Despite the dire threat to human health posed by drug-resistant bacteria, no successful therapies have been created nor implemented on a wide-scale basis. But the situation is not hopeless. Research on and usage of the essential oils from many plants suggest potential new preventions and treatments. Like many alternative and integrative therapies, however, large clinical trials on the efficacy of essential oils in preventing or treating drug-resistant bacterial infections in humans are lacking. Some say a significant and collaborative effort by complementary and conventional medicine scientists, practitioners, and industry is needed if these botanical substances are to receive the attention that could prove crucial to the future of public health.

The average person has trillions of bacteria living upon and within his or her body—more than he or she has cells.\(^1,2\) Though most of these are nonpathogenic and even helpful, such as beneficial gut flora, some bacteria can cause harm in humans and animals with compromised immunities, ranging from minor skin infections to serious diseases like tuberculosis. \textit{Staphylococcus aureus}, for example, resides on and within the bodies of about 30\% of the population and causes almost 500,000 serious illnesses each year.\(^3\)

When a bacterial infection or illness occurs, doctors must drain any infected superficial abscesses and give the patient antibiotics, which are designed to kill or slow the growth of specific bacteria.\(^4\) First used on a large-scale basis in healthcare settings in the 1940s, these infection-fighting drugs have drastically decreased infectious disease-related illness and death. But antibiotics’ widespread and sometimes inappropriate use has contributed to a situation as alarming as the sicknesses that these drugs were created to eliminate—drug resistance.

Drug-resistant bacteria withstand the intended effects of antibiotics by adapting themselves genetically and then sharing the new gene snippets with other bacteria, thus spreading the resistance ability.\(^3\) This allows them to cause more harm to living beings, increasing the risk of death, length of illness, and the opportunity for infection to spread to others. Almost every bacteria strain is stronger and less responsive to drugs than it once was; this rise in antibiotic-resistant bacteria has become one of the world’s most urgent health concerns. The US Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) both consider addressing antibiotic resistance as one of their top priorities.\(^1,5\)

In hospitals, drug resistance is a major problem. “It is a very high priority issue in clinical settings, not only for patients, but for staff who may be exposed,” said Linda Halcón, RN, PhD, an associate professor at the University of Minnesota’s School for Nursing (oral communication, April 30, 2010). Additionally, drug-resistant bacterial infections outside of hospital settings are on the rise, which many experts say is especially concerning considering that these infections once occurred mainly in the sickest hospital patients.\(^7\) A 2009 article in the \textit{New England Journal of Medicine} pointed out that it is now more difficult than ever to eradicate drug-resistant infections, and a global and collaborative effort from academia, industry, and government is direly needed.\(^6\)

WHO lists penicillin-resistant \textit{S. pneumoniae}, vancomycin-resistant \textit{enterococci} (VRE), methicillin-resistant \textit{S. aureus} (MRSA), multiresistant \textit{Salmonella}, and multi-resistant \textit{Mycobacterium tuberculosis} as the antibiotic-resistant bacteria of greatest concern.\(^5\) MRSA is especially troubling as it once comprised merely 2\% of staph infections but now accounts for at least 63\% of the total number of recorded staph infections in the United States.\(^3\) MRSA can cause skin infections and more serious sores, and it can also penetrate deep into the body, invading and infecting bones, joints, surgical wounds, and the heart, blood, and lungs.\(^7\) In 2005, the most recent year for which fatality records are available, MRSA killed 18,650 people in the United States,\(^4\) more than the number of people in the United States who die each year from AIDS (\textit{Acquired Immune Deficiency Syndrome}).\(^5\) Though vancomycin, an antibiotic that is stronger yet more toxic in humans than methicillin,\(^9\) is sometimes used as a treatment, some MRSA strains are now becoming
resistant to that drug as well.

