

# Boneset in Dyspepsia and Febrile Infections

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## Distribution and description

Boneset (*Eupatorium perfoliatum* L.) is a widespread native plant in the eastern and central United States and Canada. It ranges from Nova Scotia to Florida and west to Texas and North Dakota. It can be found growing in low damp soil over large areas and in thickets. Due to its association with swampy places, its early use by Native Americans for malaria seemed most appropriate (Foster & Duke 1990, Locock 1990).

The opposite, lanceolate and perfoliate leaves are long, wrinkled, and hairy underneath, turning dull gray after the flowers appear. A hardy perennial that grows from 1-4 feet high, it has a large, flat, terminal cluster of greyish white to pale purplish flowers that appears from July to August and persist until frost, typically in October. The leaves turn a dull gray after the flowers appear. The recently picked leaves and flowering tops are the parts normally used for medicine. An infusion of 2-4 grams of the recently harvested parts was the popular form to use both by indigenous peoples and in Anglo folk medicine as a diaphoretic, analgesic, emetic, and/or laxative. In addition, the tincture, fluid extract, and Specific Medicine were employed by Eclectics and other doctors for fevers in endemic and epidemic infections (Foster & Duke 1990, Hall 1974, Locock 1990, Mundy 1905, Powers 1928).

## Taxonomy

*Eupatorium perfoliatum* is a member of the Asteraceae (Composite) family of plants. The genus takes its name from the ancient king Mithridates Eupator of Pontus who is believed to have used one of these species in his famous poisoning-prevention formula. As many as 26 different species grow in the American northeast near

Canada, and differentiation can be difficult (Locock 1990). Former Latin synonyms for this species are *E. connatum*, *E. glandulosum*, and *E. virginicum* (Woerdenbag 1993). The species name “perfoliatum” describes how the leaves attach to each other around the stem, making the stem appear to pierce through them (Mundy 1905). Common names used included thoroughwort, thorough-stem, and crosswort (Anon. 1918). “Thorough” in this context likewise means “passing through”, another term describing the stem and the leaves, as crosswort likely also addresses this conjunction.

Of the common names applied to this plant, boneset is now more typically familiar to modern herbalists. This name refers to its use for febrile conditions with characteristic aching of the bones. Indian sage was another name used by European settlers who used it to induce a sweat for in fevers. The plant has also been known as ague weed. Wooster Beach, the father of Eclecticism, called it “vegetable antimony,” using it as a replacement for the toxic mineral drug antimony tartrate, or tartar emetic (Locock 1990, Mundy 1905, Powers 1928).

Several Composite family plants were also called boneset and in the early 20<sup>th</sup> century were occasionally misrepresented as the preferred species. Though their flowers bore a general resemblance, the leaves were completely unlike. One was *Eupatorium ageratoides*, also known as white snake-root, an herb that was diuretic, diaphoretic and antispasmodic. Another was *Gnaphalium polycephalum*, called sweet-scented life-everlasting, Indian posy, or old-field balsam, due to its very fragrant aroma. Its infusion or decoction was used as a cold and flu remedy (Anon. 1918).



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### **Ague weed employed by Native Americans**

*Eupatorium perfoliatum* is one of the first botanical remedies to be introduced to the American colonists by the Indians. In this instance it was employed to treat the common malarial fever known as the ague. This remedy was used by the Indians for malaria so often that it became known as “ague weed” (Hall 1974, Mundy 1905, Powers 1928). The leaves or the whole plant were infused, and the tea consumed as a treatment for ague and other fevers by a number of Indian tribes including the Cherokee, Delaware, Iroquois, Menominee, Mohegan, Nanticoke, Seminole, and Shinnecock (Moerman 1998).

In other debilitating circumstances such as colds, the infusion was employed as a bitter tonic and a means to increase sweating by the Cherokee, Mohegan, and Shinnecock, or simply taken as a tonic by the Rappahannock. The Indians, moreover, considered the leaves and tops a powerful remedy for use internally or locally in a variety of other conditions. The Meskwaki (Fox) drank an infusion of leaves and blossoms to expel worms. It was a well-known emetic among the Cherokee, Koasati, and Seminole and taken also as a laxative by the Cherokee and Iroquois. Iroquois applied a poultice of the smashed plant for headaches. The Chippewa (Ojibwa) made a poultice of the boiled tops for rheumatism, and applied the chewed plant locally for rattlesnake bites (Moerman 1998).

