Plants for Addressing Multidrug Resistance

An Update

Kathy Abascal, BS, JD, RH (AHG), and Eric Yarnell, ND, RH (AHG)

Abstract

Plants, with their complex variety of compounds, are likely to hold at least part of the answer to our ever-increasing problem of multidrug resistant microbes. This article provides useful information for practitioners so that they can counsel patients who are taking antibiotics. Coverage includes how to enhance the ability of these drugs to function effectively and reduce the likelihood of encountering microbes that are resistant to the antibiotics patients are taking.

Among those agents reported to have this activity are artemisinin, *Artemisia annua* (sweet Annie), *Scutellaria* spp. (skullcap), *Rauvolfia serpentina* (rauwolfia), *Dahlia versicolor* (dahlia), *Camellia sinensis* (tea), *Allium sativum* (garlic), *Grifola frondosa* (maitake), *Rosmarinus officinalis* (rosemary), *Piper* spp. (black peppers), *Cinnamomum zeylanicum* (cinnamon), *Arctostaphylos uva-ursi* (uva ursi), *Humulus lupulus* (hops), *Mentha* x *piperita* (peppermint), *Eupatorium perfoliatum* (boneset), *Marrubium vulgare* (horehound), *Salvia officinalis* (sage), *Thymus vulgaris* (thyme), *Rosa canina* (rosehips), *Hydrastis canadensis* (goldenseal), *Mahonia aquifolium* (Oregon grape), *Berberis* spp., and *Coptis* spp. (gold thread).

Introduction

Antibiotic resistance poses an ever-increasing threat to life and health. This is a problem that we have been grappling with for decades. Despite plentiful information on how to reduce this threat, we seem to be losing the battle. Our societal inability to free ourselves from a focus on patentable "silver bullet" drugs and to mandate necessary changes is hampering our ability to make choices needed to protect the efficacy of existing antibiotics. Those changes range from demanding more hand-washing and cleanliness in medical and social settings, banning the use of antibiotics to promote growth in food animals, and exploring foods and botanicals that actually might prevent and/or overcome multidrug resistance (MDR).

The authors' choice to update their 2002[1] article on the potential ability of plants to help overcome antibiotic resistance seemed quite timely, when reports of a microbe resistant to *all* antibiotics began circulating.[2] In 2002, the authors' earlier article recounted the root causes of resistance (e.g., inappropriate use of antibiotics for treating viral infections, failure of patients to take antibiotics as prescribed, lack of solid hygiene in hospitals and health care clinics, routine prophylactic use of antibiotics, and use of antibiotics to promote growth in animals).

Unfortunately, there is not much to update: Progress in these areas has been unacceptably slow although addressing them fully could definitely help solve the MDR problem. There have been good examples of this: The United Kingdom reported an 85% reduction in methicillin-resistant *Staphylococcus aureus* (MRSA) in the years 2003–2011.[3] The United States also reported progress, with a 28%–50% reduction of MRSA in hospital patients.[4] In one hospital study, better hygiene, primarily in the form of hand-washing, actually reduced MRSA by 95% in a 9-year period.[5] However this positive MRSA-reduction news was completely offset by the "inexorable rise" seen in Gram-negative organisms that more than replaced MRSA, with mortality rates of 30% for patients infected with MDR microbes.[3]

A recent study concluded that nearly one-third of antibiotic prescriptions for patients receiving dialysis were inappropriate.[6] There were no reports of dramatic changes in physician adherence to guidelines for prophylactic antibiotic use in surgical arenas, and there were no reports of hygiene changes that reduced the need for such prophylaxis. Use of antibiotics in attempting to treat viral infections has not diminished dramatically. For instance, the Centers for Disease Control and Prevention (CDC) compared data from 1993/1994 with data from 2007/2008 and reported that pediatricians prescribed antibiotics inappropriately for 58% of acute respiratory infections—a slight drop, compared with 69% in the earlier period.[7]

Laws have not been passed to prevent the routine use of antibiotics in conventionally raised food animals. The debate about the dangers of using antibiotics in factory farming continues despite research showing an antibiotic-susceptible *S. aureus* moving from humans to pigs, where it became resistant to the antibiotics tetracycline and methicillin. The MRSA then was transmitted back to humans.[8]

