Tropical American Plants in the Treatment of Infectious Diseases

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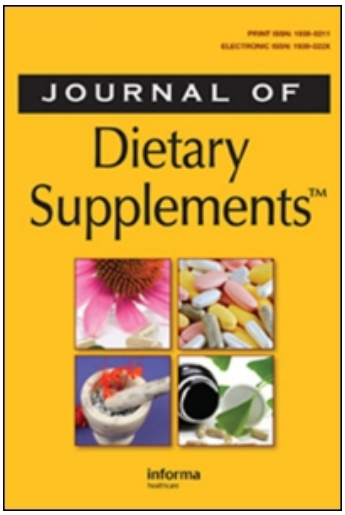

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Tropical American Plants in the Treatment of Infectious Diseases

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Tropical American Plants in the Treatment of Infectious Diseases

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ABSTRACT. The increasingly diverse U.S. immigrant populations and the growing use of medicinal herbs create a need for health care professionals to expand their knowledge in this area. This is a review of tropical plants, *Annona Muricata, Artemisia absinthium, Cinchona officinalis, Illicium verum, Momordica charantia*, *Opuntia streptacantha*, *Schinus terebinthifolius,* and *Tabebuia avellanedae (impetiginosa)*, commonly used by Latino and Haitian populations for the treatment of infectious disease. All the eight plants discussed here have one or more of the following: antibacterial, antiviral, antifungal, or antiparasitic properties. All of these plants are primarily known and used in the tropical region, but they are also readily available for purchase in the United States, specifically in the ethnic markets. This review discusses their traditional uses, chemical constituents, proven scientific evidence, and toxicities.

KEYWORDS. medicinal plants, ethnopharmacology, traditional medicine, phytotherapy, infectious diseases, antibiotics, antimicrobials,

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antiparasitic, antifungal, drug interactions, adverse effects, *Annona muricata*, *Artemesia absinthium*, *Cinchona officinalis*, *Illicium verum*, *Momordica charantia*, *Opuntia streptacantha*, *Schinus terebinthifolius*, *Tabebuia avellanedae* (impetiginosa)

INTRODUCTION

Statistics show that in the last decade the U.S. immigrant population has become increasingly diverse (Migration Policy Institute, 2000). There is a theory that many of the plants from these geographic regions have activity against common ailments of these areas, which are infectious, viral, parasitic, and fungal in nature. When immigrants from these regions migrate to different countries, they continue their use of familiar plants in the new settings (Handbook of Immigrant Health, 1998; Najm, Reinsch, Hoehler, & Tobis, 2003). The medical community is starting to recognize the importance of this information. Health care providers are motivated by concerns about the efficacy of these botanical therapies and their potential dangers (i.e., interactions and toxicities). Knowledge of phytomedicinals in immigrant populations also contributes to the new requirements for cultural competence training (Linkins, McIntosh, Bell, & Chong, 2002).

BACKGROUND

The twentieth century was a time for the development of "miraculous" compounds that have helped allopathic medicine to advance significantly—this shift in medicine is often attributed to the discovery of antibiotics. Many of the antibiotics currently used for the treatment of infections come from diverse groups of fungi—fungi imperfecti penicillium and cephalosporum were the two of the first members. Now, two-thirds of antibiotics are produced by members of the bacterial order actinomycetales (soil-living streptomyces, bacillaceae, as well as fungi such as aspergillales, algae, symbiotic lichens, mosses, and higher plants) (Lewis & Elvin-Lewis, 2003). The search for new antibiotics peaked in the 1960s to 1970s. Development of resistance is forcing many scientists to look for alternatives. Exploring the adaptive capability of plant eukaryotic (multicellular) antibiotics is still an undiscovered territory. These substances certainly have very rich historical uses against bacterial, fungal, viral, and parasitic infections (Lewis & Elvin-Lewis, 2003).

At the time when meaningful data from higher plants started to appear, it was ignored because of the coincidental discovery of antibiotics and their production through fermentative processes. The recent attempts of the pharmaceutical companies to discover compounds have not been successful because of the mechanistic screening processes. It appears, however, that when a specific condition is targeted the screening outcomes increase 3–5 fold. The best outcomes are observed when the disease studied has very clear parameters and is understood in both traditional and conventional medicine. When plants are selected based on secondary data there is a 40%–50% discovery rate, whereas using primary data, complemented by verification of therapeutic worth, can increase discovery to more than 90% (Lewis & Elvin-Lewis, 2003).

Another area of research is the concept of mimicking the complex mixture of bioreactive substances by compounding them in proportions similar to those in plants and nature. This approach may become an effective pathway for prevention of antimicrobial resistance. When investigating new antimicrobial treatments, a promising technique is to search the local habit for compounds effective against local pathogens. A perfect example is the current evaluation of the rainforest compounds effective in the treatment of *Mycobacterium tuberculosis*, a pathogen found in that environment (Lewis & Elvin-Lewis, 2003).