The root was also utilized and preferred by some tribes. The Meskwaki made a poultice of the root for snakebites. The roots or other parts of the plant were used by the Iroquois and other tribes for lung, pleuritic, stomach, urinary tract, and menstrual pains. Iroquois also decocted the root to help stop the liquor habit. Chippewa used the root to correct irregular menstruation (Moerman 1998).

### **Early history of its commendation in Euro-American medical literature**

After being introduced to settlers by the natives, the infusion and decoction of boneset were long popular with American physicians for colds and flu in spite of the disagreeable taste and nauseating effect. In one of the first published references on its use as an medicinal plant, Manasseh Cutler wrote in 1784 of the leaf infusion being used as a powerful emetic (Cutler 1903). In 1787 J.D.

Schopf, M.D., noted in his Latin text its use by Indians for fever and cough. Benjamin Smith Barton, M.D., professor of natural history and botany at the University of Pennsylvania, indicated in 1798 that thoroughwort decoction was emetic and used by Indians for intermittent fevers. James Thatcher, M.D., in 1810 declared its sudorific, emetic, and purgative powers for fevers, taken as a decoction or as powdered leaves, though he believed the flowers were the most active. By 1814 the botanist Frederick Pursh found the whole plant exceedingly bitter but effective in treating influenza and other fevers (Anon. 1918).

In 1817 Jacob Bigelow, M.D., professor of materia medica and botany at Harvard University, reported its usefulness for many cutaneous affections and for intermittent and other fevers when taken as a dried herb or its decoction. In 1818 William P.C. Barton, M.D., professor of botany at the University of Pennsylvania, declared that “few plants of our country are more deserving of the attention of physicians than this.” He found it an inestimable medicine in all cases of low typhus with hot, dry skin when given every half hour to ensure diaphoresis and avoid emesis. The next year the professor of clinical practice at the University of Pennsylvania, N. Chapman, M.D., indicated boneset was the most valuable of diaphoretics. The entire plant, but especially the flowers, hardly ever failed in this regard when used as a strong infusion. Used in early stages of catarrhal affections, he reported how 30 years prior its efficacy in treating a type of influenza called “break bone fever” led to its being given the enduring name boneset. When given hot as an infusion or decoction, it is diaphoretic, emetic, and diuretic, but as a cold decoction its tonic effects predominate (Anon. 1918). It was included under the name thoroughwort in the primary list of *materia medica* in the first edition of the *Pharmacopoeia of the United States* where it was also designated as an official infusion (*USP* 1820).

For many decades white settlers also relied on this plant as a popular remedy for malaria. Peruvian bark was considered by physicians as the treatment of choice for malaria in the early 19<sup>th</sup> century. Quinine, isolated from the bark in 1820, was a helpful refinement in making this bitter remedy more acceptable to the public. In 1824 Dr. John Sappington bought all of the quinine available in Philadelphia and brought it back to Missouri in his

saddlebags. While accepted by many, the general populace in that area was slow to abandon the use of boneset. In 1844 in his book, *Theory and Treatment of Fevers*, he stated that boneset was one of the best indigenous substitutes when quinine was unavailable or in short supply in malarious districts (Hall 1974).

In 1828 the noted naturalist C.S. Rafinesque stated that boneset acts powerfully on the skin for obstinate cutaneous diseases. Otherwise, he confirms its use for fevers such as malaria, as an emetic when the warm decoction is given in large doses, and as a powerful tonic as a cold preparation. Only its nauseous and disagreeable taste prevented its general use (Anon. 1918). In two independent updates of the original *USP*, the Philadelphia 1<sup>st</sup> revision included thoroughwort herb in its primary list (*USP* 1831), while the New York 2<sup>nd</sup> edition noted the virtues of thoroughwort or boneset were extracted by water (*USP* 1830). *Bowker's Family Instructor* of 1836 advised use of a strong tea drunk freely before going to bed to eliminate mild colds. The finely powdered leaves mixed with molasses were recommended as a gentle purge or, when steeped and drunk cold, to correct the bile (Anon. 1918). The *USPs* of the mid-19<sup>th</sup> century continued to include the tops and leaves of thoroughwort in the primary list along with instructions for preparing the infusion (*USP* 1842 & 1851).

### Physiomedical applications, preparations, and doses

Samuel Thomson declared this herb to be warming and good for coughs and other lung complaints when used as a common drink. Besides its expectorant activity, he noted it was also a mild emetic, diaphoretic, and tonic (Anon. 1918). A botanical physician's use of this remedy depended on the form utilized. As a cold infusion, it proved to be a soothing and relaxing tonic for dyspepsia. In this regard it also acted as a mild stimulant to the liver and bowels, increasing bile secretion and providing a comfortable laxative effect. Its actions were described as slow and mild but persistent and reliable. In aching throughout the lungs and for chronic coughs with irritation the infusion was found to have a soothing effect, whether prepared cold or warm (Cook 1985).

