



FEVERFEW

Also Known As:

Altamisa, Bachelor's Buttons, Featherfoiul, Featherfew, Featherfoil, Flirtwort
Midsummer Daisy, Santa Maria, Tanaceti parthenii.

CAUTION: See separate listings for Buttercup and Cornflower.

Scientific Name:

Tanacetum parthenium, synonyms Chrysanthemum parthenium, Chrysanthemum
praealtum Leucanthemum parthenium, Matricaria eximia, Matricaria parthenium,
Pyrethrum parthenium.

Family: Asteraceae/Compositae.

People Use This For:

Orally, feverfew is used for fever, headaches, prevention of migraines, and menstrual irregularities. It is also used orally for arthritis, psoriasis, allergies, asthma, tinnitus, vertigo, nausea and vomiting. Feverfew is also used for infertility, anemia, cancer, common cold, earache, liver disease, prevention of miscarriage, muscular tension, orthopedic disorders, swollen feet, diarrhea, and dyspepsia including indigestion and flatulence.

Topically, feverfew is used for toothaches and as an antiseptic and insecticide. It is also used as a general stimulant and tonic and for intestinal parasites.

Safety:

LIKELY SAFE ...when used orally and appropriately, short-term. Feverfew has been used safely in studies lasting up to 4 months (6959, 6960, 6961, 13239).

There is insufficient reliable information available about the safety of the long-term use of feverfew.

PREGNANCY: POSSIBLY UNSAFE ...when used orally. Feverfew might cause uterine contractions and abortion (12); avoid using.

LACTATION: Insufficient reliable information available; avoid using.

Effectiveness:

POSSIBLY EFFECTIVE

Migraine headache. There is some evidence that taking feverfew orally can reduce the frequency of migraine headaches and reduce symptoms of pain, nausea, vomiting, and sensitivity to light and noise (5080, 6959, 6960, 6961, 12384, 13239). It may be more effective in patients with more frequent migraine attacks (12384). But there is also evidence that feverfew does not improve migraine symptoms or reduce the occurrence of migraine headache (6938, 12153, 12384). These conflicting findings may reflect differences in the harvested feverfew plants, extracts used, or differences in bioavailability of commercially prepared feverfew products (12153). A combination product containing feverfew, riboflavin, and magnesium doesn't seem to reduce the frequency or severity of migraine any better than placebo. However, some problems with study design

suggest that more research should be conducted on this combination (12389). Most studies have used feverfew products standardized to contain 0.2% to 0.35% of the parthenolide constituent, but this standardization does not seem necessary for effectiveness (6935, 6938). Other studies have used a specific supercritical carbon dioxide extract (MIG-99), which is enriched with parthenolide (12384, 13239).

POSSIBLY INEFFECTIVE

Rheumatoid arthritis (RA). Taking feverfew orally doesn't seem to reduce the symptoms of RA (6933).

There is insufficient reliable information available about the effectiveness of feverfew for its other uses.

Mechanism of Action:

The applicable part of feverfew is the leaf. At least 39 constituents of feverfew have been identified (724). However, there has been controversy regarding which constituents were responsible for feverfew's pharmacological effects. It used to be widely believed that the sesquiterpene lactone, parthenolide, was the active constituent (6935). Parthenolide, seems to selectively inhibit cyclooxygenase-2 (COX-2) and the proinflammatory cytokines tumor necrosis factor (TNF)-alpha and interleukin (IL)-1 (12483). It was suggested that at least 0.2% of parthenolide was required for efficacy for migraine (6935, 6937). However, a study using an alcoholic extract of feverfew standardized to 0.35% parthenolide was found ineffective for preventing migraine (6938), suggesting that parthenolide may not be the active ingredient and that other constituents are necessary for benefit in the prevention of migraine (49, 6935, 6938). It's not yet clear how feverfew works in the prevention of migraine. Laboratory evidence suggests that feverfew extracts might inhibit platelet aggregation and inhibit serotonin release from platelets and leucocytes (6935, 6936, 6942, 6943, 6944, 6945); however, platelet studies in people have not found this effect (6951). Feverfew might also inhibit serum proteases and leukotrienes (6939, 6946). Feverfew also appears to block prostaglandin synthesis by inhibiting phospholipase, which prevents the release of arachidonic acid (6943, 6953, 6954). Preliminary research shows that extracts of fresh feverfew leaves and parthenolide might cause irreversible inhibition of vascular muscle contraction (6948, 6950). Chrysanthenyl acetate, an essential oil of feverfew, has been suggested as one active component (6938). Chrysanthenyl acetate inhibits prostaglandin synthetase and might have analgesic properties (6713, 12153). Feverfew also contains melatonin which might contribute to its pharmacological effect (50). Fresh or dried leaves contain significantly more melatonin than commercially prepared standardized feverfew tablets (50). Migraine attacks have been associated with decreased melatonin excretion (6712). Other pharmacological effects of feverfew include cytostatic effect on tumor cell growth (6957), inhibition of inflammation and pain transmission (6947), and anti-inflammatory effects (6941).