In addition to antimicrobial agents, other deterrent compounds include antiviral, antiparasitic, anthelmintic, and pesticide botanicals. Antiviral properties are common in many plants; however, only a few compounds are currently used to treat viral conditions in conventional medicine. Perhaps the best known is oseltamivir (Tamiflu) made from the Chinese star anise. Some of the well-known antiparasitic agents derived from phytomedicinals include quinine and artemisinin. The best known and most effective insecticides and pesticides come from synthetic chemical compounds. However, the phytochemical pesticides appear to be the safest, yet still efficacious and cost-effective. They are derived among others from the Annonaceae, Cucurbitaceae, Clusiaceae, Convolvulacae, Fabaceae families (Lewis & Elvin-Lewis, 2003).

The next eight plants described (see Table 1 for Latin, common, and family names) were chosen based on their historical use and the growing evidence of their efficacy in the scientific literature. This approach to searching for new therapies appears to be the most fruitful due to the strength of both subjective and objective evidence. Even in the absence of randomized-controlled clinical trials, conclusions can be made based on the strong evidence from basic sciences combined with parallel widespread clinical uses and efficacy described by traditional practices.

TABLE 1. Names of the Plants[a]

Latin Name	Family Name	Common Names
Annona muricata	Annonaceae	Graviola, Soursop, Corossol, Guanabana, Guanavana, Guanaba, Annona de Broquel
Artemisia absinthium	Asteraceae/ Compositae	Wormwood, Silver sage, Sage brush, Absinthe, Ajenjo, Yerba maestar, Absinthe, Istafiate, Estafiate, Green ginger, Quing Hao
Cinchona officinalis	Rubiaceae	Quinine, Quinine bark, Quina, Quinine, Kinakina, China bark, Cinchona bark, Yellow cinchona, Red cinchona, Peruvian bark, Jesuit's bark, Chinarinde, Ecorce de Quina, Fever tree, Fieberrinde, Quina-quina, Calisaya bark, Fever tree
Illicium verum	Illiciaceae	Star anise, Aniseed stars, Anisi stellati fructus, Badiana, Chinese star anise
Momordica charantia	Cucurbitaceae	Bitter melon, Balsam apple, African cucumber, Balsam pear, Papailla, Sorosi, Sorossie, Asorossi, Spanish Antugua, Sorosi, Cundeamor, Kokouli, Pawoka, Pomme couli, Calaica
Opuntia streptacantha	Cactaceae	Prickly pear cactus, Barbary-fig cactus, Cactus flowers, Cactus fruit, Cactus pear fruit, Opuntia ficus, Opuntia
Schinus terebinthifolius	Anacardiaceae	Brazilian peppertree, Peruvian peppertree, California peppertree, Aroeira, Aroeira salsa, Escobilla, Peruvian mastic tree, Mastic-tree, Aguaribay, American pepper, Anacahuita, Castilla, False pepper, Gualeguay, Jesuit's balsam, Molle del Peru, Mulli, Pepper tree, Pimentero, Pimientillo, Pirul, Christmas berry, Pirú, Perú, Arbol del peru
Tabebuia impetiginosa	Bignoniaceae	Pau D'Arco, Ipê, Ipê roxo, Lapacho, Lapachol, Trumpet bush, Tahuari, Taheebo, Trumpet tree, Ipê-contra-sarna, Tabebuia ipê, Tajy

[a]Boston Healing Landscape Project, 2004; Jellin et al., 2000; Morton, 1981; Taylor, 2003.

Annona muricata

Ethnic Uses, Interesting Facts, Historical Perspective

Annona muricata is one of the most commonly used medicinal plants in the Caribbean, believed to be native to the West Indies and introduced to

the Old World tropics and southern Florida. Annona is a slender, evergreen tree cultivated from the Bahamas through to southern Mexico and Brazil. The ovoid fruits are green and covered with fleshy spines. The edible pulp is used as an ingredient in many foods and beverages. The tea is consumed daily and often mixed with other herbal decoctions. Processed soursop is available as a concentrate. Historically, leaf decoctions are used as sedative, diuretic, antihypertensive, anti-inflammatory, and anthelmintic. Decoctions and oil from the leaves are also used to repel insects, kill head lice, and treat hematuria, influenza, and dysentery. The leaves are sprinkled on beds to promote sleep (Morton, 1981).

Annona muricata contains a wide variety of active ingredients (i.e., 220 types of acetogenins, alkaloids, isoquinolones, etc.) (Jellin et al., 2000).

Antimicrobial Activity

The three acetogenins insolated from the extracts *Annona muricata* pericarp, annonacin, annonacin A, and annomuricin A, in vitro may possess antimicrobial activity against Leishmania species (*L. braziliensis* and *L. panamensis*)(Jellin et al., 2000; Rocha, Almeida, Macedo, & Barbosa-Filho, 2005).

Antiviral Activity

In vitro, an ethanolic extract of *Annona muricata* has an antiviral effect against Herpes simplex virus-1. The extract did not show toxicity to uninfected cells (Bories et al., 1991).