Its most common use as a warm infusion was for its diaphoretic effect. Used as such to promote sweating in fevers, it retained its laxative activity and proved doubly

efficacious. If taken in large quantities or in short intervals it produced sudden vomiting. Giving emetic doses in break-bone fever appeared beneficial. In colds and influenza with rheumatic components, it effectively relieved the discomfort in the limbs. As a rectal injection, it provided effective laxative results (Cook 1985).



*Eupatorium perfoliatum* (boneset)

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In his classic 1869 text, *The Physio-Medical Dispensatory*, Dr. William Cook further described preparing water extracts by infusing one ounce of powdered leaves and flowers in one quart of boiling water. From 1-3 ounces of this were given per dose and repeated according to the desired effects. A solid extract was prepared by boiling down the decoction and was taken as a relaxing tonic in doses from 325-650 mg three times daily. It was also used as a base for other powdered herbs. Cook believed the fluid extract to be fully effective in representing the plant's qualities. One pound of boneset was macerated in one quart of 50% alcohol. Transferred to a percolator, half a pint was collected as a percolate out and was set aside. Warm water was added in the percolator until the herb was exhausted. This dilute aqueous percolate was evaporated to eight ounces and then added to the first half pint of hydroalcoholic percolate and filtered. The dose of this 1:1 extract was 20-30 drops three or more times daily (Cook 1985).

#### **Broad medical acceptance**

Besides the inclusion of *Eupatorium perfoliatum* in *The Physio-Medical Dispensatory* (Cook 1985) and all 19<sup>th</sup> century *USPs* (Boyle 1991), King's and Newton described its use in the *Eclectic Dispensatory* of 1852. They specified that, combined with potassium bitartrate and camphor, the powdered leaves were serviceable in some cutaneous diseases. In addition, they listed the usual applications of the cold infusion or extract as tonic for typhoid fevers, dyspepsia, and general debility, and the warm infusion as diaphoretic and emetic for fevers, catarrhs, and cold (Anon. 1918).

In his 1867 book *New Remedies*, the homeopathic professor E.M. Hale, M.D., of Hahnemann Medical College, indicated this plant was useful for influenza with pain in the back and limbs. Due to the multiple effects and uses of the herb, he described it as a "polychrest" that influences the whole organism in a general manner. John Scudder in his 1871 *Eclectic classic Specific Medication and Specific Medicines* described the best indications as a frequent, full pulse and flushed skin inclined to be moist, while throbbing pain was the indication for local use (Anon. 1918).

In their book *Medicinal Plants* published in London in 1880, Bentley and Trimen described preparing the infusion for influenza. One ounce of the herb was added

to a pint of boiling water. Doses of a wineglassful (2 oz.) were to be drunk every half hour while the patient remained in bed. When 4-5 doses result in profuse perspiration and possibly vomiting, relief is rapidly obtained. The infusion is then given in small repeated doses. Charles Millsbaugh, M.D., claimed in his 1887 *American Medicinal Plants* that it was unlikely that any herb in American domestic practice was used more extensively or frequently than boneset (Anon. 1918). By 1890 *Eupatorium perfoliatum* fluid extract had become official (USP 1893).

#### **Eclectic report on the cold infusion**

Dr. Joseph Adolphus reported on the value of treating intestinal problems with the cold infusion in doses that did not cause vomiting or purging. He claimed that boneset diminished the secretion of the mucous glands of the intestinal tract when their action was excessive. He also believed that there was a strong association between nervous system dysfunction and the digestive derangements. These he described as deficient innervation reflexly caused by local capillary inadequacy. He ascribed functional dyspepsia to hyperemia of the mucous membranes and felt boneset given in the early stages was the best remedy. His preferred extract that preserved well was made by soaking eight ounces of the green leaves in twelve ounces of soft water and four ounces of glycerin for two weeks, straining and pressing. This extract could be used externally for skin inflammation and ulcerations as well (Adolphus 1873).

