Herbal Medicine for Lyme Disease and Other Tick-Borne Infections

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Abstract

Numerous tick-borne infections cause problems for humans and animals worldwide. Lyme disease is the best known, but babesiosis, bartonellosis, anaplasmosis, ehrlichiosis, Rocky Mountain spotted fever, and many others are also serious problems. Many studies have confirmed that herbs and herbal extracts can help to repel the several types of ticks (as can non-chemical means such as wearing long pants and tucking them into socks) that spread these diseases, as well as inhibit their reproduction. *Corymbia citriodora* (lemon eucalyptus) and its compound *para*-menthane-3,8-diol (PMD) have most convincingly been shown to be effective. 2-Undecanone and nootkatone with carvacrol have also shown some promise. Despite many claims of efficacy, no published clinical research could be located on any herb or herbal constituent to treat any tick-borne illness and thereby validate these claims. *Dipsacus fullonum* (fuller's teasel) is used as a case study to show a promising herb that has simply no research on whether it helps people with Lyme disease or any tick-borne infection. In vitro and animal studies show some promise for herbs and herbal compounds such as *Brucea javanica* (Java brucea) and artemisinin, but they have not been studied in clinical trials. There remains a black hole in terms of supported herbal treatments for these infections that urgently needs to be filled with credible clinical trials.

Keywords: Lyme disease, tick repellent, lemon eucalyptus, 2-undecanone, herbal medicine

Introduction

A rising tide of tick-borne spirochete, rickettsial, and viral infectious diseases are causing substantial misery around the world, though this article will focus on problems in North America (see Table 1). Lyme disease is the best known of these, but babesiosis, ehrlichiosis, anaplasmosis, Rocky Mountain spotted fever, and many others are also on the list. While these infections do not affect anywhere near as many people as mosquito-borne illnesses, they are still very significant problems. Conventional medicine has offered some treatments and vaccines against some of these illnesses. There is also a raging war over the exact scope and definition of many of these conditions, most notably Lyme disease, which likely contributes significantly to the differences of opinion among various factions about how to diagnose and treat patients.[1] This is to say nothing of the many tick-borne illnesses that affect animal species that are important to humans, including dogs, cats, cows, horses, and many others.

Lyme disease, the infection caused by *Borrelia burgdorferi*, *B. mayonii*, and related organisms, is a major problem around the globe.[2] It is the most commonly reported vector-borne disease in the United States and the fifth most common notifiable disease.[3] Since 2008, there have been $>30,000$ confirmed and probable cases of Lyme disease per year reported in the United States. *B. burgdorferi* is also found in Eurasia, along with *B. afzelii* and *B. garinii*, the three known causes of Lyme disease (*B. mayonii*, *B. bissettii*, and *B. valaisiana* are also suspected of causing disease, but there are too few cases to be sure). A complete discussion of Lyme disease is beyond the scope of this article, which will focus primarily on herbal treatments for this condition and related infections (sometimes referred to as co-infections, though they can occur independently of Lyme disease).

Ticks (see Table 2) are tiny parasitic arachnids (thus adults have eight legs) that, together with their equally unbeloved cousins the mites, make up the subclass Acari. Ticks have three families, though the Ixodidae or hard ticks are most noted for spreading disease. They have prominent heads (in both nymph and adult stages) and varying sizes of scuta (shields) covering some or all of their bodies, unlike other tick families. Family Ixodidae ticks go through a complex life cycle that requires three hosts over at least 1 year. After hatching from eggs that the females lay on the ground, the larvae (which are usually the size of periods in this paragraph) seek blood meals from birds and small mammals. If successful, they detach, fall to the ground, and molt to the nymph stage. Nymphs, barely the size of poppy seeds typically, seek larger mammals for another blood meal. If successful at this stage, they again fall to the ground and molt to adults. Nymphs and larvae generally have distinctive numbers of legs (fewer than the adult) depending on the genus. Female adults then seek a final blood meal from another larger mammal, after which they can lay eggs once

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Table 1. Tick-Borne Infections in North America