Using Plants to Overcome Resistance

Updating the research on the use of botanicals as an adjunct to prevent and/or overcome antibiotic resistance also proved very disappointing. There are still no studies comparing people simply taking an antibiotic with people taking the antibiotic and drinking a few cups of tea, despite evidence dating back to 2002 that this might have a dramatic, positive effect. Instead, the research on MDR is moving slowly in a predictable direction: The goal is to find isolated, patentable silver bullets and to prove beyond a shadow of a doubt that things work before implementing even the simplest, safest changes to attempt to change the course of MDR infections or to prevent MDR from occurring in the first place.

Researchers do not even explore whether whole plants with their range of potentially synergistic compounds might prove to be both more economical and more effective than isolated constituents. An example is the use of artemisinin-containing plants as an adjunct treatment in malaria.

The current authors identified a number of such plants in an article on botanical treatments for malaria.[9] That article discussed a study showing that a tea of one of those plants—*Artemisia annua* (sweet Annie), might, safely and inexpensively, serve well as part of treatment for malaria. Instead, isolated artemisinin was pursued.

In 2004, artemisinin resistance was not an issue.[9] However, the World Health Organization recently reported that "there is concern over the emergence and possible spread of *Plasmodium falciparum* resistance to artemisinins."[10] Whether a compound is plant-derived or synthetic, microbes learn very quickly how to overcome isolated constituents but are much less able to cope with the variety and complexity of compounds found in whole plants. With respect to artemisinin, the potential benefit of using whole plants is underscored by the fact that other compounds found in sweet Annie now have been shown to prevent artemisinin resistance. See Table 1 for plants that work well synergistically with antibiotics.

This constituent-based research often uses traditional knowledge as a general guide to decide which plants to test, but seldom considers (let alone integrates) traditional knowledge of how the plants are used. No distinctions are made among a plant historically used to treat infections (such as *Scutellaria* spp. [skullcap]); a plant used cautiously, at a low-dose, to treat hypertension (such as *Rauvolfia serpentina* [rauwolfia]); and a plant not used medicinally (such as *Dahlia versicolor* [dahlia]). As a result, historical experience that certain plants are much safer than others is lost.

In the current authors' opinion, given the grave problems posed by microbial resistance, practitioners should weigh the significant potential benefits of adding plants with historical records of use and safety to the regimens of patients who are taking antibiotics, even if the degree of scientific proof of efficacy that one would prefer to have is lacking. A number of the plants with an apparent ability to diminish antibiotic resistance are part of a healthy diet such as *Camellia sinensis* (tea), *Allium sativum* (garlic), *Grifola frondosa* (maitake) mushrooms, and various berries, and vegetables. Other plants with this capacity are culinary herbs, such as *Rosmarinus officinalis* (rosemary) and spices such as *Piper* spp. (black peppers) and *Cinnamomum zeylanicum* (cinnamon). Some are plants with long histories of traditional use for treating various infections. These plants include *Arctostaphylos uva-ursi* (uva ursi) and skullcap. Others have been used medicinally, but in less-relevant contexts, including such herbs as *Humulus lupulus* (hops).

This article outlines how we might use knowledge gained from in vitro pharmacologic studies on constituent synergies to create a reasonable clinical approach. This strategy may help protect our patients from the ever-increasing scourge of MDR.

Plants as Potential MDR Synergists

Table 1 displays compounds that have shown a synergy with antibiotics. The plants designated as Tier One in Table 1 include plants that should be added to the treatment regimen for any patient who is taking antibiotics.

