

Guaifenesin for Fibromyalgia and Chronic Pain Syndromes:

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Guaifenesin has been used for years as an expectorant and mucolytic; it helps loosen sputum so that it can be coughed up easier. Mucinex is a common trade name for this medication (guaifenesin is the generic name), but it is a component in many medications, often combined with other agents to help its therapeutic effect. Guaifenesin is often mixed with dextromethorphan (DM), a cough suppressant for the additive effect of helping to increase sputum production, lessen the thickness/stickiness of the sputum while suppressing cough that would otherwise be nonproductive.

Guaifenesin has been known to help Fibromyalgia Rheumatica (FMR) more than Chronic Fatigue Syndrome (CFS) since the early 1990s. Unfortunately, it's just not well known. FMR as a diagnosis has been in use for many years. Nobody has been able to explain the root cause of the disease; what is it and why does it happen? Some believe that it's a "wastebasket" term. This does not mean that it doesn't exist, rather the concept that perhaps many various illnesses have the aches, pains & fatigue as a common final result; FMR may be more than simply *one* illness.

Certain substances however may block the benefit of guaifenesin on FMR. The main blocker of the benefit is a group of compounds known as "salicylates".

First, a bit of chemistry to put us all on the same page; an acid is a molecule that wants to lose a proton (H⁺), it often ends with the letters "-ic". Base or alkaline compounds tend to want to accept a proton. If an acid is in an alkaline solution it loses the proton and the name changes to end in "-ate". "Salicylic acid" has the proton, but in body fluids; which typically have a pH of around 7.4, it's going to lose the proton and be called "Salicylate". Acetyl-Salicylic Acid (ASA) is the chemical name for "Aspirin". Salicylates are fairly common compounds, they can be found in a variety of over-the-counter (OTC) medications, topically applied creams, etc.

Folks taking salicylate-type compounds for whatever reason, including low dose aspirin to prevent stroke or heart attack may not get the benefit of guaifenesin. They may get a partial benefit, but even without use of salicylates, we all have different body chemistries.

Unfortunately, not everybody with FMR will benefit from guaifenesin; we don't know why (yet), but it's inexpensive and can be very effective, it's certainly worth a try. When using it however, it's best to try to get it in its pure form, without "-DM" or any other added ingredient.

Thus, given the variety of symptoms and health problems that can occur in people with fibromyalgia, it is unlikely that a single remedy can treat all the symptoms that a person is likely to suffer with this syndrome. Because of this, it's common for fibromyalgia patients to use a wide range of different remedies and treatments.. In fact, [in a survey of 1200 fibromyalgia patients, no one medicine was being by more than 20% of the](#)

[patients](#). It's almost impossible to find two people with fibromyalgia, who are taking the same combination of remedies and supplements.

Guaifenesin can have many beneficial effects for FMR patients:

1. It has skeletal muscle-relaxing properties;
 - a. Guaifenesin carbamate, under the trade name “Robaxin” is a muscle relaxant, other forms are used at higher doses in veterinary medicine, mephenesin, a similar medication can even result in short-term paralysis.
 - b. Carisoprodol (Soma) & Felbamate (Felbatol, which unfortunately causes blood cells to rupture-hemolysis) are still used as muscle relaxers.
 - c. These drugs are a class of compounds known as *propanediols*. A patient who is allergic to one drug of this class will probably also have problems with other drugs of the class.
 - d. Guaifenesin’s effect as an expectorant may be in part due to relaxing smooth muscle spasm in the bronchi, it can also help with gut spasms—which makes it useful for *Irritable Bowel Syndrome (IBS)*, which frequently is found in folks with FMR.
2. It has neurologic effects; it depresses the transmission of nerve impulses in the central nervous system (CNS; brain & spinal cord), it can relieve anxiety while relaxing tense muscles.
 - a. Miltown was an early antianxiety agent that was quite addictive, based on a chemical cousin of guaifenesin.
 - b. Decreasing *central sensitization* in the CNS is a big key to reducing FMR pain.
3. It helps increase excretion of uric acid, which is responsible for gout and may have a role in FMR.
4. It inhibits platelet aggregation (like aspirin does to prevent blood clots).
 - a. In a recent study on fibromyalgia, it's been found that some fibromyalgia symptoms correlate with [lower levels of serum serotonin and higher levels of plasma serotonin](#).
 - b. But platelet activation, which causes platelet aggregation, also causes the release of serotonin, resulting in high plasma serotonin levels.
 - c. In addition, only in the last few years has it been recognized that serotonin influences many other problems, such as migraines, hypoglycemia (low blood sugar), [asthma](#), [Raynaud's](#), and IBS, all conditions which are associated with fibromyalgia.
 - d. Some of these conditions are exacerbated due to serotonin's ability to cause constriction.
 - e. Many other drugs and supplements for fibromyalgia inhibit platelet aggregation. All of the following have some affect on platelet activity:
 - i. Some antidepressants, especially tricyclic antidepressants.
 - ii. Benzodiazepines such as alprazolam (Xanax) & diazepam (Valium).
 - iii. Antihistamines such as Benadryl.
 - iv. Anesthetics such as procaine.