Organism	Disease caused	Vector[a]	Geography
Borrelia burgdorferi	Lyme disease	*Ixodes scapularis* (black-legged tick), *I. pacificus* (western blacklegged tick)	Midwestern and Eastern United States and Canada, West Coast of United States
Francisella tularensis	Tularemia	*Dermacentor variabilis* (American dog tick), *Amblyomma americanum* (lone star tick), *D. andersoni* (Rocky Mountain wood tick)	East of Rocky Mountains
Rickettsia rickettsii	Rocky Mountain spotted fever	*D. variabilis* (American dog tick), *Rhipicephalus sanguineus* (brown dog tick), *D. andersoni* (Rocky Mountain wood tick)	East of Rocky Mountains, Southwest United States, northern Mexico
Unknown	Southern tick-associated rash illness (STARI)[b]	*Amblyomma americanum* (lone star tick)	Southeastern and South Central United States
R. parkeri	*R. parkeri* spotted fever	*A. maculatum* (Gulf Coast tick)	South Central and Southeastern United States
Rickettsia spp 364D[c]	Unnamed spotted fever	*D. occidentalis* (Pacific Coast tick)	Northern California, West Coast of United States
Ehrlichia chaffeensis	Human monocytic ehrlichiosis	*A. americanum* (lone star tick), possibly *D. variabilis* (American dog tick)	Southeastern and Eastern United States
E. ewingii[d]	Human ehrlichiosis	*A. americanum* (lone star tick)	Southeastern and Eastern United States
E. muris-like	Human ehrlichiosis	*A. americanum* (lone star tick)	Southeastern and Eastern United States
Anaplasma phagocytophilum	Human granulocytic anaplasmosis	*I. scapularis* (black-legged tick), *I. pacificus* (western blacklegged tick), possibly *D. variabilis* (American dog tick)	Midwestern and Eastern United States and Canada, West coast of United States
Colorado tick fever virus	Colorado tick fever	*D. andersoni* (Rocky Mountain wood tick)	Western United States and Canada
Babesia microti, *B. duncani* and *B. divergens*	Babesiosis	*I. scapularis* (black-legged tick), *I. pacificus* (western blacklegged tick)	
Bartonella spp	Bartonellosis	*I. pacificus* (western blacklegged tick)	Western United States and Canada

[a]In North America only.
[b]Masters E, Granter S, Duray P, Cordes P. Physician-diagnosed erythema migrans and erythema migrans-like rashes following lone star tick bites. Arch Dermatol 1998;134:955–960; [c]Shapiro MR, Fritz CL, Tait K, et al. *Rickettsia* 364D: A newly recognized cause of eschar-associated illness in California. Clin Infect Dis 2010;50:541–548; [d]Buller RS, Arens M, Hmiel SP, Paddock CD, et al. *Ehrlichia ewingii*, a newly recognized agent of human ehrlichiosis. N Engl J Med 1999;341:148–155.

they mate with a male. Males do not feed, or do so minimally, and primarily inhabit larger hosts to find mates.

Larvae and nymphs are usually the stages that become infected with various parasites when they feed on smaller animals (birds, mammals, and reptiles). These initial hosts are not sickened by the microbes and so act as the reservoir of infection.

The density of tick infection with various microbes is quite variable from location to location. Studies of ticks in the wild on the West coast of the United States and Canada have found that most *Ixodes pacificus* populations are $<1\%$ infection, though "hot spots" with up to 10% infection rates have been reported.[4,5] However, other organisms may be much more common in this tick species, including one sampling in California at three sites that found 19% of western blacklegged ticks infested with *Bartonella* spp.[6] Similarly *I. pacificus* in Western Oregon were found to only be infected $<2\%$ of the time with *B. burgdorferi*, and no ticks (which were few in number anyway) in urban Portland, Oregon, were infected.[7] For comparison, *I. scapularis* ticks in Connecticut, the state with the highest Lyme disease rates in the country, were found to be infected with *B. burgdorferi* 8.6–24.4% of the time over the period 1989–1996 in one study.[8] Such variables must be considered in determining the risk of infection in a particular patient, as well as in where resources should be directed to deal with the greatest risk.

Table 2. Distinctive North American Adult Female Tick Features

Tick	Coloration	Human aggressiveness	Other distinctive features	Peak season[a]
A. americanum (lone star tick)	Brownish-red, white bands on legs	High	Single white dot in middle of back ("lone star") of adult female, move extremely quickly	Early spring through midsummer
A. maculatum (Gulf Coast tick)	Dark brown body, light brown legs	Low (prefers other hosts)	V-shaped yellow band on partial scutum[b]	Highly variable (adults prefer dry season)
D. andersoni (Rocky Mountain wood tick)	Reddish-brown body and legs	Moderate	Yellow partial scutum	Spring and summer
D. variabilis (American dog tick, wood tick)	Black-red legs and body	Moderate	Whitish/yellow/black variegated partial scutum	Spring and summer
I. pacificus (western blacklegged tick)	Very similar to *I. scapularis*	Low	Somewhat furry appearance, partial black scutum	Late spring, summer
I. scapularis (blacklegged tick, deer tick)	Black legs, red body	Moderate	Black partial scutum	Late spring, summer
R. sanguineus (brown dog tick)	Light and dark brown	Low (prefers dogs as hosts)	Rim of lighter brown around edge of body	Unknown

Nymph forms are also very prone to biting, are usually exceedingly tiny, and often appear quite different from the adult form. Also note that once engorged ticks can look extremely different (e.g., the adult female of *I. scapularis* looks silver-blue and rounded after a blood meal).
[a]Though infection can occur at any time of year, including warm winters.
[b]Scutum (Latin "shield"): a plate that partially or totally covers the body.