Adverse Reactions:

Orally, feverfew is well tolerated. It can cause gastrointestinal symptoms such as heartburn, nausea, diarrhea, constipation, abdominal pain and bloating, and flatulence. It can also cause nervousness, tension headache, insomnia, dizziness, stiffness in joints, tiredness, menstrual changes, palpitations, skin rash, and weight gain (12383). The traditional method of feverfew administration, chewing fresh feverfew leaves, can result in mouth ulceration, inflamed oral mucosa and tongue, swelling of the lips, and occasionally, loss of taste (6935, 6959). Mouth ulceration might result from direct contact with feverfew leaves during chewing, possibly attributable to the sesquiterpene lactone constituent (6959). Some researchers suggest that mouth ulceration is a systemic effect, but one study using dried feverfew capsules reported a higher incidence of mouth ulcers in subjects taking placebo than feverfew (6935, 6959).

6960). "Post-feverfew syndrome," including anxiety, headaches, insomnia, and muscle and joint stiffness, has been described in people who have taken feverfew over long periods of time (6959).

Topically, allergic contact dermatitis can occur (6958).

Overall, feverfew might be better tolerated than some conventional migraine drugs used for prophylaxis. For example, in clinical trials, feverfew did not affect blood pressure, heart rate, body weight, blood chemistry, or cytology; like some conventional drugs do such as ergot derivatives, serotonin agonists ("triptans"), beta-blockers, valproic acid, and analgesics (6959, 6960, 6961, 6965, 12153). Feverfew may cause an allergic reaction in individuals sensitive to the Asteraceae/Compositae family. Members of this family include ragweed, chrysanthemums, marigolds, daisies, and many other herbs.

Interactions with Herbs & Supplements:

ANTICOAGULANT/ANTIPLATELET HERBS AND SUPPLEMENTS: Some evidence suggests that feverfew may inhibit platelet aggregation. However, this has not been demonstrated in humans (6935, 6936, 6942, 6943, 6944, 6945, 6951). Theoretically, concomitant use of feverfew and herbs that affect platelet aggregation could increase the risk of bleeding in some people. Some of these herbs include angelica, clove, danshen, garlic, ginger, ginkgo, Panax ginseng, horse chestnut, red clover, turmeric, and others.

Interactions with Drugs:

ANTICOAGULANT/ANTIPLATELET DRUGS

Interaction Rating = **Moderate** Be cautious with this combination
Severity = High • Occurrence = Possible • Level of Evidence = D

Some evidence suggests that feverfew may inhibit platelet aggregation. However, this has not been demonstrated in humans (6935, 6936, 6942, 6943, 6944, 6945, 6951). Theoretically, feverfew might have additive effects and increase the risk of bleeding when used with these drugs.

