nervous people and reduce high blood pressure. In larger doses, the flowers are used to encourage good, restful sleep.

Animal studies tend to confirm these uses as they show that linden flowers reduce anxiety in mice, reduce blood pressure, and have a sedative effect at higher doses. The flowers contain mucilages, flavonoids, phenolic carbon acids, and essential oils.[35] It has been reported that fresh infusions of linden prolonged the swimming time of mice in a forced swimming test, which is interpreted to indicate an antistress effect.[36]

A flavonoid complex injected i.p. in mice produced a clear anxiolytic effect.[37] Another study reported that a freeze-dried aqueous extract of linden produced sedative effects in mice at doses ranging from 10 to 100 mg/kg.[38]

Linden extracts injected into rabbits produced a hypotensive effect with a large drop in diastolic arterial pressure, indicating vasodilation.[39] An aqueous extract of linden flowers stimulated lymphocyte production in vitro, with an action mimicking that of two drugs that act as agonists of the peripheral benzodiazepine receptor, perhaps suggesting that linden also is an agonist of this receptor.[40]

Some concerns have been raised that, because linden contains vitamin K, it may lessen the effect of warfarin or related anticoagulant therapy. However, the usual doses of linden are far too low to contain and deliver sufficient vitamin K to interfere. Generally, linden is considered to be a safe herb that can be used in pregnancy.

Conclusions

The nervines discussed in this article have a long history of use in many different folk traditions for improving mental functioning, moods, and sleep. These herbs continue to be widely used in a similar fashion by most botanical practitioners and appear to be very safe and effective for addressing mild-to-moderate anxiety and its many symptoms. Further research into the clinical effectiveness of these plants as a first-line treatment for anxiety should be made a high priority, reserving pharmaceutical drugs such as benzodiazepines for more persistent or difficult cases of anxiety. □

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