Tea

Dried, "unfermented" (actually unoxidized) tea is known as green tea. Fully "fermented" (oxidized) tea is known as black tea. Oolong tea is moderately oxidized, falling somewhere between black and green tea. Green tea is the second most-commonly consumed beverage in the world (water is number-one). Unfortunately, this does not hold true in the United States, where the number-one beverage is soda, water is number two, and tea is number seven.[11] Approximately 80% of the tea consumed in the United States is black tea.[12]

All tea varieties have antimicrobial properties. Preliminary controlled human trials show that various tea extracts can be useful for treating humans who have various diseases involving microbial infections, including dental caries, gut dysbiosis, and chronic gastritis.[13–15] Tea also has beneficial characteristics for treating dermal infections.[16]

Animal studies and in vitro studies confirm the potential of tea as an antimicrobial and as a protectant from damage caused by antimicrobial treatment. For instance, green tea catechins have inhibited bacterial growth in mice infected with *E coli* 0157:H7 and, when combined with levofloxacin, completely protected mice from organ damage typically seen with levofloxacin treatment.[17] The catechin dose in this study was equivalent to that found in a typical cup of green tea, and the researchers concluded that having a custom of drinking

Table 1. Plants to Use as Potential MDR Synergists

Antibiotic/antimicrobials	Synergistic herb/plants	Constituents
Tier One[a]		
Several	*Thymus vulgaris*	Thymol, carvacrol
Amoxicillin/clavulanate	Tea, fruit, vegetables, herbs	Myricetin
Ampicillin	*Berberis* spp.	Berberine
Ampicillin	*Silybum marianum*	Silybin
Ampicillin/sulbactam	Tea, fruit, vegetables, herbs	Myricetin
Artemisinin	*Artemisia annua*	Chrysoplenol D, chrysoplenetin
Berberine	*Artemisia absinthum*	4',5'-0-dicaffeoylquinic acid
Berberine	*Artemisia annua*	Chrysoplenol D, chrysoplenetin
Berberine	*Berberis* spp.	5-methoxy-hydnocarpin
β-lactams	*Arctostaphylos uva-ursi*	Corilagin
β-lactams	*Camellia sinensis*	Catechin gallate, epicatechin gallate, epigallocatechin gallate
β-lactams	*Rosa canina*	Tellimagrandin I, rugosin
β-lactams	*Scutellaria* spp.	Baicalein
Carbapenems	*Camellia sinensis*	Catechin gallate, epicatechin gallate, epigallocatechin gallate
Cefazolin	Tea, fruit, vegetables, herbs	Myricetin
Cefmetazole	Tea, fruit, vegetables, herbs	Myricetin
Cefoperazone	*Allium sativum*	Allicin
Cefoxitin	*Allium sativum*	Allicin
Cefoxitin	Tea, fruit, vegetables, herbs	Myricetin
Ciprofloxacin	*Piper nigrum*	Piperine
Ciprofloxacin	*Scutellaria* spp.	Baicalein
Clindamycin	*Cinnamomum zeylanicum*	Cinnamaldehyde
Erythromycin	*Berberis* spp.	Berberine
Erythromycin	*Piper longum*	Piperine
Erythromycin	*Rosmarinus officinalis*	Carnosol
Fluoroquinolones	*Rosmarinus officinalis*	Carnosol
Gentamicin	*Scutellaria* spp.	Baicalein
Methicillin	*Berberis* spp.	Berberine
Norfloxacin	*Artemisia annua*	Chrysoplenol D, chrysoplenetin
Norfloxacin	*Camellia sinensis*	Catechin gallate, epicatechin gallate, epigallocatechin gallate
Oxacillin	*Allium sativum*	Allicin
Oxacillin	*Berberis* spp.	Berberine
Oxacillin	*Silybum marianum*	Silybin
Tetracycline	Berry extracts	Gallic acid
Tetracycline	*Camellia sinensis*	Catechin gallate, epicatechin gallate, epigallocatechin gallate
Tetracycline	*Rosmarinus officinalis*	Carnosic acid, carnosol
Tetracycline	*Scutellaria* spp.	Baicalein
Vancomycin	*Allium sativum*	Allicin

(continued)

green tea might help to reduce the severity of enterohemorrhagic *E. coli* infections.