While these bacterial strains are becoming more and more resistant to even the most powerful antibiotics, pharmaceutical companies have been drastically reducing the amount of time and money they devote to antibiotic research and development.³ It can cost up to $800 million to bring a new drug, including an antibiotic, to market. While companies typically recover such pre-market costs through drug sales, the opportunity to do this with antibiotics is rather limited. Antibiotics do not have a long period of consumption, as most patients take them for weeks or months rather than years; also, because bacteria develop resistance unpredictably and sometimes rapidly, antibiotics often need to be replaced or discontinued within a relatively short amount of time.

Alan Goldhammer, PhD, the deputy vice president of science and regulatory affairs for the Pharmaceutical Research and Manufacturers of America (PhRMA), said that although some companies have discontinued research in this area, some promising vaccines and new classes of antibiotics are in development to combat resistance (oral communication, May 25, 2010).

According to WHO, “Most alarming of all are diseases where resistance is developing for virtually all currently available drugs, thus raising the spectre of a post-antibiotic era. Even if the pharmaceutical industry were to step up efforts to develop new replacement drugs immediately, current trends suggest that some diseases will have no effective therapies within the next 10 years.”⁵

But many healthcare professionals, including those at WHO, may be unaware of new treatment possibilities lurking below the mainstream radar. Mounting evidence suggests that the essential oils of herbs, flowers, and trees could change the future of public health in this area.

**Traditional and Modern Uses**

Drug resistance is a relatively new phenomenon, as antibiotics were not widely implemented until around the end of the Second World War.³ The contemporary usage and study of essential oils against drug-resistant bacteria is rather recent, as well. But these volatile plant-produced substances have well-established antimicrobial properties that have been used for centuries and researched for more than 100 years.

“[Essential oils] were fairly widely used in some parts of the world prior to the advent of antibiotics,” said Dr. Halcón. “Then the use of essential oils as antiseptics and antimicrobials faded from view for a time. So in a way it is a young field and in a way it isn’t.” Dr. Halcón teaches a course on aromatherapy fundamentals for health professionals at the University of Minnesota’s Center for Spirituality and Healing. Though the name aromatherapy commonly suggests the use of aromatic oils for relaxation or beauty, its actual definition encompasses the use of essential oils for therapeutic or medical purposes.¹⁰

Aromatic plants and their natural oils were used in the traditional medicine of ancient civilizations, with the oldest record of medicinal use dating back to 4500 BCE.¹⁰,¹¹ These early uses did not employ true essential oils but instead used oils obtained by combining plant material with fatty oils, which were heated under the sun and then separated so that the aromatic oil was preserved without the remaining material.¹² Egyptians, Greeks, Persians, and Romans used oils medicinally sometimes to disinfect battle wounds or to prevent disease. Though the origin of distillation, which enabled the production of true essential oils, can be difficult to trace, many references cite its creation with the invention of the refrigerated coil during the late 10th century CE by Avicenna, the great Persian physician and scholar. During steam distillation, the oldest and most common commercial production technique used today, steam is passed through a chamber of plant material, which then collects and condenses, and a separator is employed to collect the oil.

During the 19th and 20th centuries, scientists analyzed and recorded many of the medicinal properties and uses of essential oils, including cinnamon (*Cinnamomum* spp., Lauraceae), frankincense (*Boswellia* spp., Burseraceae), juniper (*Juniperus* spp., Cupressaceae), rose (*Rosa* spp., Rosaceae), rosemary (*Rosmarinus officinalis*, Lamiaceae), sage (*Salvia officinalis*, Lamiaceae), and lavender (*Lavandula angustifolia*, Lamiaceae). And in the early 19th century,
chemists identified and named some of the oils’ constituents, such as geraniol and citronellol.10,11

The rapid growth of synthetic medicine led to essential oils being used mostly in perfumes and cosmetics, though bouts of reemergence occurred. Civilian and military hospitals during World War I, for example, used thyme (Thymus vulgaris, Lamiaceae), chamomile (Matricaria recutita, Asteraceae), clove (Syzygium aromaticum, Myrtaceae), and lemon (Citrus x limon, Rutaceae) essential oils and developed ointments for antibacterial and healing purposes. Essential oils were also used as natural disinfectants on patients with battlefield injuries during World War II.10