The Ecology of Lyme Disease

Lyme disease has proven a useful model for a disease heavily influenced by ecological factors.[9]

Environmental factors therefore have to be considered in reducing the risk of tick-borne illnesses. Perhaps the most natural approach to preventing Lyme disease and other tick-borne diseases will be moving the environment back to a more natural state, affecting deer, rodent, predator, and forest populations.

Currently, deer populations are above recorded historic levels, with densities in some areas (including suburbs) reaching 100 deer/km^2.[10] Whitetail deer are important hosts for *Ixodes* nymphs and adults, and thus these and other deer play a role in maintaining and expanding tick populations. A 13-year study found that reducing deer density to $<$1.9 deer/km^2 in Connecticut reduced tick abundance by 76% and cases of Lyme disease by 80%.[11] Use of immunocontraception has also proven effective in field trials for reducing deer overpopulation.[8] Very high deer populations appear to be contributing to the spread of the prion disease known as chronic wasting disease, and are devastating to forests.[12,13] Conscious eradication of large predators, mainly wolves and cougars, by humans coupled with various impacts that have depleted efficient rodent predators, most notably the displacement of red foxes by coyotes that prefer to eat rabbits, cats, dogs, and other larger prey, have also played a major role in increasing Lyme disease.[14] Since most ticks are infected with *Borrelia* and other microbes when they feed on non-mouse rodents as larvae or nymphs, changes in rodent predation are crucial to the population dynamics of rodents and hence Lyme disease's reservoirs.[15] It is a cruel irony that gray wolves are susceptible to Lyme disease, and the current epidemic levels of this disease might make it harder to restore this predator.[16]

Deer overpopulation decimates the understory plants in the amazingly regrown Northeastern U.S./Canadian forests (which were largely cut down when Europeans settled the East Coast of North America).[17,18] This removes the grasses and other low-growing plants that weasel-family rodent predators depend on to catch rodents, making them less effective. Decreased biodiversity in the forest may also promote Lyme disease; for example, opossums and squirrels efficiently remove ticks (compared with mice, shrews, voles, and related rodents) and thus are more of a "dead-end host," as they likely overall reduce *Borrelia* populations.[19] Invasive plants in the understory of forests also contribute to favorable habitat for *I. scapularis*. One study found that the presence of *Berberis thunbergii* (Japanese barberry), an invasive Eurasian shrub, in forests in Connecticut greatly improved survival of blacklegged ticks, compared with areas where it was absent, in part because it protect ticks from drying out.[20]

Preventing Tick-Borne Infections

The most important step in preventing tick-borne infections is to prevent tick bites. This means avoiding peak habitat of ticks (grassy areas and woodlands), particularly in their peak season. If entering such areas is unavoidable, then it is recommended that people wear long sleeves, long pants, socks, and shoes to help avoid ticks reaching the skin. Ideally, pants would be tucked into socks. After being outdoors, humans and dogs should be brushed off before going indoors and then carefully checked for any ticks. If identified and not attached, they should simply be destroyed. If identified and attached, they should be removed very carefully by grasping the mouth parts, preferably with blunt, angled forceps, and easing the tick out.[21] The tick should be preserved for testing to determine if it was infected. Wrenching a tick out or irritating it by other means can cause its mouth parts to separate from the body and inject more of an infectious dose of microbes into the host. Various folkloric tricks for causing ticks to let go, such as trying to heat or burn them, are dangerous at best and should be strictly avoided. In patients with tick allergies, freezing the tick first to kill it is safer then removing it with forceps. Application of topical antimicrobials after tick removal may help reduce infection.

Non-chemical means of tick population reduction are available. Guinea hens and chickens will eat ticks in large numbers. However, guinea hens are very loud, not very good at predator avoidance, and can tend to roam excessively or not stay rooted. Hence, chickens tend to be a better option in settings that would allow for their introduction. A robot that destroys ticks has also been developed, and, in an initial field test, could reduce the levels of mostly adult lone star ticks to zero within 1 hour and kept there for 24 hours.[22] Reducing area rodent populations and deer, as discussed above, may also help control ticks.

