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File: ■ Yarrow (*Achillea millefolium*)
■ Ethnobotany

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RE: A Survey of Yarrow Ethnobotany, Bioactivity, and Biomedical Research

Applequist WL, Moerman DE. Yarrow (*Achillea millefolium* L.): a neglected panacea? a review of ethnobotany, bioactivity, and biomedical research. *Econ Bot*. June 2011;65(2):209-225.

Yarrow (*Achillea millefolium*) is used worldwide for the treatment of wounds, infectious diseases, gastrointestinal complaints, and animal bites, among many other conditions. Yarrow research, both in vitro and in vivo, supports a wide range of bioactivity; however, there has yet to be a human clinical trial investigating yarrow as a single treatment. This review summarizes the state of research on yarrow and makes the case for the progression of this traditionally-used plant into clinical trials.

In ancient texts by Dioscorides and Pliny the Elder, there are references to a plant that is most likely yarrow; the uses described are to stop bleeding and inflammation from wounds, as a douche for menstrual bleeding, and for the treatment of dysentery, among other uses. Yarrow is also mentioned in Old English medical books for the treatment of inflammation, wounds, diarrhea, intestinal pain, heartburn, lung disease, toothaches, headaches, difficult urination, and animal bites. There is also physical evidence of the historic use of yarrow. DNA confirmed that yarrow was found in the medical supplies of the ruins of a Roman ship sunk between 140 and 120 B.C.E.

In Europe today, traditional uses of yarrow include the treatment of gastrointestinal disorders, loss of appetite, inflammation, menstrual problems, and for wounds and bleeding, as well as use as a diaphoretic. The German Commission E approves of yarrow for mild gastrointestinal disturbances, dyspepsia, and loss of appetite. In Hungary, the plant is used for burns, bronchitis, kidney problems, diarrhea, and vomiting. Yarrow is also used in China for bleeding and sores, wounds, tuberculosis, hemorrhoids, varicose veins, dysmenorrhea, and snakebites. Native Americans use yarrow to treat many of the above-mentioned conditions, among others. It is postulated that the use of this plant for the same conditions across many disparate cultures worldwide supports potential efficacy.

Yarrow is native to Europe and has three subspecies: *millefolium*, *alpestris*, and *ceretanum*. Species or microspecies closely related to yarrow are considered part of the

yarrow species complex. A problem in reviewing the reported phytochemistry of yarrow is the lack of clarification as to subspecies or other taxonomic information. Proazulenes (blue compounds found in the essential oil) and alkamides are found in yarrow, and the subspecies *alpestris* has been reported to contain chamazulene, commonly found in chamomile (*Matricaria recutita* syn. *M. chamomilla*). Evidence suggests that the levels of compounds in yarrow vary greatly depending on location, and these variations are also useful in making taxonomic distinctions as seen in studies involving other species.

In vitro investigation of the bioactivity of yarrow has been wide-ranging. When testing a hexane-ether-methanol extract of yarrow for antibacterial activity, antimicrobial activity was observed against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella enteritidis*. Yarrow essential oil also inhibited *Streptococcus pneumoniae*, *Clostridium perfringens*, *Acinetobacter lwoffii*, and *Mycobacterium smegmatis*. The methanol extract was active against *Helicobacter pylori*, the bacteria associated with ulcers and gastritis, suggesting a possible explanation for the traditional use of the plant to treat gastrointestinal disorders. A hexane-ether-methanol extract of yarrow was also effective against the growth of *Aspergillus niger* and *Candida albicans*.

At a 1 mg/ml concentration, yarrow showed an 80% inhibition in both an antimalarial and antibabesial assay (*Babesia gibsoni* is a tick-borne canine pathogen). In vitro, crude extracts and fractions of yarrow also inhibited proteases associated with inflammation, such as human neutrophil elastase (HNE) and matrix metalloproteinases (MMPs). When tested for hemostyptic (stoppage of blood flow) activity, hot water extracts of yarrow significantly reduced recalcification time in human blood plasma, indicating potential hemostyptic activity. Crude yarrow extract also exhibited antispasmodic activity in the rat jejunum, and a flavonoid-rich fraction and isolated flavonoid aglycones had the same effect in the guinea pig ileum. In addition, a methanol-water extract of yarrow had estrogenic activity in an MCF-7 cell assay, while a boiling water extract inhibited liver cancer cell growth an average of 55.3% in 3 cell lines.

When tested for anti-inflammatory activity in vivo, 6% yarrow extract reduced paw edema by almost 50% in rats. Aqueous extract of yarrow healed ulcers in rodents better than the pharmaceutical ranitidine; in this study, yarrow extract limited intestinal mucosal damage caused by 70% ethanol or indomethacin. In a study of hepatitis in mice, pretreatment of the animals with an aqueous-methanol yarrow extract significantly limited histopathology, improved liver enzymes, and lowered mortality from 100% to 40%. Enriched yarrow extract, containing 48.8% dicaffeoylquinic acids and 3.4% luteolin-7-O-beta-D-glucuronide, was also found to stimulate bile production in isolated rat livers. Lastly, an aqueous flower extract of yarrow reduced conflict behavior in female rats, and diet including 1% yarrow improved the weight gain of female chicks.

A consistent adverse effect of yarrow use is contact dermatitis in certain people; the compounds responsible are sesquiterpenoids known as guaianolides. Yarrow tea, along with nettle and black tea, quercetin, and rutin, has also been found to be slightly genotoxic in the Somatic Mutation and Recombination Test using a strain of *Drosophila*. In several long and short term studies on rodents and birds, no evidence of toxicity with yarrow has been reported; however, when tested in male rodents, ethanol and hydro-alcoholic extracts of yarrow were found to impede spermatogenesis. In addition, a water extract caused a significant increase in abnormal sperm in male rats. While yarrow contains flavonoids with weak estrogenic activity, there is no evidence of estrogenic

effects in vivo; furthermore, although a study seemed to conclude that yarrow caused a decrease in fetal weight in rats and should be contraindicated for use during pregnancy, further analysis of the study revealed errors in data interpretation and methodology. Based on the analysis in this review, the conclusions are questionable and support the assertion that yarrow has yet to demonstrate reproductive toxicity.

The few human studies involving yarrow tested the plant in combination with other materials. One such product containing yarrow was found to improve cirrhosis patients but the study was underpowered. Another improvement was reported for leg ulcers when a combination of 3 herbs including yarrow was used topically. A wide range of bioactivity has been reported for yarrow when tested both in vitro and in vivo; however, human clinical trial investigations of yarrow are lacking. It is argued in this review that research into the beneficial effects of yarrow in humans should be a priority moving forward. As part of clinical investigations, it is also postulated that the chemical profiles of active compounds of yarrow are an integral part of the future research direction of this plant.

—Amy C. Keller, PhD