Antiparasitic Activity

Methanolic extracts of *Annona muricata* seeds were tested for antiparasitic activity against *Entamoeba histolytica*, *Nippostrongylus brasiliensis*, *Molinema dessetae*, *Trichomonas vaginalis*, *and Artemia salina*. Six percent crude extract did not demonstrate any activity for *E. histolytica* at a concentration 100 mg/L, but appeared active against *T. vaginalis* at a concentration 30 mg/L. The activity of crude extracts was weak against *E. histolytica* and *T. vaginalis* in comparison to metronidazole, but was potent for *N. brasiliensis* and *A. salina.* Acetogenins isolated from these extracts (i.e., annonacin, annonacinone, corossolin, corossolone, murisolin, and other) are found to be responsible for the important activity on infective larvae of *M. dessetae* (Morton, 1981; Bories et al., 1991).

Artemisia Absinthium

Ethnic Uses, Interesting Facts, Historical Perspective

Therapeutic use of wormwood dates back to ancient times. The plant is named after the goddess Artemisia because of its medicinal properties and was used by Hippocrates (Schauenberg & Paris, 1977). The green, flavored, distilled liqueur, called absinthe, was a popular drink in European cafes at the beginning of the 20th century. After many infamous events attributed to famous people under its influence, absinthe was banned from almost all countries (Tyler, 1993). Found in Europe, Asia, North and South America, bundles of fresh branches of *Artemisia absinthium* are sold in herb markets in Venezuela, Panama, and Costa Rica and in botánicas in the United States. The bitter decoction is traditionally used to calm the nerves, soothe the stomach, and control diarrhea and dysentery. In Puerto Rico and Jamaica, it is taken empty stomach for its anthelmintic properties. Fresh branches are sometimes placed in bedrooms to repel mosquitoes and the dried plant is put between clothes to repel moths. Extracts are used as a flavoring in the United States, but they must be free of thujone, the main toxic constituent (Morton, 1981) (see Table 2). Some of the ingredients of the plant include β-caryophyllene, caryophyllene oxide, α-humulene, linalool, linalooloxide, bornyl acetate, camphor, α-thujone, β-thujone, 1,8-cineole, α-pinene, p-cymene, and eugenol (Blagojevic, Radulovic, Palic, & Stojanovic, 2006; Erdogrul, 2002; Kordali, Cakir, Mavi, Kilic, & Yildirim, 2005a; Kordali et al., 2005b).

Antibacterial Evidence

Extract of 26 species from China, Japan, Thailand, and Yemen were screened for their antibacterial activity against *Bacillus cereus*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Escherichia coli*, and *Salmonella infantis*. *S. aureus* was inhibited by the maximum concentration of *A. absinthium* (2640 mg/L) while *B. cereus* was inhibited by half of this concentration (Alzoreky & Nakahara, 2003). In vitro antibacterial activities of wormwood against *S. aureus*, *B. brevis*, *B. megaterium*, *B. subtilis*, *B. subtilis var. niger*, *Mycobacterium smegmatis*, *Streptococcus thermophilus*, and *Yersinia enterocolitica* were reported. However, *L.monocytogenes*, *E. coli*, *Micrococcus luteus*, and *Pseudomonas fluorescens* exhibited resistance to antibacterial effects of the plant (Erdogrul, 2002). Research on Artemesia discusses different potencies of various chemotypes. The "(Z)-epoxyocimene + beta-thujone" chemotype appears to have high

TABLE 2. Toxicities of the Plants

Annona muricata

Toxicities

- Seeds used as a fish poison in a powdered form (Morton, 1981) .
- Seed oil used topically to kill lice (Morton, 1981)
- Graviola alkaloids—toxic to dopaminergic and GABAnergic neurons in extremely low concentrations—similar mechanism to movement disorders (i.e., Parkinson's and myeloneuropathy) (Jellin et al., 2000).

Artemisia absinthium

Common adverse reactions/Contraindications/Precautions

- Common ADR's: Seizures, bradycardia, abdominal pain, diarrhea, nausea, vomiting, decreased appetite, skin rash, fever, flu-like symptoms, and decreased reticulocyte count (Skyles & Sweet, 2004), skin irritation related to contact with flowers (Morton, 1981).
- Contraindications (strong): Gastrointestinal disorders and ulcers, avoid in pregnancy and lactation (Skyles & Sweet, 2004).

Interactions

- Reduction of efficacy of antacids, sucralfate, histamine-receptor antagonists, proton-pump inhibitors, and antiseizure medications (Skyles & Sweet, 2004).

Toxicities

- Thujone—major toxin.
- Average oil concentration of thujone—70%.
- Regular consumption of thujone-containing products can result in insomnia, nightmares, tremors, renal failure, delirium, paralysis, and death (Skyles & Sweet, 2004).
- One case of seizures and renal failure after consumption of 10 ml of wormwood oil (Weisbord, Soule, & Kimmel, 1997).

Cinchona officinalis

Common adverse reactions/Contraindications/Precautions

- Thrombocytopenia, bleeding, and hypersensitivity reactions (i.e., hives and fever, headaches, nausea, diarrhea, vomiting, ringing in the ears, vision disturbances) (Jellin et al., 2000; Waknine, 2006).
- Topical use of bark may cause contact dermatitis (Jellin et al., 2000).
- Hepatotoxicity and photosensitivity reports (Jellin et al., 2000).
- Contraindicated in patients hypersensitive to quinine, and those with myasthenia gravis (Jellin et al., 2000).