Chemical tick repellants and killing agents (acaricides) are also helpful at preventing tick bites, most notably pyrethrum, pyrethroids, and permethrin.[23] Permethrin is a mixture of four synthetic, fat-soluble stereoisomers. Its structure is based on natural pyrethroids found in various plant species, but most notably *Tanacetum cinerariifolium* = *Chrysanthemum cinerariifolium* (Dalmatian pyrethrum), and to a much lesser extent *Tanacetum coccineum* = *Chrysanthemum roseum* (Persian pyrethrum) and *Glebionis coronaria* = *Chrysanthemum coronaria* (garland chrysanthemum).[24] All of these species are native to the Mediterranean basin and South Central Asia. Tasmania, Kenya, Tanzania, and Ecuador are major growers of Dalmatian pyrethrum today. There is evidence that crude extracts of Dalmatian pyrethrum repels brown dog ticks.[25]

Pyrethrum flowers contain varying levels of pyrethroids that act as nerve toxins to insects, ticks, and other pests. They are fairly rapidly biodegradable, unlike permethrin, which is far more persistent in the environment. This does make permethrin useful to add to clothing as an ongoing insecticide, particularly because it does not degrade any known natural or synthetic fiber and has no odor once it dries. It acts as an on-contact acaricide, preventing the ticks from ever reaching the skin. It has minimal absorption and toxicity, even when applied directly to the skin, though such use is not recommended for preventing tick bites.[26] By comparison, the synthetic neurotoxin diethyltoluamide (DEET) only repels ticks, and has the distinct disadvantages of dissolving various synthetic fibers, having its absorption increased by sunscreen (thus necessitating it being applied 15 minutes or more after oxybenzone sunscreen is applied), has more toxic risk than permethrin, and has a disagreeable odor.[27,28] Unfortunately, permethrin resistance has begun to develop in dog ticks in the United States, and other tick species will likely follow, given the widespread use of this chemical and the inevitable history of resistance developing to prior single chemicals in various disease vectors.[29]

Numerous natural acaricides have been researched and may be a reasonable alternative to the failing single molecular entity approach that permethrin and DEET represent (see Table 3 for recent examples, though many others could have been cited). Most research on natural products has been conducted with *Rhipicephalus microplus*, the southern cattle tick, a hard tick that infests many economically important species. It was eradicated from the United States after 1917. Nevertheless, it gives an idea for agents that should be studied further and specifically applied to human-infesting species. It is also still present along the Rio Grande bordering Texas and New Mexico, and with rising resistance to pyrethroids in populations coming from Mexico, it may re-establish in the United States.[30] Those that have been tested against human-biting ticks will be discussed in more detail here.

C. citriodora (lemon eucalyptus, formerly *Eucalyptus citriodora*) in the Myrtaceae family is a native Australian tree. Commercially it is largely grown in Brazil and China (Fig. 1). The leaves contain high levels ($\sim 80\%$) of lemon-scented citronellal in its steam-distilled volatile oil. This naturally breaks down into the two isomers (cis- and trans-) of PMD. Numerous studies have shown that both the crude volatile oil and PMD are active but somewhat short-lived (4–6 hours) mosquito repellants.[31] In a randomized trial, 111 Swedish adults living in an area heavily infested with *I. ricinus* (castor bean tick), the main vector of Lyme disease in Europe, either applied lemon eucalyptus spray containing 64% PMD twice daily to their legs or no repellant for 2 weeks (then the groups crossed-over).[32] Significantly fewer attached ticks were found during use of PMD spray compared with no repellant with no adverse effects. Two other small, human field trials found that 30% lemon eucalyptus lotion and 40% spray efficiently repelled both *I. pacificus* and *I. ricinus*.[33] Though larger, more rigorous trials would still be helpful. It appears that relatively safe and natural lemon eucalyptus oil products, reapplied two to three times daily before entering tick-infested areas, is a reasonable strategy for reducing tick bites.