Today, numerous physicians, nurses, other healthcare practitioners, and laypersons use essential oils for their antibacterial properties, as well as their antiviral, sedative, stress-reducing, and antiseptic properties. According to Mindy Green, founder and president of the herbal and aromatherapy consulting company Green Scentsations and co-author of a leading book on aromatherapy, physicians in France prescribe essential oils externally and internally, and they sometimes specially formulate essential oil products for specific patients. In some European pharmacies, people can also purchase over-the-counter (OTC) oral capsules of essential oils to treat headaches, menstrual cramps, stomach problems, and many other ailments, she said (oral communication, April 21, 2010).

The UK Royal College of Nursing accepts all methods of aromatherapy except oral use, and nurses in Australia, New Zealand, Canada, Germany, and Switzerland also use aromatherapy on their patients.10 Though therapeutic essential oil use in the United States is more limited, some physicians, nurses, and complementary and alternative medicine (CAM) practitioners employ essential oils in their treatments.

Current use in US hospitals primarily concerns palliative care, such as reducing stress and pain and increasing relaxation, but some physicians have begun using essential oils in their operating rooms to prevent infection of the surgical patient as well as crossinfection among staff.10 Depending on the institution’s policy, nurses can also incorporate essential oils into their interventions. Jane Buckle, RN, PhD, a noted aromatherapist and author of several essential oil books, including Clinical Aromatherapy, has trained about 2,000 US nurses on the uses of essential oils (oral communication, May 5, 2010). As of 2003, about 70 hospitals and other medical centers in the United States were incorporating some form of essential oils into their treatment practices.10

According to Green and Dr. Buckle, the general public uses essential oils as antibacterials more frequently than does the healthcare community, especially with the growing interest in natural health. The majority of topical essential oils and essential oil products sold in the United States that do not make medicinal claims are considered cosmetics (as opposed to drugs), a designation accompanied by less stringent regulation, thus allowing for widespread availability and use in self-care.13 (To be classified as a dietary supplement, the essential oil would have to be administered orally with the intention of supplementing the diet.)

A Google search for essential oil cleansers returns hundreds of sites, pages, and forums providing advice and/or suggesting products for making essential oil cleaners—many of which call for tea tree (Melaleuca alternifolia, Myrtaceae) and lavender oils. Many brands also currently offer antibacterial products containing essential oils. CleanWell™, for example, is a brand of soaps and hand sanitizers containing thyme oil, and according to its website, the product has been shown in laboratory studies to be effective at killing MRSA, E. coli, and Salmonella.14 CleanWell products have been used by Equinox Health Clubs, Carnival Cruise Lines, The Great Neck Unified School District in New York, Brigham and Women’s Hospital in Boston, and the Lincoln Park Zoo (R. Diamond, e-mail, May 4, 2010).

Research

Human Studies

Though not as extensive as the antimicrobial history, emerging human research and case reports support the specific use of essential oils against drug-resistant bacteria. “I think the fact that there’s anything at all in the literature that shows that essential oils have an efficacious effect is enormous,” said Dr. Buckle. “And I think it’s the tip of the iceberg.”
In 2007, for example, a study at Wythenshawe Hospital in Manchester, England found that a vaporizer diffusing a blend of East Indian lemongrass (*Cymbopogon flexuosus*, Gramineae) and sweet-scented geranium (*Pelargonium graveolens*, Geraniaceae) essential oils into the air effectively reduced airborne bacteria, including MRSA, by 89% when operated for 15 hours. For 9 months, the vaporizer was kept in the hospital’s burn unit, causing a disappearance of MRSA infections and a dramatic decrease in all other infections. As a control, the essential oil blend was removed from the hospital’s vaporizing machines during the last 2 months of investigation. This resulted in a MRSA outbreak.