Dr. Adolphus described a case of a skeletal patient who had been dyspeptic for years and was unable to hold down food. After eating he would experience intense acidic belching, his heart raced to 160 beats per minute, and a precordial constriction accompanied by intense anxiety ensued. These symptoms would be relieved in several hours as vomiting of the partially digested food took place. The man had been treated by numerous digestive medications (e.g., bismuth, ipecac, pepsin, bitter tonics, potassium iodide, quinine, morphine, sodium sulphate), all of no benefit. Dr. Adolphus prescribed a boneset extract made by soaking one ounce of the green leaves in a quart of soft water at 80°F to which two ounces of glycerin had been added. His diet was Graham (whole wheat) mush and milk. The man, after taking four ounces of the boneset extract every four

hours for one day had remarkably reduced symptoms. After four days his “spells” entirely abated and never returned. However, for ten days he experienced a nervous agitation over his upper and lower extremities for 15-20 minutes that ended with profuse sweating on the palms, soles, and abdomen. The treatment was continued for six weeks, at which time his disposition was serene and composed, his countenance was rejuvenated, and his formerly constipated bowels functioned with regularity (Adolphus 1873).

### Small doses and specific prescribing of Eclectics

John Scudder first described boneset used as an “essential tincture” (his early version of Specific Medicines). The advantage of using this form was the much smaller doses compared to the amounts of the infusion normally consumed. Eight ounces of the recently dried herb was tinctured with one pint of 50% alcohol. Given in doses of one teaspoon, it increased excretion through the skin as a nauseant diaphoretic for respiratory infections. In doses as low as 5 drops, it was believed to stimulate the vegetative nervous system and improve visceral functions (Scudder 1862a & 1862b).

Scudder declared that boneset occupied a front rank in the Eclectic indigenous remedies but was little used because of the unpleasant practice of using large doses as was formerly popular. He would later mix only 10-30 drops of the tincture in four ounces of water and give a teaspoonful of this mixture every hour (0.3-1.0 drop of tincture hourly). This was used for many rheumatic conditions, especially in cases of chest pain and cough or fever. To obtain the best results, he believed the skin must be full (not dehydrated) and tending toward perspiration. He also described the tongue and pulse as full. His brief description of a patient with “dull pain, full tissues, leaden color, inclination to sweat” was one for whom boneset would work best (Scudder 1875).

The fluid extract was employed by Ellingwood in a larger dose to resolve an interesting case of severe hiccoughs. A patient with extreme exhaustion from intestinal inflammation and hemorrhage resembling the later stage of fatal typhoid, but with less fever, had suffered from hiccoughs for four days. The tongue and mouth had a dry membranous coating with a dark red base. He first tried an infusion of *Capsicum*, but when

that failed he gave 15 drops of boneset fluid extract in hot water every 1-2 hours. Relief was rapid, and the remedy stopped. The hiccough returned in 2-3 hours, then after 6-8 hours, and finally only once or twice daily before disappearing entirely (Ellingwood 1908). A similar case of intractable hiccoughs in an old man in which every prior remedy had failed was cured when 15 drops of boneset fluid extract was added to *Capsicum* infusion and given hourly (Ellingwood 1994).

Mundy noted that the cold infusion in small doses acted as a simple bitter tonic. The infusion given warm in larger doses was diaphoretic and anti-malarial, and in even larger doses it acted as an emetic and cathartic. He considered the tincture a digestive tonic and antimalarial. The dose he recommended for the Specific Medicine was 1-60 drops (Mundy 1905). The infusion was at such times considered superior to the tincture (Bloyer 1901), though this was disputed. The bitterness of the infusion made it unacceptable to some (Felter 1924).

In cases of malaria that were unresponsive to quinine or had relapsed, the use of boneset was most effective, especially when general sluggishness and intense aching were predominant, particularly intermittent headache or severe browache with other symptoms of ague. The Eclectic Dr. Locke recommended infusing one ounce in a quart of boiling water and giving a half to a full teacupful every 15 minutes until vomiting ensued. The patient was then put to bed and kept sweating with smaller doses for two hours. After drying the patient, this treatment was followed with other tonics and stimulants (Ellingwood 1994, Powers 1928).

### Lloyd's colloidal preparation

Specific Medicine Eupatorium was described by Dr. Bloyer as a remedy par excellence in rheumatism. He claimed the chief indication was sluggishness (Bloyer 1901). Deep-seated, general aching continued to be regarded as the prominent indication for the use of boneset; severe pain in the muscles and bones, in the head, in the chest, in the limbs and back, aching eyes, or soreness over the entire body. The skin was usually described as moist and the pulse as full (Bloyer 1901, Felter 1924, Mundy 1905).