2-Undecanone is a strong-smelling, naturally occurring, 11-carbon ketone found in such medicinal plants as *Zingiber officinale* (ginger), *Ruta graveolens* (rue), *Syzygium aromaticum* (cloves), and *Houttuynia cordata* (houttuynia, yú xīng cǎo) and such foods as bananas, strawberries, and tomatoes. Most of it is made synthetically in modern times. It is often described as having a floral, fruity odor somewhat akin to pineapple. A repellant product containing 7.75% 2-undecanone has been tested in human field trials for tick repulsion. In one such study, volunteers in North Carolina wore one sock treated with 2-undecanone or DEET and one sock treated only with a

Table 3. Tick Repellent and Acaricidal Herbs and Extracts in Recent Preclinical Research

Herb/extract	Model and effect	Reference
Chrysopogon zizanioides (vetiver, khus), Poaceae, SDVO of rhizome	*Amblyomma cajennense* and *Rhipicephalus microplus*: reduced egg laying and hatching, larvicidal	Campos et al. 2015[a]
Lippia alba (bushy lippia), Verbenaceae, SDVO of leaf, citral chemotype	*Rhipicephalus microplus*: larvicidal, adulticidal (at fairly high concentrations)	Peixoto et al. 2015[b]
Argemone mexicana (Mexican poppy), Papaveraceae, whole plant tincture	*Rhipicephalus microplus* (pyrethroid-resistant and non-resistant): acaricidal, reduced egg laying	Ghosh et al. 2015[c]
Datura metel (devil's trumpet), Solanaceae, fruit tincture	*Rhipicephalus microplus* (pyrethroid-resistant and non-resistant): acaricidal, reduced egg laying	Ghosh et al. 2015[c]
Murraya koenigii (curry tree), Rutaceae, leaf tincture	*Rhipicephalus microplus* (pyrethroid-resistant): acaricidal, reduced reproduction	Singh et al. 2015[d]
Artemisia absinthium (wormwood), Asteraceae, leaf tincture	*Rhipicephalus microplus*: acaricidal, reduced egg hatching	Parveen et al. 2014[e]
Atropa belladonna (belladonna), Solanaceae, leaf tincture, scopolamine, atropine	*Rhipicephalus microplus*: acaricidal, larvicidal, reduced egg laying and hatching (100% w/ pure alkaloids)	Godara et al. 2014[f]
Ocimum spp (basil), Lamiaceae, SDVOs, eugenol, thymol, elemicin	*Rhipicephalus microplus*: larvicidal	Hüe et al. 2015[g]
Syzygium aromaticum (clove), Myrtaceae, SDVO	*Rhipicephalus microplus*: acaricidal, reduce egg laying and hatching	De Mello et al. 2014[h]
Hyptis suaveolens (pignut, chan), Lamiaceae, SDVO	*Ixodes ricinus*: tick repellant	Ashitani et al. 2015[i]
Calendula officinalis (calendula), Asteraceae, flower tea and tincture	*Rhipicephalus microplus* (pyrethroid-resistant): acaricidal, reduced egg laying and hatching; tincture superior	Godara et al. 2015[j]
Allium sativum (garlic), Amaryllidaceae, SDVO	*Rhipicephalus microplus*: larvicidal	Martinez-Velazquez et al. 2011[k]

[a]Campos RN, Nascimento Lima CB, Passos Oliveira A, et al. Acaricidal properties of vetiver essential oil from *Chrysopogon zizanioides* (Poaceae) against the tick species *Amblyomma cajennense* and *Rhipicephalus* (*Boophilus*) *microplus* (Acari: Ixodidae). Vet Parasitol 2015;212:324–330; [b]Peixoto MG, Costa-Júnior LM, Blank AF, et al. Acaricidal activity of essential oils from *Lippia alba* genotypes and its major components carvone, limonene, and citral against *Rhipicephalus microplus*. Vet Parasitol 2015;210:118–122; [c]Ghosh S, Tiwari SS, Kumar B, et al. Identification of potential plant extracts for anti-tick activity against acaricide resistant cattle ticks, *Rhipicephalus* (*Boophilus*) *microplus* (Acari: Ixodidae). Exp Appl Acarol 2015;66:159–171; [d]Singh NK, Jyoti, Vemu B, et al. In vitro acaricidal activity of *Murraya koenigii* (L) Spreng (Rutaceae) extracts against synthetic pyrethroid-resistant *Rhipicephalus* (*Boophilus*) *microplus*. Parasitol Res 2015;114:1531–1539; [e]Parveen S, Godara R, Katoch R, et al. In vitro evaluation of ethanolic extracts of *Ageratum conyzoides* and *Artemisia absinthium* against cattle tick, *Rhipicephalus microplus*. Scientific World J 2014;2014:858973; [f]Godara R, Katoch M, Katoch R, et al. In vitro acaricidal activity of *Atropa belladonna* and its components, scopolamine and atropine, against *Rhipicephalus* (*Boophilus*) *microplus*. Scientific World J 2014;2014:713170; [g]Hüe T, Cauquil L, Fokou JB, et al. Acaricidal activity of five essential oils of *Ocimum* species on *Rhipicephalus* (*Boophilus*) *microplus* larvae. Parasitol Res 2015;114:91–99; [h]de Mello V, Prata MC, da Silva MR, et al. Acaricidal properties of the formulations based on essential oils from *Cymbopogon winterianus* and *Syzygium aromaticum* plants. Parasitol Res 2014;113:4431–4437; [i]Ashitani T, Garboui SS, Schubert F, et al. Activity studies of sesquiterpene oxides and sulfides from the plant *Hyptis suaveolens* (Lamiaceae) and its repellency on *Ixodes ricinus* (Acari: Ixodidae). Exp Appl Acarol 2015;67:595–606; [j]Godara R, Katoch R, Yadav A, et al. In vitro acaricidal activity of ethanolic and aqueous floral extracts of *Calendula officinalis* against synthetic pyrethroid resistant *Rhipicephalus* (*Boophilus*) *microplus*. Exp Appl Acarol 2015;67:147–157; [k]Martinez-Velazquez M, Rosario-Cruz R, Castillo-Herrera G, et al. Acaricidal effect of essential oils from *Lippia graveolens* (Lamiales: Verbenaceae), *Rosmarinus officinalis* (Lamiales: Lamiaceae), and *Allium sativum* (Liliales: Liliaceae) against *Rhipicephalus* (*Boophilus*) *microplus* (Acari: Ixodidae). J Med Entomol 2011;48:822–827.
SDVO, steam-distilled volatile oil.