- v. Supplements such as *MSM, ginkgo, pycnogenol, quercetin, and bromelain*.
 - vi. *Magnesium* (many folks in developed countries with highly refined diets have chronically low magnesium levels, simple serum levels won't pick it up as it's an intracellular ion).
 - vii. *Vitamin B12* (homocysteine increases platelet aggregation).
 - viii. *Whey* (treats glutathione deficiency, which causes platelet aggregation).
 - ix. Amino acids such as *taurine and arginine, and relaxin* (presently experimentally used for fibromyalgia).
- f. One could hypothesize that some of the people in the guaifenesin study, who did not see any benefit from guaifenesin, might have already been taking a supplement or medicine that inhibited platelet activation, and thus were not affected by the addition of guaifenesin.
- g. An excess of anything that causes vasodilation, which then leads to capillary permeability can also cause edema. Abnormally high levels of *cortisol* are known to cause this, and studies have shown higher that levels are increased in some people with fibromyalgia. Other substances such as *serotonin and histamine* can also cause vasodilation. These substances are released when blood platelets are activated.
5. Analgesic (pain reducing) effects.
- a. This is probably due to its effect in the CNS by increasing levels of the amino acid *glycine* and by decreasing the effect of excitatory amino acid (EAA) neurotransmitters such as *glutamate* (of note, *glutamine* is an inhibitory amino acid and may also help control pain in FMR).
 - b. [Combined glutamate \(excitatory\) & glutamine \(inhibitory\) amino acid neurotransmitters are found in the posterior cingulate cortex.](#)
 - c. [Guaifenesin at such sub effective doses, is able to increase the analgesic effect of paracetamol \(Tylenol\).](#)
 - d. [Plus, guaifenesin is believed to have an additive effect on narcotics.](#)
 - e. The addition of guaifenesin to doxepin may be of particular value when painful spasticity is present." Doxepin is a tricyclic antidepressant.
 - f. As an aside, [neurontin at low doses is able to potentiate the analgesic property of opioids such as morphine.](#) This potentiating property is likely due to an antagonistic effect on excitatory amino acids.
 - g. Increased levels of EAAs are known to cause tolerance and [the loss of antinociceptive \(pain-relieving\) response to morphine,](#)
 - h. Given the possibly unique mode of action of guaifenesin, i.e. an anti-excitatory amino acid effect, it might explain why some people with fibromyalgia have noticed an effect from it, while others have not.
 - i. Many drugs used for fibromyalgia have varying success between patients. For example, different [people respond to different painkillers, showing that not all people with fibromyalgia are experiencing the same pain problems.](#)
 - j. Some people who have a higher baseline level of pain have fewer flare ups; this may be due to the production of more endorphins by the body to

control the higher baseline pain covers the flare up of their symptoms. With the use of guaifenesin, the improvement in the base cause of illness may lower pain, making patients more susceptible/noticeable of these flare-ups.

6. Guaifenesin helps lower anxiety with [higher levels of glutamate & glutamine compounds in the right amygdala of the brain](#) this is associated with decreased levels of pain intensity, more fatigue and depression

Pharmacology of Guaifenesin (ADME);

Absorption;

Guaifenesin is well absorbed from the GI tract.

Distribution;

Guaifenesin is widely distributed in the aqueous compartment of the body.

Metabolism;

Guaifenesin is metabolized to inactive metabolites in the liver Cytochrome P450 subsystems (including 1A2, 2C9, 2D6, 3A4) as many other drugs are. Rapidly hydrolyzed (60% within seven hours) and then excreted in the urine, with beta-(2-methoxyphenoxy)-lactic acid as its major urinary metabolite. It's half-life (time it takes for half of it to be removed from the body) is about an hour)

Excretion;

Inactive metabolites, mainly glucuronates & sulfates are excreted through the kidneys. With this metabolism and excretion, disorders of liver and kidneys may require dosage reductions to avoid toxic effects.