In the most well-known human study, in 2001 researchers conducted a randomized, controlled trial looking at the effect that a tea tree oil cream and body wash had on 224 patients infected with MRSA. They found that almost as many patients receiving treatment with the tea tree oil products were free of MRSA (41%) as were patients receiving the control, a standard treatment of the antibiotic mupirocin, chlorhexidine gluconate, and silver sulfadiazine (49%). While the standard antibiotic treatment more effectively killed MRSA in the nasal region, the tea tree cream and body wash were better at clearing MRSA from the skin and wounds. Additionally, anecdotal reports have arisen, telling of aerosolized tea tree oil reducing hospital-acquired infections.

“[Tea tree oil] has broken down the door,” Dr. Buckle said of the existing research. “And I think a lot of other ones are coming.”

Case reports document similar success. In 2000, for example, researchers in Australia used botanical-containing antiseptic beads to treat a man whose leg wound was infected with MRSA and was not responding to antibiotics. The beads, containing mostly tea tree and eucalyptus (*Eucalyptus globulus*, Myrtaceae) oils, as well as a mixture of lemongrass, clove, thyme, butylated hydroxytoluene, 0.3% triclosan, and 69.7% ethanol (Polytoxinol™, Eucanol Pty Ltd, Wollongong, NSW, Australia) were inserted through a funnel into the MRSA-infected bone. After 3 months, the man’s wound had healed, his symptoms resolved, wound cultures cleared, and a plain x-ray showed resolution of the infected bone.

In a separate study a year later, 8 out of 9 patients with wound infections, including 4 infected with MRSA, experienced reduced inflammation and rapid healing after being given Polytoxinol. Some patients had had the infection for more than 2 years. Six of the original 9 patients took only Polytoxinol while 3 took the essential oil medicine in addition to systemic antibiotics.

“It was quite surprising to see how active these oils are,” said Patrick Warnke, MD, PhD, one of the researchers involved in the Polytoxinol studies (oral communication, August 2, 2010). According to Dr. Warnke, a professor of surgery at Bond University in Australia and an internationally renowned stem-cell researcher and plastic surgeon, it was very difficult to get a respected medical journal to accept an additional article he co-wrote on essential oils against drug-resistant bacteria. But now, he said, it is the journal’s most downloaded article, and people from around the world contact him for advice on using essential oils to combat critical infections in their patients. “This is very important,” he said, noting the duality of essential oils’ antibacterial and anti-inflammatory properties. “It sounds a bit dodgy in many eyes, but we are clinical scientists. I’m coming from the old-school [medical establishment]. There is so much potential that could really have an impact on clinical hospital treatments today.”

Additional case reports further show the activity of essential oils against other types of infections. In October of 2009, an elderly woman in hospice care who had had MRSA in her eyes and nostrils for 3 years was cleared of infection after a month-long treatment with lavender essential oil and saline. In another, a woman with tuberculosis, many strains of which are resistant to drug therapy, inhaled a blend of Australian eucalyptus oils in a water base with 29% ethanol 3 times per day for 10 days. This resulted in her having no clinical symptoms and testing negative for tuberculosis.

Though these human studies and case reports have shown essential oils to be effective against drug-resistant bacterial infections, more rigorously-controlled human clinical research is needed.

“There are tons of laboratory studies on the effectiveness of a variety of essential oils,” said Dr. Halcón of the University of Minnesota. “They’re very good laboratory studies. But they’re not human studies.”
Conducting human studies has not been easy, however. The US National Center for Complementary and Alternative Medicine (NCCAM) currently has no research portfolio or grants dealing with the use of essential oils against drug-resistant bacteria (K. Danielson, e-mail, May 13, 2010). According to Dr. Halcón, it is more difficult to obtain funding from NCCAM if the proposed research does not relate to one of its current prioritized research areas.

