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File: ■ Boneset (*Eupatorium perfoliatum*)

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RE: Review of Traditional and Scientifically Substantiated Applications of Boneset

Hensel A, Maas M, Sendker J, et. al. *Eupatorium perfoliatum* L.: phytochemistry, traditional use and current applications. *J Ethnopharmacol.* December 8, 2011;138(3):641-651.

A perennial North American herb, boneset (*Eupatorium perfoliatum*) was used by Native Americans long before European colonization. Leaves and flowering parts were used in North American traditional medicine primarily to treat fever and cause sweating. Many tribes knew about boneset, using it for colds and fevers. It was also called feverwort by Europeans.* The Chippewa and Cherokee used it as an antirheumatic. Early European settlers adopted Native American uses, adding treatment of malaria, yellow fever, dengue fever, and influenza. Boneset was grown as a substitute for quinine (*Cinchona* spp.). Early in the US, it was used for rheumatism, gout, and arthritis. In the late 19th century, it was widely used mostly in colds with fever and in rheumatism by the Eclectic and Physiomedicalist physicians. It appeared in the US Pharmacopeia until 1900 and the National Formulary until 1945. Current European use includes homeopathic treatments for colds, flu, and liver and biliary diseases associated with fever and rheumatism. A 1985 monograph by the former German Federal Office for Drugs and Medicinal Products, Commission D, indicates its homeopathic use. It appears in the German Homeopathic Pharmacopoeia (HAB 2010).

There are about 38 *Eupatorium* spp. Europe's one indigenous species is hemp agrimony (*E. cannabinum*). Boneset for medicinal use mostly originates in North America; however, it is now also cultivated in Europe. Pharmacognostic and analytical differences between boneset and hemp agrimony are of concern, especially because of potentially hepatotoxic pyrrolizidine alkaloids in hemp agrimony and other *Eupatorium* which are absent in boneset. The German Homeopathic Pharmacopoeia does not provide a definitive identification method; other literature describes an identification and fingerprinting method by capillary zone electrophoresis. One of the authors has described a validated high-performance liquid chromatography (HPLC) method to verify boneset identity and quality.

Whether or not dried boneset leaves and flowers contain volatile essential oils (EOs) remains unsettled, with different studies reporting different results. The authors say the data indicate boneset accumulates only small quantities of EOs, with inconsistent

composition, and a broad analysis is needed to consider variables like seed material, growth conditions, harvest time, etc. Profuse trichomes and EO glands on leaves seem to indicate that EOs are produced, but may not persist after harvest and drying.

Many flavonoids, e.g., kaempferol and quercetin, and methylated flavonoid aglycones, including eupafolin, are found in dried boneset. Eupafolin has anti-inflammatory effects in vivo, inhibiting transcription nuclear factor-kappa B (NF- κ B). Several sesquiterpene lactones (STLs) and related compounds, including euperfolid, have been reported with an exocyclic methylene group. Many STLs with this structure have anti-inflammatory effects in vitro, also inhibiting NF- κ B. Eupafolin and euperfolid likely contribute to the potent anti-inflammatory effects of boneset reported in vitro for homeopathic extracts and in vivo for other extracts, validating its traditional use in inflammatory conditions. Boneset extracts and fractions, especially those with flavonoids and protocatechuic acid as dominant compounds, also have strong antioxidant properties.

Many triterpenes and sterols; caffeic acid derivatives; fatty acids and fatty alcohols; and some polysaccharides have been reported in boneset extracts and fractions. A fructan found by enzymatic assay of a hot water extract is thought to be inulin-like, chemotaxonomically typical of the Asteraceae plant family. Two polysaccharides, characterized as 4-O-methyl-glucurono-xylans, increased in vitro phagocytosis of human granulocytes by 30% over untreated controls. In vivo studies using the carbon clearance test also showed increased phagocytosis. An STL, usually eufoliatin, increased phagocytosis in vitro. Other studies report contradictory results. Only one non-placebo-controlled open trial, on 53 patients with colds, has been conducted using boneset. One group took a homeopathic preparation; the other, aspirin. Outcomes did not differ. In trials reporting benefits against colds, homeopathic boneset extracts were combined with other extracts. None of the studies reported applied Good Clinical Practice (GCP) protocols. Constituents accounting for a proposed immunostimulatory effect and claimed efficacy of homeopathic boneset cold remedies remain unclear. Polysaccharides such as those reported, for example, are not normally extracted by virtue of their strong cell wall association, and would occur in insignificant amounts in commercial or traditional remedies. Reported immunostimulation could be caused by lipopolysaccharide (LPS)-depletion of polysaccharides before testing.

Boneset extracts are strongly active against *Plasmodium falciparum*, the protozoan causing malaria, validating another traditional use. An unusual dimeric guaianolide was most active.

Finally, a lack of cytotoxic effects has been reported.

—Mariann Garner-Wizard

* The common name boneset comes from a characterization of severe fevers as "bone-breaking."

The American Botanical Council has chosen not to reprint the original article.

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