

Name of Herb: Feverfew, A member of the *Asteraceae* or *Compositae* family¹

Scientific names: *Tanacetum Parthenium*^{1,2}, *Tanacetum Parthenium*^{1,2}, *Chrysanthemum parthenium*^{1,2}, *Leucanthemum Parthenium*^{1,2}, *Pyrethrum Parthenium*^{1,2}

Common names: Altamisa^{1,2}, Bachelor's Button¹, Featherfoil^{1,2}, Featherfew^{1,2}, Featherfoil^{1,2}, Flirtwort Midsummer Daisy^{1,2}, Santa Maria¹, Mother-herb², Febrifuge plant²

Description of active ingredients:

The chemical constituents are sesquiterpene lactones, which include germacranolides (parthenolide), guaianolides (chrysanthemin and partholide) and eudesmanolides (magnolialide, reynosin and santamarin).² All of these are α -unsaturated γ -lactones.² The effectiveness of various feverfew preparations in inhibiting the release of serotonin from human blood platelets has been found to correlate with parthenolide content in freeze-dried or air-dried whole feverfew leaf.³

Mechanism of Action:

In 1985, it was reported that extracts of feverfew inhibited the release of 2 inflammatory substances; serotonin from platelets and prostaglandin from white blood cells.³ Both are thought to contribute to the onset of migraine attacks and perhaps even to play a role in rheumatoid arthritis.³ By inhibiting these amines as well as the production of histamine, the herb controls inflammation that constricts the blood vessels in the head, and prevents blood vessel spasms which may contribute to headaches.⁴

Other possible mechanisms are that it suppresses production of prostaglandin, thromboxane and leukotriene, constituents prevent formation of inflammatory mediators by inhibiting cellular phospholipases and release of arachidonic acid from cell membrane, and extracts inhibit platelet aggregation.² There has not been proof of these pharmacologic actions to have an effect on migraine prophylaxis.² This remains to be unclear.²

Current indications and efficacy:

Feverfew is indicated for the prophylaxis of migraines, but has not been approved by the German Commission E.² Feverfew is described in folklore references to treat fever, arthritis, toothache and insect bites, but these uses are without clinical or scientific support.² Uses supported by peer-reviewed human data showed subjects who took one capsule of dried feverfew leaves a day (2.19 μ mol parthenolide over 4 months) was associated with a reduction in the number (24%) and a trend towards severity of migraine attacks, and significantly showed improvement in visual analogue scores with feverfew in a randomized, double-blind, placebo controlled trial with 76 subjects.⁶ This study supported an earlier smaller trial of 17 subjects who took 50mg of freeze-dried feverfew vs. placebo.⁷ Another trial, however, showed no difference when compared to placebo with an equivalent dose of 0.5mg parthenolide in an alcoholic extract of feverfew leaves.⁸ This trial however was different than the previous two because it used an alcoholic extract of the herb, and the participants were allowed to ingest additional conventional medications when necessary.⁸ The most recent trial compared a new stable extract (MIG-

Original Author Nicole Garcia

Reviewed by Susan Paulsen Pharm D

99) of feverfew to placebo.⁹ The primary objective was to show a dose-response of feverfew by looking at the number of migraine attacks during the last 28 days of the treatment period compared with baseline.⁸ The doses they used were 2.08mg, 6.25mg, and 18.75mg TID. MIG-99 failed to show a significant migraine prophylactic effect in general. A dose response relationship could not be observed. It was only effective in a small pre-defined subgroup with at least four attacks during the 28 day baseline period with a dosage of 6.25mg TID per day. The incidence of adverse events were similar in all treatment groups.⁹ This was true also with all the other studies. This trial (n=147) does need to be verified with a larger sample study to conclude the safety and efficacy of feverfew.⁹ From the conclusions of these four studies, there is still conflicting evidence for its efficacy in the prevention of migraine headaches.

A double-blind placebo controlled trial of 41 patients with arthritis concluded that dried feverfew (70-80mg, equivalent to 2-3 μ mol parthenolide) taken for 6 weeks as an adjunct to existing NSAID treatment showed no benefit over NSAID alone in relieving symptoms of arthritis.¹⁰

Dosage forms, recommended doses, duration:

Feverfew is supplied in a capsule, tablet, tincture, crude leaf, powder or seed dosage forms.¹¹ The Canadian Health Protection Branch allows the following dose for the prophylaxis of migraines in adults: 125-250mg daily of dried feverfew leaf preparation containing a minimum of 0.2% parthenolide.² MICROMEDEX alt med PDA: 200-250mg daily capsule or 1 fresh leaf daily.⁹ Feverfew is considered safe when used short term for no more than 4 months.^{1,2} The safety long term is unknown.^{1,2}

Drug interactions and Drug-Disease interactions:

There has been no documented drug interactions, but feverfew may potentiate the activity of anticoagulants such as warfarin in theory.² There is some concern that feverfew might increase the risk of bleeding if taken with aspirin, clopidogrel, dalteparin, enoxaparin, heparin, ticlopidine, and warfarin.¹ The effectiveness of feverfew might be decreased when used with anti-inflammatory medications such as aspirin, ibuprofen, ketoprofen, naproxen and many others.¹

Other Safety issues

Side effects are rare, but may include upset stomach, diarrhea, flatulence, nausea, and vomiting.^{1,2} Mouth sores may occur and this warrants discontinuation of feverfew.^{1,2} Although the effect of feverfew long term is unknown, it may increase the chance of having additional side effects such as anxiety, headaches, insomnia, and muscle/joint stiffness.¹

Feverfew is contraindicated in pregnancy.² Animal studies in cattle have shown its ability to cause abortion.² It has also been shown to cause changes in menstrual flow.² Uterine contractions in full-term women have reportedly been induced by feverfew.² Feverfew should not be ingested if you are allergic to plants in the Asteraceae Compositae family including ragweed, chrysanthemums, marigolds, daisies, and other herbs.^{1,2}

The safety of its use during lactation or by children has not been established, nor has safety of long term use.²

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People taking anticoagulants should use feverfew with caution because feverfew may potentiate the activity of anticoagulants such as warfarin.²

Other Comments

- Reference #2 did not give a reason to why this herbal product has not been approved by the German Commission E.
- It's possible that the extract doesn't work, but the synergy of the whole leaf that carries the medicinal properties.

References

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