Interactions

- Increases gastric acidity—theoretical decrease in effectiveness of antacids, H2 blockers, and proton-pump inhibitors (Jellin et al., 2000).
- Increased bleeding when used with anticoagulant/antiplatelet medications (Jellin et al., 2000).
- Do not take with its synthetic counterparts (Taylor, 2003).
- Potential interaction with cytochrome P-450 substrates—carbamazepine, phenobarbital—decreased plasma concentration, increased urinary excretion, and reduced effectiveness of antiepileptics (Jellin et al., 2000).

(Continued on next page)

TABLE 2. Toxicities of the Plants *(Continued)*

Toxicities

- Toxicity: Extremely severe.
- Treatment of overdose: Generally supportive.
- Acute quinine poisoning: Visual toxicities, some cases of permanent visual deficit, deaths (Boland, Roper, & Henry, 1985).
- Fatal adult at single oral dose of 2–8 g pure quinine alkaloids (Yarnell, & Abascal, 2004).

Illicium verum

Common adverse reactions/Contraindications/Precautions

- Usually well tolerated orally.
- Certain types may be contaminated with poisonous Japanese anise (Lee & Balick, 2006).
- Not clear whether events reported were caused by the Chinese or Japanese star anise (Lee & Balick, 2006; Ulbricht, & Basch, 2005).
- Reactions include nausea, vomiting, tremors, hypertonia, seizures, convulsions, nervousness, rapid eye movements, and other serious neurologic symptoms (Lee & Balick, 2006; Ulbricht, & Basch, 2005).
- Contraindication: Hypersensitivity to star anise or any member of the Illiciaceae family.

Interactions

- Animal studies—increase in activity of 7-ethoxycoumarin O-deethylase—theoretical increase in risk of bleeding (Ulbricht, & Basch, 2005).
- Avoid before surgeries or when taking anticoagulants and antiepileptic medications (Ulbricht, & Basch, 2005).

Toxicities

- Several cases (neurological and gastrointestinal toxicities in infants ingesting tea); use with extreme caution in infants (Ize-Ludlow et al., 2004a; Ize-Ludlow et al., 2004b; U.S. Food and Drug Administration, 2003).

Momordica charantia

Common adverse reactions/Contraindications/Precautions

- Purgative and emetic properties in seeds.
- Convulsions in children and dogs consuming the fruit (Morton, 1981).
- Avoid in pregnant and lactating women—traditional use as abortifacient (Morton, 1981).

Interactions

- Blood glucose levels lowering and potential additive effects with antihyperglycemic medications (Jellin et al., 2000).

Opuntia streptacantha

Common adverse reactions/Contraindications/Precautions

- Usually well tolerated orally (Jellin et al., 2000).
- Mild side-effects: Diarrhea, nausea, increased stool volume, abdominal fullness, headaches (Jellin et al., 2000).
- Some dermatologic effects from contact with cactus spines (Jellin et al., 2000).
- Contraindication: Hypersensitivity to plant (Jellin et al., 2000).

Interactions

- In diabetics: With concurrent use of chlorpropamide potential additive effects on insulin and blood glucose levels, increased risk of hypoglycemia, closely monitor blood glucose levels (Meckes-Lozyoa & Roman-Ramos, 1986).

(Continued on next page)

TABLE 2. Toxicities of the Plants *(Continued)*

Toxicities
• No toxicities reported after oral administration to adult mice, horses, and humans (Ahmad, Davies, Randall, & Skinner, 1996).
Schinus terebinthifolius
Common adverse reactions/Contraindications/Precautions
• Some Florida grown species—respiratory distress and irritation of the mucous membranes—high urushiol content.
• Not the case with species growing elsewhere (Morton, 1981).
Toxicities
• Low toxicity in mice in dose 2.5 times greater than daily human consumption (Pires, Corsi Taquemasa, Akisue, De Oliveira, & Pulz Araujo, 2004).
• In overdose cases—reversible effects in first 12 hr—depressed response to touch, righting reflex, body tonus (Pires et al., 2004).
Tabebuia impetiginosa (avellanedae)
Common adverse reactions/Contraindications/Precautions
• Severe nausea, vomiting, diarrhea, dizziness, anemia, increased risk of bleeding at high doses (Abt & Hammerly, 2004).
• Occupational asthma in workers exposed to Ipe (Tabebuia spp.) dust (Algranti, Mendonca, Ali, Kokron, & Raile, 2005).
• Avoid in pregnancy and possibly lactation—at least one isolated phytochemical—extreme abortifacient properties in animal study (Guerra, Mazoni, Brandão, & Peters, 2001).
Interactions
• Cases of increased risk of bleeding at high doses
• Contraindicated in coagulation disorders or anticoagulant and antiplatelet medications and herbs (Block, Serpick, Miller, & Wiernik, 1974; Morrison, Brown, Oleson, & Cooney, 1970).

antibacterial and antifungal activities. The "(Z)-epoxyocimene + chrysanthenyl acetate" chemotype, lacking thujone, exhibits only a moderate antimicrobial activity (with no activity against bacterial strains such as *E. coli*, *S. aureus*, and *Enterococcus hirae*) (Juteau et al., 2003). Other studies have found high antibacterial and antifungal activity for the following constituents: ß-thujone, linalool, ß-caryophyllene, and 1,8-cineole. *A. absinthum* root oil lacks thujones but has a high and nonselective antimicrobial activity possibly related to the presence of geraniol and geranyl derivatives (Blagojevic, Radulovic, Palic, & Stojanovic, 2006).