Another in vitro study found that combining green tea extracts with *Mentha* x *piperita* (peppermint) volatile oil enhanced its action against *E. coli*.[18] Other studies have found that black tea extracts appeared to be protective against *Vibrio cholerae* 01 and *Shigella* spp. *in vitro*, and had a dramatic curative effect on guinea pigs infected with

Table 1. Plants to Use as Potential MDR Synergists (continued)

Antibiotic/antimicrobials	Synergistic herb/plants	Constituents
Tier Two (use cautiously, only if needed)[b]		
Berberine	*Geranium caespitosum*	Polyacylated neohesperidosides
Ciprofloxacin	*Geranium caespitosum*	Polyacylated neohesperidosides
Ciprofloxacin	*Humulus lupulus*	Xanthohumol, lupulon
Erythromycin	*Lycopus europaeus*	Methyl-1a-acetoxy-7a-14a-dihydroxy-8,15-isopimardien-18-oate; methyl-1a,14a-diacetoxy-7a-hydroxy-8,15-isopimaradien-18-oate
Norfloxacin	*Chamaecyparis nootkatensis*	Diterpene 416, totarol
Norfloxacin	*Geranium caespitosum*	Polyacylated neohesperidosides
Polymyxin B sulfate	*Humulus lupulus*	Xanthohumol, lupulon
Rhein	*Geranium caespitosum*	Polyacylated neohesperidosides
Tetracycline	*Chamaecyparis nootkatensis*	Diterpene 416, totarol
Tetracycline	*Lycopus europaeus*	Methyl-1a-acetoxy-7a-14a-dihydroxy-8,15-isopimardien-18-oate; methyl-1a,14a-diacetoxy-7a-hydroxy-8,15-isopimaradien-18-oate
Tobramycin	*Humulus lupulus*	Xanthohumol, lupulon

[a]Tier One includes plants that should be added to the treatment regimen for any patient taking antibiotics.

[b]Tier Two includes plants that are used medicinally but not usually to treat infections. This category also includes species of plants related to those that may, or may not, have compounds needed to prevent resistance.

Note: Plants lacking sufficient relevant data on traditional use were not included.

Source: Adapted from ref. 36.

experimental shigellosis.[19–21] Tea's bactericidal in vitro effects have occurred at well below standard "cup of tea" concentrations.[22]

Myricetin-Containing Foods and Herbs

Tea, fruits, vegetables, and herbs generally contain myricetin. In turn, myricetin has shown a synergistic effect on several resistant microbes. When a patient is prescribed any antibiotic, it makes sense to advise that patient to increase the amount of vegetables, fruits, and culinary herbs in the diet to gain the benefit of this potential synergy. A list of foods highest in myricetin that can be provided to patients is provided in Myricetin-Rich Foods.

Gallic-Acid Containing Foods and Herbs

Although only listed as berry extract in Table 1, gallic acid is found in a wide variety of useful plants, and a list of them is available on James Duke, PhD's, plant database.[23] Foods rich in gallic acid include pomegranates; berries, including strawberries, raspberries, and blueberries; soy; cashews; walnuts; cocoa; and tea.[24] Also included are herbs that are often used to treat respiratory ailments; these herbs include *Eupatorium perfoliatum* (boneset), *Marrubium vulgare* (horehound), and *Salvia officinalis* (sage).

Culinary Herbs and Spices

Cinnamon is used worldwide to add flavor to foods and botanical formulas. It is also used medicinally for everything from dyspepsia to colds.[25] This spice is one of the primary ingredients in William A. Mitchell, Jr., ND's, antiviral tea.[26] Black pepper is, of course, a well-used spice, but it is one that also has interesting potentiating properties. It is used in Asia to enhance the effectiveness of medicinal formulas. In fact, black pepper's main constituent, piperine, has enhanced curcumin absorption dramatically, and curcumin is an important inflammation-modulating constituent of *Curcuma longa* (turmeric).[26] Both rosemary and *Thymus vulgaris* (thyme) are known to have antibacterial and antifungal properties, with thyme having a well-established history of treating respiratory infections.[25]

Rosehips

Although *Rosa canina* (rose hips) today is primarily used as a flavor in herbal teas and as a source of flavonoids and proanthocyanidins, rose hips have a long history of being used to treat a variety of gastrointestinal (GI) disorders.[25]