carrier.[34] 2-Undecanone and DEET were equally effective at preventing lone star ticks from adhering to the socks compared with the placebo socks. There was evidence that 2-undecanone worked partly through olfactory repellency of the ticks. In laboratory conditions, 2-undecanone at a concentration of 40% was as effective as pure DEET at repelling lone star ticks, while 30% was as effective as pure DEET at repelling blacklegged ticks.[35] When impregnated into cloth and kept at room temperature, 2-undecanone 7.75% provided 5 weeks of at least 90% repellency against lone star ticks.[36] 2-Undecanone is also an effective mosquito repellant.[37]

Another product contains the natural terpenoids nootkatone, originally found in grapefruit, and carvacrol, which is common in many Lamiaceae family plants such as *Origanum vulgare* (oregano) and *Thymus vulgaris* (thyme). In field trials, clothing treated with this combination were just as effective as permethrin at repelling both lone star and blacklegged tick nymphs.[38] This effect, at least for the nootkatone component,

Figure 1. ***Corymbia citriodora*****. Permissions: Drawing by Meredith Hale and reprinted with permission.**

endured with 100% repellency for 3 days. In a similar study, nootkatone applied to clothing retained repellency after 7 days more effectively than permethrin.[39]

Herbs Against Tick-Borne Illnesses

No clinical trials of any herb or herbal product for Lyme disease or co-infections could be located. This is moderately unusual for a disease such as Lyme disease that has been clearly described since 1975 and indistinctly known for at least 200 years before that. While not every disease has had studies published about it using herbs, this is unusual for something as common and significant as Lyme disease. It is problematic because many companies and practitioners make claims for products helping Lyme disease, but none has apparently been willing or able to conduct or publish any clinical trials confirming their contentions. This situation urgently needs to be remedied so that practitioners can make a more informed and reasoned choice among the various natural programs being promoted for Lyme disease (and other tick-borne infections to a lesser degree).

D. fullonum = *D. sylvestris* (fuller's teasel) is a plant native to Eurasia and North Africa that was historically used in combing out tangles or naps in wool and other fabrics (a process referred to as fulling). It provides a good example of the current dilemma in which herbs to use for people with Lyme disease. Fuller's teasel is an invasive weed in North America and many other parts of the world. Apparently based on traditional use of the root of the plant to treat arthritis and other chronic inflammatory diseases, it has come to be used as a treatment for chronic symptoms of Lyme disease, which commonly includes arthralgias and arthritis.[40] This in significant part comes from a description by Matthew Wood of using the herb for people with Lyme disease.[41] Other species of *Dipsacus* are also used in Traditional Chinese Medicine.