Adverse Effects;

Guaifenesin can have adverse effects, most notably [headaches, dizziness](#), diarrhea, nausea, vomiting, rash, stomach pain, and hives. It also has effects throughout the body on Dopamine D3 receptors, Substance-K receptors, Leukotriene C4 synthase, Thromboxane-A synthase, Beta-2 adrenergic receptors & matrix metalloproteinase-9. The lethal dose required to kill 50% of rats given the medication (LD₅₀) is 1,510 mg/kg.

Notes;

These side effects may represent the clearance of toxins related to the illness. FMR symptoms also are known to cycle; some days are better, some days are worse, "flare ups". It's possible that the changes in symptoms are due more to this cycling than to any benefit or harm from any given therapy. In order to correct for this variability, longer-term monitoring of symptoms is necessary.

Safety;

Guaifenesin is pregnancy category "C"; there are no adequate studies in pregnant women (but it's been used for years without known problems).

Breastfeeding; no adequate studies have been done.

Dosing;

200-400 mg every 4 hours for adults, 100-200 mg every 4 hours for children 6-12 years old, 50-100 mg every 4 hours for children 4-6 years old and not recommended for children under 4 years of age.

12 mg/kg/day orally in 6 divided doses

To achieve short-term paralysis in large animals, a dose of 50 mg/pound is needed, thus for a 100 pound person, a dose of 5,000 mg would be needed—this would be for a single

dose however as it's a short-acting medication. Doses of up to 5,000 mg/d can be safe, but are not recommended without medical supervision.

What causes FMR?

Central Sensitization of Pain-role of the spinal cord & brain and chronic pain;

"FMR pain is frequent in the general population but its pathogenesis is only poorly understood. Many recent studies have emphasized the role of central nervous system pain processing abnormalities in FMR, including central sensitization and inadequate pain inhibition. However, increasing evidence points towards peripheral tissues as relevant contributors of painful impulse input that might either initiate or maintain central sensitization, or both. It is well known that persistent or intense nociception can lead to neuroplastic changes (biochemical & microscopic brain tissue changes) in the spinal cord and brain, resulting in central sensitization and pain. This mechanism represents a hallmark of FMR and many other chronic pain syndromes, including irritable bowel syndrome, temporomandibular disorder, migraine, and low back pain. Importantly, after central sensitization has been established only minimal nociceptive (pain resulting from an injury) input is required for the maintenance of the chronic pain state. Additional factors, including pain related negative affect and poor sleep have been shown to significantly contribute to clinical FMR pain. Better understanding of these mechanisms and their relationship to central sensitization and clinical pain will provide new approaches for the prevention and treatment of FMR and other chronic pain syndromes."

This theory explains why people with different conditions and symptoms can all have fibromyalgia. Anything that causes pain, can initiate fibromyalgia. The nervous system is transformed, resulting in a centralized chronic pain state, such that even much lower amounts of pain will continue to maintain the condition. Other factors that increase pain sensitivity, such as a sleep disorder, will further maintain the condition.

If you have only a single source of pain, then if you treat that single source, perhaps this might cause the fibromyalgia to resolve. On the other hand, for people who problems are not treatable, then the fibromyalgia will be maintained, as it will continue to have sources of pain that will constantly aggravate it.

This theory of fibromyalgia explains why so many widely different treatments are claimed to help fibromyalgia. Treating any source of pain will reduce fibromyalgia symptoms. And if some people had the specific problem that the treatment was best designed to treat, then in those people, their fibromyalgia would essentially resolve. If you look on the web, you will find numerous claims of people find a cure for fibromyalgia. Unfortunately, some people deduce from this that their treatment could cure fibromyalgia for everyone, which might not likely be the case.