Antifungal Evidence

In vitro testing of the French essential oil of wormwood, which lacks thujone, confirmed the inhibition of growth of *Candida albicans* and *Saccharomyces cerevisiae* var. chevalieri. (Juteau et al., 2003). Essential oils extracted from Turkish *A. absinthium* showed potent wide-spectrum

antifungal activity. The results were not entirely conclusive but it appeared that the oils completely inhibited the growth of numerous fungal species particularly *Alternaria alternate*, *Fusarium oxysporum*, *F. sambucinum*, and *F. solani* (Kordali et al., 2005a, 2005b). In another study, these essential oils were tested against 11 plant fungi. The oils showed potent inhibitory effects at very broad spectrum against all of the tested fungi (Kordali et al., 2005a; Skyles & Sweet, 2004).

Antiparasitic Activity

As its common English name, "wormwood" implies, Artemisia is an effective anthelmintic agent used to destroy intestinal worms (Tyler, 1993). In an in vitro trial, aqueous and alcoholic extracts of wormwood strongly inhibited the growth of *N. fowleri* (Mendiola, Bosa, Perez, Hernandez, & Torres, 1991). A 96.2% suppression of *P. berghei* was reported in another trial in which Swiss mice were given ethanolic extract of wormwood leaves (Zafar, Hamdard, & Hameed, 1990). *Artemisia annua*, a Chinese relative of *Artemisia absinthium*, is the source of a new class of antimalarial drugs showing great promise especially in treating drug-resistant malaria (Price, 2000).

Cinchona Officinalis

Ethnic Uses, Interesting Facts, Historical Perspective

The bark of various species of the Cinchona tree has been used medicinally since 1630. The name was derived from the story of the cure produced in the Countess of Cinchon, wife of a Peruvian viceroy in 1638. Jesuit missionaries spread the powdered bark and tales of its efficacy against malaria around the world. Other historical uses of quinine include treatment of fever, indigestion, mouth and throat diseases, and cancer. In 1820, quinine alkaloid was identified and isolated from the cinchona bark by the French chemists, Joseph Caventou and Joseph Pelletier (DeStefano, 2001). Up to the present time, quinine usage has been extended to mild attacks of influenza, enlarged spleen, muscle cramps, arrhythmias, diarrhea, hangover, neuralgia, pneumonia, typhoid, headache, hemorrhoids, and varicose veins (Jellin et al., 2000; Taylor, 2003). Quinine is also used topically in ophthalmic preparations for astringent, bactericidal, and anesthetic effects. Cinchona trees are native to Colombia, Ecuador, Peru, and Bolivia and their bark contains at least 6.5% of total alkaloids. Cinchona trees are an

important crop and of great economic importance to countries in South America, Asia, and Africa. The history of quinine is a classic example of how the developed world can discover and patent a natural drug, and develop its pharmaceutical manufacture with no monetary return to the people or countries of Peru and Bolivia where cinchona was discovered (Taylor, 2003). Although partially replaced by synthetic drugs, quinine remains a major treatment for malaria (Trease & Evans, 1983). In addition, cinchona also contains the alkaloid quinidine, a successful cardiac drug since the 19th century. Quinidine has not been synthesized, and this, along with the use of quinine as a bitter flavoring, accounts for the continued cultivation of cinchona trees (Taylor, 2003).

Antimicrobial Activity

Ethanol extract of *Cinchona officinalis* has demonstrated antimicrobial activity against *S. aureus*, *B. cereus*, *Streptococcus B hemolytic*, and *Pseudomonas aeruginosa*, whereas hexane extract has demonstrated activity against *Bacillus cereus* and *E. coli* (Rojas, Ochoa, Ocampo, & Munoz, 2006). Quinine sulfate appears to interfere with invasion of *E. coli* into host cells (Wolf et al., 2002). In other experiments it was observed that *Streptococcus pneumoniae*, *Salmonella typhimurium*, and *Shigella flexneri* are sensitive to quinine (Munoz, Garcia, & De la Campa, 1996; Wolf et al., 2005).

Antiparasitic Activity

Quinine is an effective antimalarial agent. In a randomized, controlled, open-label trial, 204 patients received 10 mg/kg of quinine three times a day for the treatment of multidrug-resistant *Plasmodium falciparum* malaria producing an 87% cure rate (Pukrittayakamee et al., 2000). An addition of second antibiotic (such as clindamycin or tetracycline) to the regime yields an even higher cure rate (Kremsner et al., 1995; Parola et al., 2001). Another randomized, controlled, clinical trial involving 30 patients with uncomplicated *P. falciparum* malaria demonstrated quinine's effectiveness and evaluated its ability to prevent relapses (Pukrittayakamee et al., 2003).