In 1918 Lloyd Brothers made a new Colloidal Specific Medicine Eupatorium, recommending it for the

same indications. This followed isolation of two distinct component complexes of entirely different chemical qualities and pharmacological effects. One was pleasantly bitter and soluble in water, alcohol, glycerin or syrup. It possessed the diaphoretic and tonic qualities useful in influenza, coughs, and colds. This was found present in the dried herb, infusions, decoctions, and alcoholic extracts. The other complex contains oils, fats, and glycosides insoluble in water, glycerin or syrup but very soluble in alcohol. It is found in all tinctures and fluid extracts, hot decoctions and the fresh infusion, but is largely cast down as a precipitate when water extracts are cooled and allowed to sit for 12 hours. Though not bitter, this complex is nauseating and also produces the cathartic action of boneset. The wine-colored Colloidal Specific Medicine retained the fragrance and mild herb flavor but excluded the second complex, flavone derivatives, and glucosides such as rutin. It could be mixed with water, glycerin, and/or alcohol. This Colloidal Specific Medicine was found to be especially useful as a treatment and especially as a preventative in the influenza epidemic of 1918 (Anon. 1918).

### Influenza epidemics

Boneset was often given in combination with complementary remedies (Cook 1985). One formula used by Dr. Hoener to cure over 700 cases in the flu epidemic of 1891 contained 1.5 ounces each of elixirs of boneset and *E. alternifolium* (false boneset), along with 1.0 ounce each of *Verbena hastata*, *Leptandra virginica*, and *Agrimonia eupatoria*. Used alternatively as a decoction, these quantities of dried herbs could be extracted with 6 pints of boiling water and given as 2-4 tablespoon doses every 2-3 hours (Nowell 1926).

The consensus among Eclectic physicians was that boneset was one of the safest and most successful remedies employed during flu epidemics, especially the severe influenza pandemic from 1918-19. Both the infusion and Lloyd's Specific Eupatorium were effective. Eventually, boneset began to be used as a prophylactic. Cases were milder, the severe pain in the back and limbs was quickly relieved, cough and irritation were reduced, and recovery hastened with its liberal use (Powers 1928, Felter 1924, Best 1928). The simple infusion of the leaves and flowers was found to be safer and of greater advantage than the bacterins, coal-tar compounds,

quinine sulphate, and opiates that were typically prescribed (Powers 1928, Best 1928).

For acute aching with chilliness, depression and subnormal vitality that characterized the first stages of influenza, boneset was considered one of the top remedies (Best 1928). In a discussion of this remedy for the flu, a Dr. Bixel claimed that in 1918 he lost only two of 500 influenza cases he treated. A Dr. Ilgenfritz stated that he treated 628 cases and lost only three using the infusion. He had his druggist make up a half-dozen one-gallon bottles of infusion daily that he carried in his car (Powers 1928).

Specific Eupatorium became a routine treatment of influenza, taking its place alongside vaccines and serums (Powers 1928). In the aged and debilitated Specific Eupatorium helped bring relief to coughs with abundant secretions that could not be expelled. It was also used for the cough of measles (Bloyer 1901, Felter 1924). It was considered admirable in breaking up the common cold, but in children needed to be administered in an aromatic syrup. It relieved the pleuritic pains and those associated with the cough of broncho-pneumonia (Felter 1924). In these types of cases it acts both as a diaphoretic and expectorant (Best 1928).

### Use diminishes and antibacterial activity discovered

*Eupatorium perfoliatum* and its infusion had been official from the first edition of the *USP* in 1820 through the eighth revision in 1900 (Boyle 1991). Due to the growing professional disregard for many herbs, but in recognition of its continuing popular utilization, it was transferred from the *USP* to the *National Formulary (NF)*.

By the 1920s naturopathic physiomedical use as described by Dr. Nowell in the Dominion Herbal College postgraduate course had not changed significantly from former times. The cold infusion was valued for its tonic properties, good for ague and dyspepsia, and as a mild laxative when constipated. The warm infusion was diaphoretic and invaluable in colds, fevers, and asthma. Its effect on the liver and bowels was marked. Large warm doses produce emesis. Boiling the decoction down, a solid extract could be made and rolled into pills that helped reduce night sweats of tuberculosis. The solid extract was not as relaxing but did act as an antispasmodic (Nowell 1926).

The physiomedicalist Dr. William Cook has stated in 1689 that the dose of the powder would be from 0.65-1.3 grams (10-20 grains), but that it was not given in that form (Cook 1985). *E. perfoliatum* retained in the *NF* through the 8<sup>th</sup> edition published in 1946. The dose of the powdered leaves and flowering tops was given there as 2 grams or about 30 grains (*NF* 1946). Following World War II and the expansion of the synthetic pharmaceutical industry, boneset was relegated to the growing group of traditional remedies unused by most professional prescribers.