A treatment that directly affects muscle pain, would likely have the most success. [Muscle pain has been found to be particularly efficient at stimulating centralized pain](#), so that muscle pain may especially cause fibromyalgia to persist. One possible reason for muscle pain in FMR, is the reduction of microcirculation blood flow in muscles, which has been seen in some studies. Some researchers theorize that this is the most common reason for fibromyalgia. For a description of this theory, see the [2005](#)

[article written by Professor Charles J. Vierck, former head of the Department of Neuroscience at the University of Florida College of Medicine](#), who has published a number of studies on fibromyalgia. In that article, he concludes: “The majority of FM cases develop as a consequence of a peripheral insult and associated nociceptive input [pain resulting from injury] that is long-lasting because of inadequate healing. Centrally enhanced nociceptive input produces sympathetic activation. Also, chronic, persistent pain from any source, local or generalized, causes stress. Nociceptive input to the cerebral cortex and limbic system causes stress reactions involving the hypothalamic pituitary axis (HPA) and sympathetic nervous system. Abnormally high sympathetic activation results in not enough blood flow to deep tissues. Muscle nociceptors are highly sensitive to low blood flow, which produces FMR pain in deep tissues. Therefore, focal pain of peripheral origin can produce widespread effects with chronic magnification by CNS processing. This also appears to create a predisposition toward development of IBS and interstitial cystitis by FMR patients.”

If the peripheral generator(s) for chronic pain could be silenced, all components of FM should not develop or would fall away, and FM would be prevented or cured.” This researcher’s theory is that increased sympathetic nervous system activity (i.e. elevated norepinephrine) is the reason for reduced blood flow in muscles, which then causes muscle pain, and this becomes a major source of pain that sustains the hyperactive central nervous system. Other researchers also believe that norepinephrine is a significant factor. Elevated levels can occur due to a number of reasons. Stress is the most common reason, and pain can be a source of stress. Thus, fibromyalgia in some people could be a cyclic problem, i.e. stress causes pain, and pain causes stress. However, other factors may also be present. Elevated levels of the inflammatory cytokine IL-8 has been found to be elevated in some fibromyalgia studies, and this can increase sympathetic activity.

According to the above article, one way to combat the reduced blood flow is via physical therapy and exercise, as trained muscles have increased blood flow (and also lower insulin resistance).

Another way to increase blood flow is by reducing muscular tension: “when (EMG) biofeedback procedures have been utilized to directly reduce muscular tension, 5 of 6 studies reported reductions of clinical pain and tender point numbers or sensitivity. For one of these investigations, EMG biofeedback was significantly effective compared to subjects receiving false EMG feedback. A 4.5-year prospective study has included EMG recordings and concluded that reductions in muscular tension correlated with pain reduction (Wigers, 1995).”

The muscle relaxant Flexeril is commonly used in fibromyalgia. But since that drug also has beneficial effects on sleep, some doctors attribute its usefulness for fibromyalgia on its ability to improve sleep, rather than its muscle relaxant capabilities. However, this may not be the case. Recently, one researcher has found that [low doses of both Flexeril, and the muscle relaxant Zanaflex, were both effective for fibromyalgia, even at doses lower than suggested by the Physicians Desk Reference](#). The doses were given both in

the morning and the afternoon, which would seem to imply that the positive effects were possibly due to muscle relaxation, rather than due to a direct effect on sleep. Guaifenesin's effects on the nervous system are totally different from most other muscle relaxants. People who respond to one muscle relaxant, may not respond to another, and vice versa.

In any event, if it is true that reduced blood flow in muscles is capable of causing fibromyalgia, the beneficial effects from muscle relaxants may be due to an improvement of blood flow. And if this was the only major source of pain that a person with fibromyalgia had, then in theory the fibromyalgia could be reversed by a muscle relaxant. This could explain any claim of reversal of fibromyalgia by guaifenesin. However, many people with fibromyalgia have multiple sources of pain. A treatment that only reduces one source of pain will not be successful at treating fibromyalgia in people who have other sources of pain, such as inflammation, physical defects, sleep disorders, immune dysfunctions, infections, and hormonal imbalances. In those cases, several treatments will have to be used together, in order to have a chance at effectively treating fibromyalgia.

Hormones affect FMR;

Estrogen may be a factor in women, since it's known to inhibit platelet aggregation. Fibromyalgia is more likely to occur in older women, when estrogen levels are decreasing.

Other hormonal imbalances, such as a deficiency of either progesterone or testosterone, can play a major role in fibromyalgia symptoms. Progesterone not only has hormonal effects, but also has many neurological ones. A progesterone deficiency can lead to symptoms commonly found in fibromyalgia, such as [disturbed sleep and migraines](#). The effect that causes migraines, may be related to a release of substance P, a neurotransmitter that is involved in the pain process, and known to be elevated in fibromyalgia. [Studies show that progesterone can reduce levels of substance P. Progesterone also appears to be able to relieve pain, via an effect on NMDA neuron receptors](#), receptors that play a role in pain perception.