Antifungal Activity

Ethanol extract of *Cinchona officinalis* has demonstrated some activity against *Candida albicans* (Nino, Espinal, Mosquera, & Correa, 2003; Rojas, Ochoa, Ocampo, & Munoz, 2006).

Illicium Verum

Ethnic Uses, Interesting Facts, Historical Perspective

Star anise, an evergreen tree 4–10 m in height, immigrated to Latin America from China and Vietnam. Flowers vary from yellowish-green to red. The fruits have a distinctive star shape with eight segments, each containing a shiny brown seed. Traditionally, the fruit and its oil are used as an expectorant and for antispasmodic effects. The oil is used as a flavoring, perfume, and carminative and is blended with oil from *Pimpinella anisum* to create the official preparation of anise oil (Trease & Evans, 1983; Wyk & Wink, 2004).

Antibacterial and Antifungal Activity

An in vitro study found that the star anise constituent, anethole, had the strongest antimicrobial activity. Anethole inhibited the growth of saprophytic filamentous fungi, dermatophytes, plant pathogens, yeasts, and bacteria (De, De, Sen, & Banerjee, 2002). A methanol extract of *Illicium verum* was tested against eight bacteria responsible for periodontic infections and found strong activity against *Eikenella corrodens*, but not against the other seven bacteria tested (Iauk, Lo Bue, Milazzo, Rapisarda, & Blandino, 2003).

Antiviral Activity

Shikimic acid from Chinese star anise was used in the development of Tamiflu®(Roche Pharmaceuticals), a neuraminidase inhibitor, one of the most recent antiviral medications. Tamiflu® is an important weapon in the arsenal against the H5N1 virus as well as influenza A and B. Shikimic acid interacts with the surface structures of the virus preventing replication (Bertelli, 2006; Lee & Balick, 2006).

Momordica Charantia

Ethnic Uses, Interesting Facts, Historical Perspective

Momordica charantia is a climbing vine commonly seen growing on walls and shrubs in tropical and subtropical regions. The textured leaves look as though a bite has been taken from them giving the plant its Latin

name, Momordica, meaning "to bite." The plant is known for its peculiar musky odor. The orange fruits are soft when ripe and have black seeds with a red covering. This plant is one of the most popular traditional remedies in the Caribbean area decocted as a tonic, cold and fever remedy, antihypertensive, vermifuge, and as an anti-inflammatory. Momordica is used as a food, bitter flavoring, and medicine. The plant is sold by many herb vendors either fresh or dried (Morton, 1981).

Antimicrobial Activity

Water, ethanol, and methanol leaf extracts of *Momordica charantia* have clinically, as well as experimentally, demonstrated broad-spectrum antimicrobial activity, especially against *Escherichia coli*, *Salmonella*, *and Shigella* (Omoregbe, Ikuebe, & Ihimire, 1996; Vashishta, Sahu, Sharma, Choudhary, & Dixit, 2006). The fruit extract has shown activity against *Helicobacter pylori* (Yesilada, Gurbuz, & Shibata, 1999). In a phase-II study, leaf extract inhibited *Mycobacterium tuberculosis* (Frame et al., 1998). These compounds may have therapeutic use in future (Grover & Yadav, 2004).

Antiviral Activity

Momordica charantia and several of its isolated phytochemicals, i.e., alpha and beta-momorcharin, lectin, and Momordica anti-HIV protein (MAP 30), have documented in vitro activity against Epstein-Barr, herpes, HIV, coxsackievirus B3, and polio viruses. Many of these compounds are found in the seeds and fruits of the plant. MAP 30 is nontoxic to noninfected cells, as it is unable to penetrate healthy cell membranes, but capable of dose-dependent blockade (mediated through inhibition of protein synthesis) of infection and replication of HIV-1, HSV-1, and HSV-2. This compound maybe useful as nonspermicidal protection against sexually transmitted diseases (Bourinbaiar & Lee-Huang, 1996; Lee-Huang et al., 1990; Schreiber et al., 1999).

In vitro studies looked at several common plant ribosome-inactivating proteins (RIPs) including agrostin, gelionin, luffin, α-momorcharin, β-mormorcharin, saporin, and trichosanthin, found in seeds, fruit, and leaves of Momordica. Their ability to interfere with HIV-1 replication was assessed in a variety of mechanistic assays. All the RIPs tested could strongly inhibit HIV-1 intergrase with the exception of agrostin, with the extent of inhibition ranging from 26.1% to 96.3% in an ELISA-based assay. Ribosome-inactivating proteins inhibit poliovirus replication by blocking

protein synthesis. In addition, lyophilized extracts showed high antiviral activity against Sindbis and HSV-1 (Au et al., 2000; Beloin et al., 2005; Grover & Yadav, 2004; Wang & Ng, 2001).