An early antimicrobial study found the ether extract of *E. perfoliatum* fresh plant produced complete to partial inhibition of *Staphylococcus aureus* culture *in vitro* (Carlson et al 1948). *E. perfoliatum* was shown to be one of the more active antibacterial plants of the 209 obtained from Nova Scotia that were studied. Ten grams of stems, leaves, flowers, and roots were macerated in 50 ml of water for 5-10 minutes. The water extract was filtered off and combined with the fluid pressed from the plant material. The extracted plant material was then extracted again with 95% ethanol, filtered and pressed. This procedure was then repeated with the solvents ethyl ether, acetone and benzene. When tested for inhibition of bacteria the water, alcohol, ether, and acetone extracts all produced inhibition of *Staph. aureus* (diameter of inhibition 16, 12, 23, and 17 mm, respectively) but not of *Escherichia coli* (Bishop & MacDonald 1951).

### Phytochemical analysis

Scientific interest in boneset appeared dormant for decades until phytochemical studies on this plant began in the 1970s. Flavonoids isolated from *E. perfoliatum* methanolic extract of the aerial parts include the glycosides hyperoside, astragalín, rutin and kaempferol rutinoside (Wagner et al 1972). A number of sesquiterpene lactone components were isolated from *Eupatorium* spp. including *E. perfoliatum* (Bohlmann et al 1977). Two of these are germacranolides, euperfolín and euperfolítín, identified along with the diepoxyguianolide, eufoliatín, and a novel dilactone, eufoliatórin (Herz et al 1977).

Terpene derivatives, known as chromenes, were isolated from *E. perfoliatum* and related species (Bohlmann & Grenz 1977). The sterols campesterol, beta-sitosterol (Hooper & Chandler 1984), and

stigmasterol were discovered from this species, along with the triterpenes including alpha-amyrin and others (Dominguez et al 1974). An ethyl acetate fraction of a methanol and water extract of the herb contained 6 caffeic acid derivatives. These included chlorogenic acid, neochlorogenic acid, 3,5-dicaffeoylquinic acid, and 3 new depsides of caffeic acid with glucaric acid (Maas et al 2008).

### Medical and pharmacological studies

A clinical study using boneset was published in Germany in 1981. The trial involved a comparison of the effects of aspirin with a homeopathic dilution (D2) of *Eupatorium perfoliatum* when used to treat the common cold. This D2 preparation is a 1:100 dilution of the mother tincture made from the plant. Ten drops or two tablets of this remedy were taken five times daily (amounting to one half drop daily of mother tincture) by ten men and twelve women, while one aspirin tablet was taken three times daily by 14 men and 17 women. The effects were assessed on day 1, 4, and 10 by reported subjective complaints and physical examinations. Symptoms, body temperature, and lab findings were not significantly different between the groups, indicating equivalent efficacy (Gassinger et al 1981). This dosage is more than ten times less than even Scudder's relatively low recommended daily dose for his essential tincture in febrile respiratory infections (Scudder 1875).

Subsequent laboratory investigations into boneset's pharmacological effects began in earnest in Germany. The sesquiterpene lactone eufoliatín has been shown to enhance phagocytosis by neutrophils in a chemiluminescence immunostimulation assay (Wagner et al 1985b). A screening test of *Eupatorium perfoliatum* water and alkaline-water extracts of the leaves and their isolated heteroglycan polysaccharides showed significantly enhanced phagocytic activity *in vitro* and *in vivo* (Wagner et al 1984, Wagner et al 1985a). Phagocytosis was stimulated in human granulocytes *in vitro* at a concentration of 0.001 mg/ml (Wagner et al 1985a). Two homogeneous polysaccharides were isolated from the alkaline aqueous extract by ethanol precipitation and shown to be 4-*O*-methylglucuronoxylans with  $M_r$ s of 40,000 and >500,000. These polysaccharides showed a phagocytosis-enhancing effect in carbon clearance, granulocyte-, and

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chemiluminescence tests (Vollmar et al 1986). The immune-enhancing effects could be valuable in treating infections, especially viral.

In combination with *Echinacea angustifolia* extract, *E. perfoliatum* extract helps increase phagocytosis in the carbon-clearance test more than the *E. angustifolia* extract alone. Furthermore, with the successive additions of *Baptisia tinctoria* extract and *Arnica montana* extract to this combination, the phagocytosis was incrementally increased as indicated in both the granulocyte and carbon-clearance tests. The four-extract combination was over 50% more effective than the *E. angustifolia* mono-extract (Wagner & Jurcic 1991). In another antibacterial test the crude ethanolic extract was mildly antibacterial against the Gram-positive species *Staph. aureus* and *Bacillus megaterium* but not the Gram-negative *E. coli* or *Pseudomonas aeruginosa* (Habtemariam & Macpherson 2000).