Dr. Halcón was able to obtain an Investigational New Drug (IND) designation for a tea tree oil product created specifically for use in her pilot study on wound healing and a seed grant from the University of Minnesota’s Academic Health Center. But a large trial would require much more funding.

“The FDA was very supportive once I entered this process,” she said. “They called me periodically to tell me, ‘Don’t give up, we believe in this,’ and, ‘Keep going.’ Then in the same breath, they said, ‘You know you won’t be able to do large clinical trials without help from the pharmaceutical companies.’”

Because raw botanicals have historically been used in traditional medicine and contain numerous phytochemical constituents that can vary from plant to plant, many of these plants, or their extracts, are difficult to standardize and are usually not patentable. Thus, the pharmaceutical industry is not usually interested in funding such botanical research, as it prefers to focus on patentable single-chemical entity products, generally necessary to protect the large financial investment required to meet the high costs of FDA’s extensive New Drug Application process.

While conducting her tea tree oil study, Dr. Halcón also experienced difficulty in recruiting participants, as she works in the academic world without a patient pool of her own. “It is necessary to have a team for this kind of research,” she said, noting the need for researchers and healthcare providers to join together in testing innovative and promising therapies.

Despite there being very few human studies, the low number of toxicity reports from the many years that essential oils have been used by the public and some healthcare providers indicates that they are generally nontoxic and safe when used appropriately. Dr. Buckle surveyed documented cases of toxicity for her book Clinical Aromatherapy and found that few adverse event reports exist regarding essential oils taken orally, an administration route with greater chance of toxicity. Most of the adverse events that have been reported pertain to children who ingested a greater amount than is normally used. Even in those cases, the children fully recovered.

“Enough people are using essential oils throughout the world that if these things were not safe, then we’d know about it,” said Dr. Buckle.

Sometimes toxicity does occur, however, ranging from minor to more serious skin reactions, oral poisoning, respiratory depression, and even several deaths. This is an area that warrants more investigation, particularly since the amount of essential oils that can result in adult fatalities has varied widely, with some adults having died after ingesting 4 or 5 ml of eucalyptus essential oil and others having recovered after ingesting 220 ml.

In Vitro Studies

Much more extensive than the body of existing human studies on essential oils against drug-resistant bacteria is the collection of in vitro research. Cinnamon, thyme, lemon, lemon balm (Melissa officinalis, Lamiaceae), lemongrass, sage, clary sage (S. sclarea, Lamiaceae), and eucalyptus oils have been found to be active against several bacterial strains, such as MRSA, S. aureus, E. coli, S. epidermidis, Candida krusei, S. pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. Zataria multiflora (Lamiaceae), a medicinal plant in Iran, has been found to have high antibacterial activity against MRSA and methicillin-sensitive S. aureus (MSSA). It has also been found to work synergistically with the antibiotic vancomycin. Carrot (Daucus carota, Apiaceae) seed oil has been found to be active against S. aureus and Helicobacter pylori, which is developing resistance to drugs and is associated with gastric and duodenal ulcers, as well as gastric carcinoma. Additionally, tea tree oil has been shown as effective against Mycoplasma
pneumoniae, strains of which are also drugresistant.\textsuperscript{29}

Older \textit{in vitro} studies have documented the drug-resistant antibacterial efficacy of the essential oils from bay (\textit{Laurus nobilis}, Lauraceae), clove, marjoram (\textit{Origanum majorana}, Lamiaceae), and geranium; and French tarragon (\textit{Artemisia dracunculus}, Asteraceae) was found effective against several strains including \textit{Enterococcus faecalis}, which can lead to meningitis, food-borne illnesses, urinary tract infections, and life threatening VRE.\textsuperscript{10} In 1960, researchers found that lemongrass, oregano (\textit{Origanum vulgare}, Lamiaceae), savory (\textit{Satureja} spp., Lamiaceae), thyme, and cinnamon were the most effective of 133 oils against \textit{S. aureus}, \textit{E. coli}, \textit{E. faecalis}, and \textit{Mycobacterium avium}, which can be resistant to drugs and cause infections associated with HIV, pulmonary disease, and cervical lymphadenitis.