Another protein isolated from ripe fruit and seed of Momordica, MRK29, inhibits HIV-1 reverse transcriptase with 50% relative inhibitory ratio. Concentrated MRK29 produced 82% reduction of viral core protein p24 expression in HIV-infected cells. MRK29 is thought to have immunomodulatory role, because of three-fold increase in TNF activity in the presence of this compound (Au et al., 2000; Grover & Yadav, 2004; Jiratchariyakul et al., 2001).

The galactose-binding lectin extracted from the Momordica directly inhibits HIV-1 reverse transcriptase (Zheng, Ben, & Jin, 1999). Plant juice appears to reduce apoB secretion, apoC-III mRNA expression, and to normalize apoA-I expression in protease inhibitor-treated HepG2 cells. Therefore, the plant may be a valuable nutritional therapy to manage HIV-1-protease inhibitor-associated hyperlipidemia (Nerurkar et al., 2006).

Antiparasitic Activity

Anthelmintic activity of Momordica is due to the presence of terpene glycosides, momordicine I and II, in the leaves. These compounds are active against *Caenorhabditis elegans* (Beloin et al., 2005). Momordica also produces in vitro anthelmintic effects against *Ascaridia galli* worms and appears to be more effective than piperazine hexahydrate (Grover & Yadav, 2004). The lipophilic extract of Momordica has a weak in vitro antiplasmodial activity (Kohler et al., 2002). Momordica inhibits the growth of *Plasmodium falciparum* in a dose-dependent manner (Gbeassor et al., 1990). Moderate in vivo activity against rodent malaria *Plasmodium vinckei petteri* 279 has been demonstrated in some experiments (Munoz et al., 2000), but not in in vitro studies involving *Plasmodium berghei* (Amorim, Marques, & Cordeiro, 1991; Ueno, Doyama, Padovani, & Salata, 1996). The extract of the whole plant inhibited activity of *Entamoeba histolytitca* (Khan & Omoloso, 1998).

Antifungal Activity

A refolded napin-like protein from *M. charantia* expressed in *Escherichia coli* demonstrated antifungal activity against *Trichoderma hamatum* (Vashishta, Sahu, Sharma, Choudhary, & Dixit, 2006). Momordica

extract appears to have genotoxic activity against *Aspergillus nidulans* (Ramos Ruiz et al., 1996).

Opuntia Streptacantha

Ethnic Uses, Interesting Facts, Historical Perspective

Prickly pear cactus grows up to 5 m in height with elliptical joints. The sweet, juicy red fruits have white flesh with many seeds and are eaten raw, cooked, or preserved. Native to tropical America, the plant is cultivated commercially in Mexico and the United States. Traditionally, the roasted fruits are used as a poultice. The pulp is used to quench thirst, and as a shampoo. People drink infusions and decoctions to treat a wide variety of ailments ranging from stomachaches, dysentery, and hangover to benign prostatic hypertrophy, gonorrhea, and rabies (Jellin et al., 2000; Morton, 1981). Currently, prickly pear is widely used in diabetes and for the treatment of HIV, especially in Mexican cultures (Rivera et al, 2005).

Antiviral Activity

A promising animal and human cell study examined the inhibitory effect of cactus extract on the replication of DNA viruses (Ahmad, Davies, Randall, & Skinner, 1996). The extract completely inhibited the replication of HSV-2. The replication of other herpes viruses (pseudorabies, bovine mammilitis, equine, human herpes, cytomegalovirus, and varicella zoster viruses) was significantly inhibited as well. Prickly pear also appeared to inhibit the replication of RNA viruses (influenza A, respiratory syncytial virus, and HIV-1). Greater effect was observed following preinfection incubation in prickly pear medium. Prickly pear failed to inhibit the replication of picornavirus even at high concentrations (Ahmad, Davies, Randall, & Skinner, 1996).

Schinus Terebinthifolius

Ethnic Uses, Interesting Facts, Historical Perspective

Brazilian pepper tree is an evergreen shrub or small tree native to South America. It remains a staple of Brazilian medicine, sometimes replacing

common black pepper as part of the diet. The dark green leaves and small bright red berries have earned it the name of Christmas berry. The intertwining branches and aroma are similar to juniper. The sweet bright red fruits are usually sold dry. In Brazil, a decoction is widely used for its anti-inflammatory and wound-healing properties. The plant is extremely invasive import into the southern United States and Hawaii and a threat to native ecosystems (Katzer, 2002).

Antibacterial Activity

An in vitro study testing 25 traditional Brazilian medicines including ethanolic extracts from *Schinus terebinthifolius* tree bark recorded antimicrobial activity against *Staphylococcus aureus*, but not against *Escherichia coli* (de Lima et al., 2006). However, in 2003, cell death was reported for strains of *E. coli* and *Salmonella* in the presence of *S. terebinthifolius* extract (de Carvalho, Barca, Agnez-Lima, & de Medeiros, 2003).