As one example of the claims made, one Web site states that teasel will "pull the bacterium [*B. burgdorferi*] from tissue, and into the blood stream, exposing it to antibiotics and the immune system."[42] No references are given for the basis of this, and no research could be found confirming this supposed effect. One study found a tincture of teasel root did not kill or inhibit *B. afzelii* in the test tube, while less polar ethyl acetate extracts did inhibit growth of the bacterium.[43] Most clinical sources do not suggest teasel is antimicrobial or directly affects *Borrelia*, but instead that it helps with symptoms, perhaps by modulating inflammation, which is supported by in vitro and some clinical research on *D. asperoides* and *D. japonica* (xù duàn, Japanese teasel) root.[44,45] Anyhow, the exact place, form, and dose of teasel for anyone with any form of Lyme disease or any co-infection remains uncertain.

A handful of other herb products have been studied in vitro for their activity against *Borrelia* and other tick-borne infectious agents (see Table 4). *Brucea javanica* (Java brucea, yā dǎn zǐ) fruit in the Simaroubaceae family is a shrub or small tree native to eastern Asia. Its intensely bitter fruit is a traditional treatment for dysentery.[46] It is also traditionally used to treat malaria, and in vitro research confirms it kills

Table 4. Preclinical Research on Herbs for Tick-Borne Infectious Organisms

Herb/extract	Organism and effect(s)	Reference
Cistus creticus (pink rock rose), Cistaceae, leaf SDVO and hexane extract	*B. burgdorferi*: growth inhibition in vitro	Hutschenreuther et al. 2010[b]
Citrus x *paradisi* (grapefruit), Rutaceae, seed extract[a]	*B. afzelii*: killing of motile spirochetes and latent rounded forms, degeneration of cysts in vitro	Brorson and Brorson 2007[c]
Camellia sinensis (green tea), Theaceae, (–)-epigallocatechin gallate	*B. microti*: cleared mice of infection after 14 days at 5 mg/kg	Aboulaila et al. 2010[d]
Aloe marlothii (mountain aloe), Asphodelaceae, leaf acetone extract	*Ehrlichia ruminantium*: blocked host cell entry in vitro	Naidoo et al. 2006[e]
Elaeocarpus nitidus (xiao ye du ying, small-leaf elaeocarpus), Elaeocarpaceae, bark ellagic acids	*B. gibsoni*: moderate growth inhibition in vitro	Elkhateeb et al. 2005[f]
Phyllanthus niruri (bhumiamalaki), Phyllanthaceae, flavonoid	*B. gibsoni*: bactericidal	Subeki et al. 2005[g]
Arcangelisia flava (yellow root), Menispermaceae, isoquinoline alkaloids including berberine	*B. gibsoni*: bacteriostatic	Subeki et al. 2005[h]
Achillea millefolium (yarrow), Asteraceae, leaf aqueous extract	*B. gibsoni*: bacteriostatic	Murnigsih et al. 2005[i]
Curcuma zanthorrhiza (Java ginger), Zingiberaceae, rhizome constituents	*B. gibsoni*: bacteriostatic	Matsuura et al. 2007[j]
C. zedoaria (white turmeric), Zingiberaceae, bark extract and constituents	*B. gibonia*: bacteriostatic	Kasahara et al. 2005[k]

[a]There is credible evidence that the production of this product results in formation of benzalkonium chloride and similar molecules which are arguably not healthy or particularly advisable for internal use, or at least that they are not really different from synthetic antibiotics (Ganzera M, Aberham A, Stuppner H. Development and validation of an HPLC/UV/MS method for simultaneous determination of 18 preservatives in grapefruit seed extract. J Agric Food Chem 2006;54:3768–3772; Takeoka G, Dao L, Wong RY, Lundin R, et al. Identification of benzethonium chloride in commercial grapefruit seed extracts. J Agric Food Chem 2001;49:3316–2220.)