Garlic

Garlic has been used medicinally for millennia. Egyptian slaves were fed garlic to maintain their health, and the Romans used garlic for treating GI disorders, asthma, and consumption. Today, garlic continues to be used as a common home remedy for upper respiratory–tract infections.[27] Researchers claim that garlic's antimicrobial action in vitro is comparable to that of standard antibiotics.[28] Thus, garlic has been effective against a wide variety of bacteria, including *Pseudomonas, Proteus, Staphylococcus aureus, Escherichia coli, Salmonella, Klebsiella, Micrococcus, Bacillus subtilis,* and *Clostridium;* and a variety of fungi, including *Candida, Torulopsis, Trichophyton, Cryptococcus, Aspergillus, Trichosporon,* and *Rhodotorula* in vitro.[29]

Skullcap

Skullcap has a worldwide history of traditional use. In Traditional Chinese Medicine, skullcap, usually in combination formulas, is viewed as useful for treating patients with high fevers, coughs, and expectoration of thick, yellow sputum. This herb is also used to treat diarrhea or dysenteric disorders presenting with fever.[30] Native Americans used *S. lateriflora* as a febrifuge, to treat diarrhea, and to prevent smallpox.[31] *S. baicalensis* had antimycotic properties against *Aspergillus fumigatus, Candida albicans, Geotrichum candidum,* and *Rhodotorula rubra.*[32] The herb has also shown in vitro antimicrobial activity against *Klebsiella pneumoniae, Proteus vulgaris,* and *Mycobacterium smegmatis.*[33]

Berberine-Containing Plants

Hydrastis canadensis (goldenseal), *Mahonia aquifolium* (Oregon grape), *Berberis* spp., and *Coptis* spp. (gold thread) contain berberine in their roots and stem bark. These berberine-containing plants have a long, worldwide history of use for treating a wide range of infections.[1] Berberine has an antiadhesive effect.[34] These plants are highly complex, and studies suggest that the whole plants are superior to isolated berberine when it comes to inhibiting microbes.[35]

Uva Ursi

Uva ursi is most famous for its ability to cure bladder infections. This herb has also shown a remarkable bacteriostatic effect against numerous microbes.[26]

Choosing and Using Tier-One Plants

Myricetin- and gallate-containing foods are healthy choices that have beneficial effects beyond any ability to prevent or overcome MDR in microbes. In the current authors' opinion, any patient who is taking an antibiotic should be given a list of these foods and be advised to make them a regular part of his or her diet while taking the medication. These foods will also provide fiber and complex sugars to help support beneficial flora.

Myricetin-Rich Foods

- Blackberries
- Blueberries
- Carrots
- Currents
- Ginger
- Grapes
- Parsley
- Potatoes
- Lettuce
- Spinach
- Walnuts

Source: Adapted from Ref. 23.

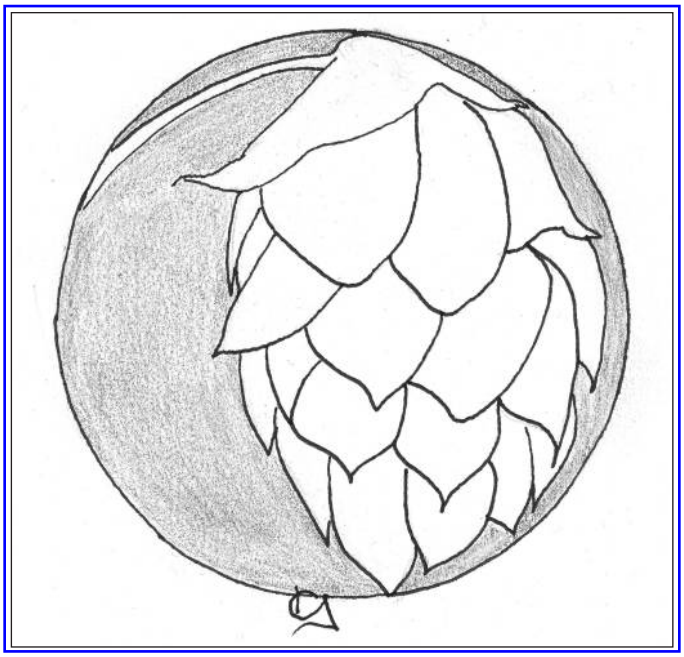
Certainly, patients who are taking antibiotics that these foods have had positive effects on (amoxicillin, ampicillin, cefazolin, cefmetazole, cefoxitin, and/or tetracycline) should be advised to emphasize these foods. Rather than recommending any particular amount to patients, clinicians should tell patients to make a number of the foods on this list the centerpiece of their diets while taking medications.