In an animal study *S. terebinthifolius* was assessed for efficacy against *Enterococcus*, *Streptococcus*, *Pseudomonas*, and *E. coli* in the presence of dry socket (alveolitis) after dental surgery (after upper jaw extraction) (de Melo Junior et al., 2002). In vitro antibacterial activity against all gram-positive bacteria studied and one gram-negative bacterium (*Enterococcus Group D*, *Bacillus coryneform*, *Streptococcus beta hemolyticus*, *Streptococcus* not belonging to group A.B.D., *Streptococcus viridans*, *S. aureus*, *E. coli*, *P. aeruginosa*, *Citrobacter freundii*) was observed. Gentamicin was used as a positive control and reduced bacterial growth completely (de Melo Junior et al., 2002). Ethanolic leaf extract inhibits growth of *S. aureus*, *P. aeruginosa*, and *C. albicans*. The oil is used to treat respiratory problems, mycosis, and candidal infections. The activity is attributed to high concentrations of monoterpenes (de Lima et al., 2006).

Antifungal Activity

In an in vitro study aqueous extract of *S. terebinthifolius* was tested against *Candida albicans*, *Trichophyton rubrum*, and *Cryptococcus neoformans.* The extract produced a pronounced inhibition zone for Candida and diminished activity against Trichophyton and Cryptococcus (Schmourlo, Mendonca-Filho, Alviano, & Costa, 2005).

Tabebuia Avellanedae (Impetiginosa)

Ethnic Uses, Interesting Facts, Historical Perspective

Tabebuia impetiginosa (also known as *T. avellanedae)* is an evergreen tree growing from Northern Mexico to Argentina. The dried inner bark harvested from wild trees is used medicinally. The tree has clusters of pink flowers, broad leaves, oblong fruit, and flat, winged seeds (Wyk & Wink, 2004). Medicinal use of Tabebuia tea dates back to the ancient Incas. Traditional healers often select hardy trees that are rich with protective, medicinal secondary compounds. Tabebuia wood is widely used in construction because of its attractive color and indestructible properties. Pau D'Arco tea is one of the most popular and expensive supplements people use to treat cancer (DeStefano, 2001). However, many Pau D'Arco supplements sold in the United States are purportedly prepared from the sawdust of Brazilian lumber mills from species lacking medicinal properties (Taylor, 2003; Tyler, 1993).

Antibacterial Activity

The extracts of Pau D'Arco bark containing naphthoquinones have definite antibacterial, antifungal, antiviral, analgesic, anti-inflammatory, and carcinogenic properties (Wyk & Wink, 2004). The naphthoquinones activity has been tested against *methicillin-resistant Staphylococcus aureus* (MRSA) strains in vitro in animals. The effectiveness of the naphthoquinones against *methicillin-susceptible S. aureus* (MSSA), MRSA, *Staphylococcus epidermidis*, and *Staphylococcus haemolyticus* was confirmed (Machado et al., 2003; Nagata, Hirai, Koyama, Wada, & Tamura, 1998). Other Pau D'Arco constituents, anthraquinone-2-carboxylic acid and lapachol, inhibit the growth of human intestinal bacteria. Anthraquinone-2-carboxylic acid effectively inhibits the growth of *Clostridium paraputrificum*. Lapachol, weakly inhibits *C. paraputrificum*. Both compounds do not inhibit *Clostridium perfringens* and *E coli* (Park et al., 2006). On the other hand, lapachol demonstrated potent inhibition of Staphylococcus, Streptococcus, Enterococcus, Bacillus, and Clostridium (Nagata et al., 1998). Bark constituents have also inhibited growth of *Helicobacter pylori* (Nagata et al., 1998). A mixture of *Punica granatum* (pomegranate) and *T. avellanedae* demonstrated antibacterial activity against *S. aureus* (Machado et al., 2003).

Antifungal Activity

Lapachol showed antifungal activity against *C. albicans*, *Candida tropicalis*, and *Cryptococcus neoformans* possibly due to its interaction with the cellular membrane.

T. avellandedae bark significantly inhibits *A. fumigatus*, *C. neoformans*, *M. gypseum*, *P. purpurogenum*, *S. cerevisiae*, and *T. mentagrophytes* (Cowan, 1999; Portillo, Vila, Freixa, Adzet, & Canigueral, 2001).

Antiparasitic Activity

In vitro and animal studies have found antimalarial activity in several Pau D'Arco constituents. Phenazines from lapachol, beta-lapachone, and its derivatives were effective against *Plasmodium falciparum* and *Plasmodium berghei*, especially those resistant to chloroquine. These compounds are considered promising leads for new low-cost antimalarial drug development (de Andrade-Neto et al., 2004). Lapahol in the diet (less toxic option) or administered by gavage is secreted by the skin. A study in mice found that lapahcol protects against *Schistosoma mansoni* infection (Austin, 1974). Several studies have found that various constituents of beta-lapachone are effective against protozoal parasites causing trypanosomiasis (e.g., Chagas' disease) (Menna-Barreto et al., 2005).

CONCLUSION

With the increased use of botanicals in the United States and mounting concern about antibiotic resistance, interest in plants that can offer antibacterial, antiviral, antiparasitic, and antifungal effects is growing. Because infectious diseases are so prevalent in tropical regions, plants from these areas develop a protective mechanism using potent phytochemicals. Many of these constituents can help to protect human health. Even though the plants discussed in this paper have not been part of extensive human trials, the combination of their traditional use over centuries and in vitro and animal research offers promise of finding new treatments for infectious diseases.

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