“I would think that we are actually at a pivotal stage where there are enough \textit{in vitro} studies and anecdotal evidence to suggest that we need to move along to more human studies,” said Dr. Buckle.

\textbf{Action Mechanisms}

How do essential oils work against such smart and powerful bacteria when even the strongest drugs fail? Though their mechanisms of action are complex and not completely understood, several factors are thought to contribute to their demonstrated efficacy.

As plants grow in the wild, they are susceptible to many dangers, including wild animals, climatic and environmental stressors, and disease. To protect themselves, they produce molecules called secondary metabolites, some of which produce a bitter smell or taste, induce loss of appetite if consumed, or emanate a pleasant aroma in order to attract seed and pollen dispersers.\textsuperscript{30} Essential oils are secondary metabolites that can affect the activities of bacterial membranes and can also interfere with bacterial membrane or surface proteins, thus changing the bacteria’s viability.\textsuperscript{31}

“There are many different molecular targets in the bacteria with which the essential oils interact,” said Kurt Schnaubelt, PhD, a chemist and scientific director of the educational and research organization Pacific Institute of Aromatherapy (oral communication, April 29, 2010). “The actual mechanisms of how these things occur are actually very well established.”

Additionally, essential oil components can interfere with membrane vesicles and, eventually, the primary energy metabolism. Components such as thymol disrupt or partially disintegrate the membrane’s outer layer,\textsuperscript{30,32} and some oils can denature the bacteria’s functional proteins, as is the case with tea tree oil’s activity against \textit{E. coli}.

“Conventional antibiotics only interfere with one specific target, often a very specific step in the reproduction of a bacterial membrane,” said Dr. Schnaubelt. “This is only a single step that the antibiotic is attacking, whereas the essential oil is attacking many targets at the same time.”

Though some have asserted that the solvent, usually ethanol, in which oils are diluted could be the source of the active properties, an international group of researchers found that when using only 70\% ethanol, essential oils “consistently demonstrated inhibition zones larger than 70\% ethanol alone.”\textsuperscript{25} Additionally, their controls of olive and paraffin oils had no effect, showing that the effect of the essential oils was not caused by an effect of an oily medium on microbial membranes.

Essential oils’ complex compositions, as well as their evolutionary history, make it unlikely that bacteria will develop resistance to them, Dr. Schnaubelt continued. “I don’t think it is justified to say that this is impossible, but it is really, really unlikely. The complex mixtures in plants have been designed by nature to prevent resistance. In addition, essential oil composition continuously changes throughout the season and from year to year. This contributes to the goal of the plant. They have the same interest as we do.” Supporting Dr. Schnaubelt’s comment, a 2008 study found that bacteria like MRSA and \textit{E. faecalis} have very low frequencies of resistance to higher concentrations of tea tree oil.\textsuperscript{33}
This ability to avoid resistance might be compromised, however, when the essential oils are used in lower levels of concentration, though this is also debated. In 2007, researchers at the University of Ulster found that bacteria such as MRSA, E. coli, and Salmonella exposed to low doses of tea tree oil were more resistant to antibiotics. They warned that because the concentration of tea tree oil used in cosmetic products is not always specified, consumers could be using low concentrated products, which might increase the risk that the tea tree oil will fail to kill bacteria and increase the bacteria’s resistance to antibiotics.

Several studies have reported that some essential oils work synergistically with antibiotics to increase activity and decrease drug resistance. It is thought that some botanicals, like epigallocatechin gallate (EGCG) from green tea (Camellia sinensis, Theaceae), overcome resistance by inhibiting the synthesis of bacterial enzymes that target, destroy, or modify antibiotic drugs, thus increasing antibiotic drugs’ activity when combined. Additionally, essential oil constituents like thymol and carvacrol can increase the permeability of bacteria’s outer membranes that work to keep out antibiotics. Other plant components, such as carnosic acid from rosemary, can decrease the amount of antibiotics flushed out of bacteria’s cells.