Tea constituents have a significant potential benefit as an adjunct to β-lactams, carbapenems, norfloxacin, and tetracycline. Given tea's potential benefit for treating other infections, ranging from *E. coli* to shigella, any patient taking an antibiotic should drink *at least* 1 cup of unsweetened tea per day—black, green, or oolong; caffeinated or decaffeinated.

To these recommendations, the current authors also suggest adding a blend of the herbs that have been shown to have a positive effect on the particular antibiotic (see Table 1), taken at the general medicinal dose for that plant. In other words, for a patient taking ciprofloxacin, the current authors would add a

Table 2. Doses for Botanicals

Botanicals	Forms & dosages
Allium sativum	1–10 cloves of fresh garlic qd
Arctostaphylos uva-ursi	*Cold infusion:* 4–5 tbsp/quart of water, steeped overnight & consumed in divided doses over the next day
Cinnamomum spp.	Tincture, 0.5–1 mL tid
Eupatorium perfoliatum	Tincture, 3–5 mL tid
Humulus lupulus	Tincture, 3–5 mL tid
Hydrastis canadensis, Mahonia aquifolium, Berberis spp., & *Coptis* spp.	Tincture, 5–15 gtt tid
Marrubium vulgare	Tincture, 3–5 mL tid
Piper nigrum & *P. longum*	Tincture, 0.5–1 mL tid
Rosa canina	Tea, steep 2–2.5 g of crushed rose hips in 150 mL of water for 10–15 minutes, strain before drinking, 2–3 cups/day
Rosmarinus officinalis	Tincture, 3–5 mL tid
Salvia officinalis	Tincture, 3–5 mL tid
Thymus vulgaris	Tincture, 3–5 mL tid



Humulus lupulus (hops). Drawing © 2013 by Kathy Abascal, BS, JD, RH (AHG).

tincture of skullcap and pepper. In contrast, for a patient taking vancomycin, the recommendation would be a medicinal dose of garlic. Doses for these botanicals are shown in Table 2.

Second-Tier Choices

The ideal treatment choice would be a food that has been established as being part of a healthy diet or an herb with a history of relevant, traditional use that has also shown to have a synergy with a particular antibiotic. The herbs referred to as second-tier choices are herbs used medicinally but not usually in the context of treating infections. In Table 1, Tier Two also includes species of plants related to those in the table that may, or may not, have the needed compounds to prevent resistance.

However, if there are indications that these plants may have attributes needed for a particular antibiotic, and if their use is safe, certainly they should be brought in. For instance, hops is primarily used as a sedative, but if tobramycin is being used, adding hops to a formula is not going to pose any harm and may indeed prove to be beneficial. Similarly, various species of *Geranium* (geranium) related to *Geranium caespitosum* and various species of *Thuja* (cedar) related to *Chamaecyparis nootkatensis* (Alaskan yellow cedar) are used topically to treat infections and wounds. It makes sense to explore uses for these herbs if using them topically can help antibiotics function more effectively.

Synergistic Plants to Avoid

The current authors eliminate from consideration plants that are lacking traditional data as either foods or relevant medicines. A long history of use is a form of proof that a plant can be used safely. Take, for instance, the use of *Berberis* spp. leaves as a synergist. A compound in Oregon grape leaves (5'-methoxy-hydnocarpin) has prevented microbes from developing resistance to berberine, an antimicrobial compound found in all members of this plant family.