Low levels of testosterone, both in men and women, can also play a role in chronic pain. [Testosterone may be the reason why many more women have chronic pain problems, such as fibromyalgia, than men](#). A study has shown that [testosterone is significantly lower in some groups of women with fibromyalgia](#). And another study has shown that [low testosterone can lead to low levels of ATP in muscles](#). Additionally, there is ongoing research to [develop a testosterone patch to help treat fibromyalgia patients that have low testosterone](#).

And, as an aside, one of the reasons why some people with fibromyalgia can't tolerate narcotics may be because [opioids are known to suppress hormones such as testosterone, progesterone, and growth hormones](#).

Certain infections, such as candida, can increase platelet activity, as platelets secrete toxins against infections. [Lyme disease might also increase platelet aggregation](#).

The use of amino acids, which have been found to be low in diabetes. Taurine and arginine have been successfully used to reduce platelet aggregation. Since amino acid levels have been found to abnormal in both fibromyalgia and CFS, this is another possible factor.

["Tendons and ligaments are often the last to clear so always expect aches and pains of considerable duration in those regions."](#) Thus, according to the treatment, it's possible to be on guaifenesin for years, but still continue to experience pain.

The guaifenesin treatment also has major psychological benefits. The main benefit is that one is able to picture one's pains in a more optimistic positive light. One's normal response to pain is to reduce activity, as pain is usually a signal to the body that an injury has occurred. Unfortunately, inactivity leads to unconditioned muscles, which is a major problem in many people with fibromyalgia. Constant pain and inactivity can then lead to other problems, such as myofascial pain. Gentle exercise and stretching can be beneficial to both problems. [Studies have shown if one is assured that pain is not indicative of an injury, this makes the person more willing to keep active and exercise and work through the pain, and this can lead to the lowering of pain levels.](#) While on the guaifenesin treatment, pain is attributed to the reversal process, and is thus thought to be a good sign. Pain is less frightening. Combining this outlook, with increased physical activity, and a possible neurological effect on pain and muscles, could lead to a significant improvement of fibromyalgia.

Thyroid under activity should be investigated and treated.

Glycine is another amino acid that may be depleted in FMR sufferers; it should be looked for and corrected with glycine supplements. It is used up when the liver metabolizes salicylates (which should be avoided anyway) as well as benzoates (from benzoic acid, a preservative) & cinnamic acid (from cinnamon).

What is causing the platelet aggregation? There are many possible reasons. A magnesium deficiency can be the cause. Another interesting possibility is that low levels of certain antioxidants factors, glutathione and thiols, [can also be the cause.](#) This is interesting because some people with fibromyalgia and CFS appear to have this condition, and people have found benefit from taking supplements that increase glutathione, such as special forms of whey. Elevated blood homocysteine levels is also a possible cause. This can be due to a B12 deficiency, and many people with CFS and fibromyalgia find benefit from taking B12 shots. Homocysteine levels are also increased in hypothyroidism, and hypothyroidism is commonly found in fibromyalgia patients. [The present TSH normal range, is still viewed by some people as being too wide.](#)

Additional aids to FMR Relief;

Sleep apnea and sleep-disordered breathing can aggravate FMR; evaluation in a sleep lab can be helpful.

Glutathione (GSH) deficiency can be partially corrected by taking supplemental amino acids such as Cysteine which is important component of GSH (GSH isn't absorbed well when swallowed). GSH is an important anti-oxidant that removes free radicals.

Sulfur deficiency should be sought & corrected.

Overuse of Acetaminophen (Tylenol) can cause depletion of sulfur.

Sulfur deficiency can also cause hypoglycemia (low blood sugar) should be considered and corrected with the appropriate high-protein diet.

Hypoglycemia aggravates FMR.

Serotonin, which is important on the clotting effects of guaifenesin, is also important with hypoglycemia. Serotonin can increase insulin levels, which cause blood sugar to drop.

[Platelet aggregation sensitivity is increased due to hypoglycemia.](#)

For those suffering from gluten sensitivity, also known as celiac sprue, [plasma serotonin in celiac patients has been found to be elevated.](#)

In addition, platelet activity causes a release of other substances that might be affecting fibromyalgia. For example, ATP is also released, and this might be the cause of reduced levels of ATP found in red blood cells of people with fibromyalgia.