[b]Hutschenreuther A, Birkemeyer C, Grötzinger K, et al. Growth inhibiting activity of volatile oil from *Cistus creticus* L against *Borrelia burgdorferi* s.s. in vitro. Pharmazie 2010;65:290–295; [c]Brorson O, Brorson S. Grapefruit seed extract is a powerful in vitro agent against motile and cystic forms of *Borrelia burgdorferi* sensu lato. Infection 2007;35:206–208; [d]Aboulaila M, Yokoyama N, Igarashi I. Inhibitory effects of (-)-epigallocatechin-3-gallate from green tea on the growth of *Babesia* parasites. Parasitology 2010;137:785–791; [e]Naidoo V, Zweygarth E, Swan GE. Determination and quantification of the in vitro activity of *Aloe marlothii* (A Berger) subsp *marlothii* and *Elephantorrhiza elephantina* (Burch) Skeels acetone extracts against *Ehrlichia ruminantium*. Onderstepoort J Vet Res 2006;73:175–178; [f]Elkhateeb A, Subeki, Takahashi K, et al. Anti-babesial ellagic acid rhamnosides from the bark of *Elaeocarpus parvifolius*. Phytochemistry 2005;66:2577–2580; [g]Subeki S, Matsuura H, Takahashi K, et al. Anti-babesial and anti-plasmodial compounds from *Phyllanthus niruri*. J Nat Prod 2005;68:537–539; [h]Subeki, Matsuura H, Takahashi K, et al. Antibabesial activity of protoberberine alkaloids and 20-hydroxyecdysone from *Arcangelisia flava* against *Babesia gibsoni* in culture. J Vet Med Sci 2005;67:223–227; [i]Murnigsih T, Subeki, Matsuura H, et al. Evaluation of the inhibitory activities of the extracts of Indonesian traditional medicinal plants against *Plasmodium falciparum* and *Babesia gibsoni*. J Vet Med Sci 2005;67:829–831; [j]Matsuura H, Nomura S, Subeki, et al. Anti-babesial compounds from *Curcuma xanthorrhiza*. Nat Prod Res 2007;21:328–333; [k]Kasahara K, Nomura S, Subeki, et al. Anti-babesial compounds from *Curcuma zedoaria*. Planta Med 2005;71:482–484.

Plasmodium parasites.[47] Based on these results, it is not too surprising that in vitro its constituents inhibit the growth of *Babesia gibsoni*.[48,49] A study of three dogs infected with *B. gibsoni* found that bruceine A, a quassinoid extracted from Java brucea fruit, completely protected two of them from developing any symptoms (though anemia did develop over 4 weeks, and total clearance of the parasite was not achieved) while the one untreated dog became extremely ill.[50] This promising treatment needs to be assessed in human babesiosis patients. Java brucea is a potentially very toxic herb that is absolutely contraindicated in pregnancy and lactation.

Artemisinin is a sesquiterpene lactone found in *Artemisia annua* (sweet Annie, qīng hāo) leaf in the Asteraceae family. It is a famous treatment for people with malaria and may also be active in patients with cancer.[51] In vitro testing found artemisinin very active against *B. burgdorferi* round bodies, a non-motile persistent form of the organism, particularly when combined with cefoperazone and doxycycline.[52,53] Artemisinin and its semi-synthetic derivative artemether were active against *B. gibsoni* in vitro.[54] Artesunate, a water-soluble semi-synthetic artemisinin derivative, effectively treated mice infected with *B. microti*.[55] Clearly, sweet Annie, artemisinin, and its derivatives are also deserving of study in humans affected with some tick-borne infections.

Absolutely no research published in peer-reviewed journals was identified on the effect of any herb or constituent on *Ehrlichia* spp, *Bartonella* spp, *Rickettsia* spp, or *Anaplasma phagocytophylum.* Many of the most recommended herbs for treating Lyme disease, notably *Reynoutria japonica* = *Polygonum cuspidatum* (Japanese knotweed), *Cryptolepsis sanguinolenta* (cryptolepsis), *Uncaria* spp (uña de gato), *Andrographis paniculata* (king of bitters), *Guaiacum officinale* (lignum vitae), *Stillingia sylvatica* (queen's root), and *Sida acuta* (common wireweed), also appear to have no credible evidence published supporting their efficacy. Publications in non-peer-reviewed publications on proprietary extracts of *Uncaria* suggest it might have some activity, but until more credible evidence is presented this should be viewed as extremely preliminary.[56] These herbs may have inflammation-modulating and other actions that might help in Lyme disease, and some do have evidence of efficacy against other infections organisms. So while the theoretical basis for their use may be as sound as any other extrapolations for other diseases, they remain theoretical. It cannot be overstated how unfortunate and shocking this lack of research is regarding herbs to treat such relatively common and serious conditions. The situation needs to be urgently remedied.

Conclusion

There is ample evidence that herbal medicines have a role to play in preventing tick bites and therefore the spread of numerous serious tick-borne illnesses, most notably Lyme disease. Several field trials have confirmed a range of safe herbal extracts reliably repel several of the worst offending ticks. Unfortunately, when it comes to clinical use of herbs to treat people infected with these tick-vectored organisms, whether it be acutely or chronically, evidence is severely lacking. In vitro and animal studies for a handful of herbs have not been followed up with human clinical trials in any case. Such trials are desperately needed so clinicians can know which treatments really are useful to recommend to patients. Until such information is forthcoming, it is extremely difficult to make recommendations outside of research studies. ■

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