CYTOCHROME P450 1A2 (CYP1A2) SUBSTRATES

Interaction Rating = **Moderate** Be cautious with this combination
Severity = Moderate • Occurrence = Possible • Level of Evidence = D

There's preliminary evidence that feverfew might inhibit cytochrome P450 1A2 (CYP1A2) (12479). So far, this interaction has not been reported in humans. However, watch for an increase in the levels of drugs metabolized by CYP1A2 in patients taking feverfew. Some drugs metabolized by CYP1A2 include amitriptyline (Elavil), haloperidol (Haldol), ondansetron (Zofran), propranolol (Inderal), theophylline (Theo-Dur, others), verapamil (Calan, Isoptin, others), and others. Use feverfew cautiously or avoid in patients taking these drugs.

CYTOCHROME P450 2C19 (CYP2C19) SUBSTRATES

Interaction Rating = **Moderate** Be cautious with this combination
Severity = Moderate • Occurrence = Possible • Level of Evidence = D

There's preliminary evidence that feverfew might inhibit cytochrome P450 2C19 (CYP2C19) (12479). So far, this interaction has not been reported in humans. However, watch for an increase in the levels of drugs metabolized by CYP2C19 in patients taking feverfew. Some drugs metabolized by CYP2C19 include proton pump inhibitors including omeprazole (Prilosec), lansoprazole (Prevacid), and pantoprazole (Protonix); diazepam (Valium); carisoprodol (Soma); nelfinavir (Viracept); and others.

CYTOCHROME P450 2C9 (CYP2C9) SUBSTRATES

Interaction Rating = **Moderate** Be cautious with this combination
Severity = Moderate • Occurrence = Possible • Level of Evidence = D

There's preliminary evidence that feverfew might inhibit cytochrome P450 2C9 (CYP2C9) (12479). So far, this interaction has not been reported in humans. However,

watch for an increase in the levels of drugs metabolized by CYP2C9 in patients taking feverfew. Some drugs metabolized by CYP2C9 include nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac (Cataflam, Voltaren), ibuprofen (Motrin), meloxicam (Mobic), and piroxicam (Feldene); celecoxib (Celebrex); amitriptyline (Elavil); warfarin (Coumadin); glipizide (Glucotrol); losartan (Cozaar); and others. Use feverfew cautiously or avoid in patients taking these drugs.

CYTOCHROME P450 3A4 (CYP3A4) SUBSTRATES

Interaction Rating = **Moderate** Be cautious with this combination
Severity = Moderate • Occurrence = Possible • Level of Evidence = D

There's preliminary evidence that feverfew might inhibit cytochrome P450 3A4 (CYP3A4) enzyme (12479). So far, this interaction has not been reported in humans. However, watch for an increase in the levels of drugs metabolized by CYP3A4 in patients taking feverfew. Some drugs metabolized by CYP3A4 include lovastatin (Mevacor), ketoconazole (Nizoral), itraconazole (Sporanox), fexofenadine (Allegra), triazolam (Halcion), and numerous others. Use feverfew cautiously or avoid in patients taking these drugs.

Interactions with Foods:

None known.

Interactions with Lab Tests:

None known.

Interactions with Diseases or Conditions:

CROSS-ALLERGENICITY: Feverfew may cause an allergic reaction in individuals sensitive to the Asteraceae/Compositae family. Members of this family include ragweed, chrysanthemums, marigolds, daisies, and many others.

SURGERY: Feverfew has antiplatelet effects. Feverfew might cause excessive bleeding if used perioperatively. Tell patients to discontinue feverfew at least 2 weeks before elective surgical procedures.

Dosage/Administration:

ORAL: For migraine headache prophylaxis, clinical studies have used 50-100 mg of feverfew extract daily. Most extracts used in clinical studies were standardized to 0.2% to 0.35% parthenolide content, however, this standardization does not appear to be necessary for effectiveness (6935, 6938, 6959, 6960, 6961). Other studies have used a specific supercritical carbon dioxide feverfew extract (MIG-99) enriched with parthenolide (12384, 13239).

TOPICAL: No typical dosage.

Editor's Comments:

Some feverfew tablet products can contain little or no feverfew. The Therapeutic Products Directorate of the Health Products and Food Branch of Health Canada issued a Drug Identification Number (DIN) to a feverfew leaf (capsules) product standardized to 0.2% parthenolide, with the labeling claim "used as a prophylactic against migraines" (724).

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