However, while the roots and stem bark of various *Berberis* species are traditionally used as medicines, the leaves are not. As a result, we do not have the benefit of long use of the leaves to indicate safety. *R. serpentina* can be a highly useful medicinal when used in small doses in patients who have hypertension, but it is not a plant the current authors would use casually. In fact, researchers did conclude that the potential toxicity of its constituent reserpine outweighed its potential benefit as an MDR synergist.[36] It is critical to make sure that traditional uses are evaluated fully before adopting a synergist based on pharmacologic data.

Conclusion

MDR microbes pose a very real threat—a threat that our society is not responding to adequately. Along with continuing to demand better implementation of existing guidelines on the use of antibiotics and a ban on the use of antibiotics in factory-farmed animals, the current authors suggest that practitioners begin mining pharmacologic studies on plants with compounds that can help prevent and/or overcome resistance. This simply involves analyzing whether the plants at issue have a sufficient history of relevant use and then helping patients who are taking antibiotics to integrate relevant plants in their treatment regimens. ■

References

1. Abascal K, Yarnell E. Herbs and drug resistance: Part 1–herbs and antimicrobial resistance to antibiotics. Altern Complement Ther 2002;8:237–241.

2. Centers for Disease Control and Prevention. New Carbapenem-Resistant Enterobacteriaceae Warrant Additional Action by Healthcare Providers. February 14, 2013. Online document at: www.bt.cdc.gov/HAN/han00341.asp Accessed April 20, 2013.

3. Kessel AS, Sharland M. The new UK antimicrobial resistance strategy and action plan. BMJ 2013;346:11601.

4. Centers for Disease Control and Prevention. MRSA Statistics. Online document at: www.cdc.gov/mrsa/statistics Accessed April 15, 2013.

5. Virginia Commonwealth University. Simple Prevention Strategy Found For Reducing MRSA Infections. Science Daily, October 24, 2012. Online document at: www.sciencedaily.com/releases/2012/10/121024124842.htm Accessed April 15, 2013.

6. Snyder GM, Patel PR, Kallen AJ, et al. Antimicrobial use in outpatient hemodialysis units. Infection Control Hosp Epidemiol 2013;4:349–357.

7. Centers for Disease Control and Prevention. Office-Related Antibiotic Prescribing for Persons Aged ≤ 14 Years—United States, 1993–1994 to 2007–2008. Online document at: www.cdc.gov/mmwr/preview/mmwrhtml/mm6034a1.htm Accessed April 19, 2013.

8. Price LB, Stegger M, Hasman H, et al. *Staphylococcus aureus* CC398: Host adaptation and emergence of methicillin resistance in livestock. MBio 2012; 3:e00305-11.

9. Yarnell E, Abascal K. Botanical treatment and prevention of malaria: Part 2—selected botanicals. *Altern Complement Ther* 2004;10:277–284.

10. World Health Organization. Update on Artemesinin Resistance—April 2012. Online document at: www.who.int/malaria/publications/atoz/arupdate042012.pdf Accessed April 15, 2013.

11. Zmuda N. Bottom's Up! A Look at America's Drinking Habits. Advertising Age,® June 27, 2011. Online document at: http://adage.com/article/news/consumers-drink-soft-drinks-water-beer/228422/ Accessed April 15, 2013.

12. WiseGEEK. Which Beverages Do People Drink the Most of in the US? Online document at: www.wisegeek.com/which-beverages-do-people-drink-the-most-of-in-the-us.htm Accessed April 15, 2013.

13. Hamilton-Miller JMT. Anti-cariogenic properties of tea (*Camellia sinensis*). J Med Microbiol 2001;50:299–302.

14. Goto K, Kanaya S, Nishikawa T, et al. The influence of tea catechins on fecal flora of elderly residents in long-term care facilities. Ann Long-Term Care 1998;6:43–48.

15. Setiawan VW, Zhang ZF, Yu GP, et al. Protective effect of green tea on the risks of chronic gastritis and stomach cancer. Int J Cancer 2001;92:600–604.

16. Pazyar N, Felly A, Kazeouni A. Green tea in dermatology. Skinmed 2012; 10:352–355.

17. Isogai E, Isogain H, Hirose K, et al. In vivo synergy between green tea extract and levofloxacin against enterohemorrhagic *Escherichia coli* 0157 infection. Curr Microbiol 2001;42:248–251.