A combination of mother tinctures of *E. angustifolia* (40%), boneset (40%), and *Thuja occidentalis* (20%) was given in 3 ml daily doses orally for 4 weeks to 23 surgically-cured malignant tumor patients. However, blood samples taken before treatment and after two and four weeks of therapy showed no significant alteration in lymphocyte cytokine production compared to pretreatment levels or to blood samples from 12 surgical tumor patients used as a control. Also, no significant change in leukocyte populations was identified at this dose when compared to pretreatment levels (Elsasser-Beile et al 1996).

### Modern British herbalists' and naturopathic applications

By the 1980s British herbalists and naturopaths were teaching the combined use of boneset for acute fevers and for flu with night sweats and aching bones together with *Achillea millefolium* (yarrow) in the first stage and *Anemone pulsatilla* in the third stage. Post-influenzal gastric upset and constipation could also be treated with boneset, *Chelone glabra* (turtlehead) and *Juglans cinerea* (butternut) syrup. It was also combined with *Asclepias tuberosa* (pleurisy root) and *Inula helenium* (elecampane) for pulmonary inflammation with cough and soreness (Priest & Priest 1982).

The emphasis of professional British herbalists has been in using boneset for influenza epidemics,

respiratory infections, and febrile conditions, and its action to enhance stomach and liver secretions. The usual fluid extract dose is 30 minims or 2 ml (Priest & Priest 1982). David Hoffman noted its speedy relief of the associated aches and pains and clearing respiratory mucosal congestion. Its cleansing laxative action and symptomatic relief of rheumatism make it a good general agent outside of acute febrile conditions. His tincture dose is 2-4 ml three times daily. Collected in late summer or early fall after the flowers open, 1-2 teaspoonsful of the dried herb per cup infused for 10-15 minutes makes a tea to be drunk hot every half hour for fevers or flu (Hoffman 1996).

The naturopathic profession in America adopted the traditional physiomedical and Eclectic indications for boneset's use, utilizing either the infusion, tincture (10-40 drops), or, while it was available, the Specific Medicine (5-60 drops). The hot infusion was used as a diaphoretic and mild laxative to dissipate colds in their incipiency. Its sedative effect on aching tendencies was applied not only for influenza but also rheumatoid conditions. In measles it helped bring out the rash and control the cough. In moderate doses (1 teaspoon of the cold infusion 3-6 times daily) it acts as a bitter stomachic tonic for improving the appetite and digestion. Hot infusions are nauseating and emetic if too strong, so cold infusions or alcoholic extracts are considered preferable when its diaphoretic effects are not desired. Administering in a palatable vehicle is best for children and delicate subjects (Kuts-Cheraux 1953, Lust 1974).

Dr. Bill Mitchell obtained much traditional botanical knowledge from his mentor, the eclectic naturopathic doctor John Bastyr. Dr. Bastyr described the flowering tops and leaves of boneset as an excellent diaphoretic and one of his favorite flu remedies, using  $\frac{1}{4}$  of standard tea every half hour until sweating begins. Dr. Mitchell gave 30 drops of tincture four times daily in hot water, considering it one of the finest flu remedies. He also combined it together with elder (*Sambucus* spp.) flowers and buds. For fevers such as typhoid or yellow fever, sip wineglass doses until the fever is reduced or use 15-40 drops of the tincture. As a stimulating stomachic tonic, the cold tea twice daily or 10 drops of the tincture in a cup of cold water may be used. A dose of 5-60 drops of tincture serves as a stomachic that benefits dyspepsia and people who cannot keep food down. He further

recommended 150 drops of tincture (comparable to the Eclectic dose of 3 cups of strong tea) to induce emesis if that was desired (Mitchell 1982 & 2003).

### Possible adverse effects

The obvious side effects from excessive consumption of boneset are the vomiting and diarrhea. Vomiting occurs more readily when the tea is taken hot. Diarrhea occurs after 6-7 hours and is accompanied by profuse sweating. Since these effects are sometimes the purpose for which boneset is taken, they are not in that case considered adverse events. Vomiting appears to be due to the flavone eupatorin, which also has cytotoxic effects (Woerdenbag 1993). The ethanolic extract of the dried leaves was also overtly cytotoxic to the three mammalian cell lines tested (Habtemariam & Macpherson 2000). The cytotoxic activity may also be due to its sesquiterpene lactones, but this has not been validated (Woerdenbag 1993).