18. Osawa K, Saeki T, Yasuda H, et al. The antibacterial activities of peppermint oil and green tea polyphenols, alone and in combination, against enterohemorrhagic *Escherichia coli*. Biocontrol Sci 1999;4:1–7.

19. Toda M, Okubo S, Ikigai H, et al. The protective activity of tea against infection by *Vibrio cholera* 01. J Appl Bacteriol 1991;70:109–112.

20. Vijaya K, Ananthan S, Nalini R. Antibacterial effect of teaflavin, polyphenon 60 (*Camellia sinensis*) and *Euphorbia hirta* on *Shigella* spp.: A cell culture study. J Ethnopharmacol 1995;49:115–117.

21. Vijaya K, Ananthan S. Therapeutic efficacy of medicinal plants against experimentally induced shigellosis in guinea pigs. Ind J Pharmaceut Sci 1996;58: 191–193.

22. Yam TS, Shah S, Suguiura T, et al. Microbiological activity of whole and fractionated crude extracts of tea (*Camellia sinensis*), and of tea components. FEMS Microbiol Lett 1997;152:169–174.

23. Dr. Duke's Phytochemical and Ethnobotanical Databases. Online document at: www.ars-grin.gov/cgi-bin/duke/highchem.pl Accessed April 18, 2013.

24. LIVESTRONG.™ Foods with Gallic Acid. Online document at: www.livestrong.com/article/535607-foods-with-gallic-acid/ Accessed April 18, 2013.

25. van Wyk B-E, Wink M. Medicinal Plants of the World. Portland, OR: Timber Press, 2004.

26. Yarnell E, Abascal K, Rountree R. Clinical Botanical Medicine, rev. exp. ed. New Rochelle, NY: Mary Ann Liebert Inc., 2009.

27. Harris JC, Cottrell SL, Plummer S, et al. Antimicrobial properties of *Allium sativum* (garlic). Appl Microbiol Biotechnol 2001;43:3045–3048.

28. Khan MR, Omolosa MD. *Momordica charantia* and *Allium sativum:* Broad spectrum antibacterial antibiotics. Korean J Pharmacog 1998;29:155–158.

29. Sharma VD, Sethi MS, Kumar A, et al. Antibacterial properties of *Allium sativum* in vivo and in vitro studies. Ind J Exp Biol 1977;15:466–468.

30. Bensky D, Gamble A. Chinese Herbal Medicine, Materia Medica, rev ed. Seattle: Eastland Press, 1986.

31. Moerman DE. Native American Ethnobotany. Portland, OR: Timber Press, 1998;524–525.

32. Shang X, He X, He X, et al. The genus *Scutellaria* an ethnopharmacological and phytochemical review. J Ethnopharmacol 2010;128:279–313.

33. Franzblau SG, Cross C. Comparative in vitro antimicrobial activity of Chinese medicinal herbs. J Ethnopharmacol 1986;15:279–288.

34. Sun D, Abraham SN, Beachey EH. Influence of berberine sulfate on synthesis and expression of Pap fimbrial adhesion in uropathogenic *Escherichia coli*. Antimicrob Agents Chemother 1988;32:1370–1374.

35. Bhandari DK, Nath G, Ray AB. Antimicrobial activity of crude extracts from *Berberis asiatica* stem bark. Pharmaceut Biol 2000;38:254–257.

36. Abreu AC, McBain AJ, Simoes M. Plants as sources of new antimicrobials and resistance-modifying agents. Nat Prod Rep 2012;29:1007–1021.

Kathy Abascal, BS, JD, RH (AHG), is executive director of the Botanical Medicine Academy in Vashon, Washington. **Eric Yarnell, ND, RH (AHG),** is chief medical officer of Northwest Naturopathic Urology, in Seattle, Washington, and is a faculty member at Bastyr University in Kenmore, Washington.

To order reprints of this article, e-mail Karen Ballen at: Kballen@liebertpub.com or call (914) 740-2100.