Boneset should be used with caution when allergic hypersensitivity to Composite family plants exists, since this may result in contact dermatitis from the sesquiterpene lactone constituents that are common in the *Eupatorium* genus (Woerdenbag 1993). Though most *Eupatorium* spp. have been shown to contain hepatotoxic pyrrolizidine alkaloids, these have not been isolated from *E. perfoliatum*. Uncharacterized alkaloids have been reported (Locock 1990, Woerdenbag 1993).

The plant is known to contain high amounts of nitrate that has been considered responsible for spontaneous abortions that occur in cattle grazing on this plant. Free nitrate ingestion leads to methemoglobin formation and tissue anoxia that can precipitate a miscarriage (Locock 1990, Sund et al 1957). So its use is preferably avoided during pregnancy, due to its potential fetotoxic, cathartic, and abortifacient effects produced by consumption of large amounts.

### Unnecessary confusion

The species *E. rugosum*, known commonly as white snakeroot or richweed, has been designated by the FDA as a poisonous plant, since it caused many deaths in the 19th century. It is noted for its unique component tremetol that is responsible for stock poisoning and milk sickness in those consuming milk, butter, or possibly even meat from livestock that have grazed on this plant. Symptoms of milk sickness include anorexia, tremors,

violent vomiting, and severe constipation. The syndrome also involves blood glucose changes and severe ketosis (Woerdenbag 1993). Drying the plant reduces the tremetol toxicity (Spoerke 1980). Concern has been expressed in relation to its supposed similarity in appearance to *E. perfoliatum* (Woerdenbag 1993).

Both of these species can be found from Canada south through the eastern, midwestern, and Great Plains states to the Gulf of Mexico. However, as noted earlier, *E. perfoliatum* leaves are lanceolate, wrinkled, and perfoliate, that is, the stem appears to puncture the middle of the pairs of opposite leaves. The opposite leaves of *E. rugosum* on the other hand are heart-shaped with toothed margins and rest on slender petioles (Foster & Duke 1990). Whatever unnecessary confusion existed between these species was exaggerated when a text on herbal medicines identified both *E. perfoliatum* and *E. rugosum* as boneset, or alternatively richweed and white snakeroot. This text stated that *E. rugosum* was “the most toxic member of the group” but that it was hard to differentiate it from other species, failing to distinguish it from *E. perfoliatum* morphologically or phytochemically (Spoerke 1980). Unfortunately, this error of mistaken association was perpetuated in early editions of my own clinical toxicology handbook (Brinker 1989).

### Conclusions

The bitters in boneset have tonic effects on the alimentary tract and digestion. Increases in both secretions and motility are common physiologic responses to bitter botanical compounds. The prevalent use of boneset by native Americans and pioneers for common febrile conditions such as malaria could be explained by its diaphoretic effect of controlling fever through sweating. This does not, however, explain its ability to dramatically relieve the associated body aches in these conditions.

Its ability to protect against viral diseases such as influenza may be attributed at least partially to an enhancement of nonspecific immune resistance. The tea provides a proper extract for the polysaccharides that have been shown to actively improve phagocytosis. However, the tinctures that have been popularly used and tested are also known to be effective in these conditions, possibly due to the sesquiterpene lactone eufoliatin that contributes to an immune-enhancing

effect. It may be other sesquiterpene lactones or undiscovered phytochemical components that make this plant a special contributor to the management of common viral complaints. Inhibition of Gram-positive bacteria by water and ethanolic extracts is an additional feature that could contribute to treating or preventing secondary infections caused by these organisms.

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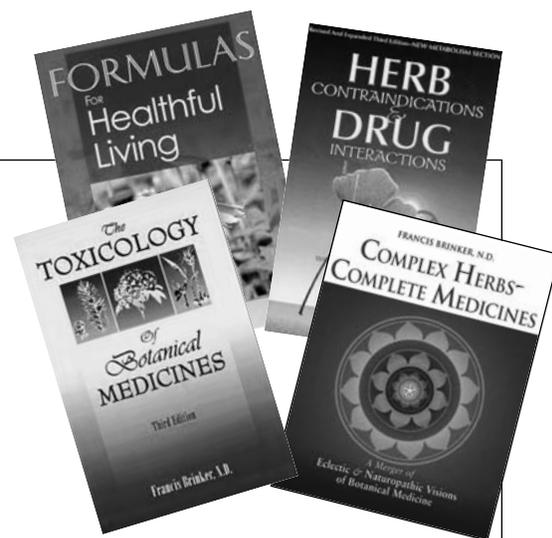
## The writings of Francis Brinker...

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