Fewer studies have been conducted on essential oils’ activity against beneficial bacteria, said Dr. Schnaubelt. “Very little is known about that. However, the experience within the aromatherapy community suggests that they do not. Some of the studies suggest that the good bacteria can use some essential oil components as nutrients.”

While some components of essential oils have been found to be most active, such as thymol and eucalyptol, it is thought that the synergistic relationship between all of the molecules might be important as well.

“It really depends on who you’re talking to,” said aromatherapist Green. She noted that there are several schools of thought on the effectiveness of isolated constituents versus the whole herb or essential oil. Holistic therapists often favor using the whole herb, while other practitioners might lean toward using an isolated component based on research showing its efficacy.

In the 1970s and 1980s, French physicians Christian Duraffourd, MD, and Jean Claude Lapraz, MD, studied the antimicrobial effects of essential oils and concluded that their activity stems from the synergistic interaction among their molecules, and not one key “active principle.” Their research found an essential oil to be effective against a given microbe in vitro regardless of the presence of commonly recognized active principles.

In addition, essential oils have the ability to encourage a healing response in patients through antioxidant activity, immunomodulation, and/or neuroendocrine and genetic activity. Drs. Duraffourd and Lapraz found the most effective therapy is to treat patients at regular intervals with a combination of mild essential oils, regardless of the relative level of key “active” ingredients, and to tailor the essential oils to the individual patient and his or her terrain—the biologically qualitative and quantitative state of the body and its internal milieu. This process of considering the totality of a patient’s sickness is the basis of the endobiogenic method, or clinical “phytoaromatherapy.”

According to Dr. Schnaubelt, just because pharmacology has not yet conclusively determined if all molecules have a stronger combined effect does not mean it is not happening.

Clearly the isolated components do have an effect,” said Dr. Schnaubelt. “But we also know, when you use a natural mixture, such as essential oils, you have many different components and you do observe effects. If you adopt an evolutionary perspective, you realize that plants have evolved for all secondary metabolites to have more or less pronounced physiological effects.”

**Future Outlook**

Drug-resistant bacteria present a potentially serious threat to the health, wellbeing, and even survival of people throughout the world. Despite the situation’s dire nature and the potential of essential oils as a new therapy, several obstacles could prevent or slow their widespread clinical usage.
Because recent essential oil usage has mainly been within the perfume and food-flavoring industries, therapeutic essential oils are much farther behind herbs when it comes to complementary and integrative therapies, said Green.

“Medical use of essential oils is still very, very new in this country,” she said. “I think aromatherapy is still making its way in the role of modern medicine. To most Americans, ‘aromatherapy’ is a product you buy on the drug store shelf that might be peach flavored bubble bath.” While essential oils have aromas with restorative and healing effects, they also have potent and strong properties that work to mitigate conditions like infection, leading many within the aromatherapy community to want a new name for the practice, she added.

Additionally, one bottle of essential oil requires a great deal of plant material, making sustainability a potential concern for widespread usage. Although the amount of essential oil produced from plant material varies based on a number of factors, the yield of essential oils in plants is typically only between 0.005 and 10%.35 Plants like sage and rosemary, which produce a relatively high percentage of essential oil, can require about 500 pounds of plant material to produce a mere 32 oz of essential oil. Dr. Buckle recognizes that this could potentially be a problem. “Wild crafted is probably not a good idea, but there is no reason why we can’t grow [essential oil plants],” she said. “On the whole, I don’t think the world is running out of them.”

Green, on the other hand, thinks the plants from which essential oils are derived can be wild crafted in a sustainable way. In the book Aromatherapy: A Complete Guide to the Healing Art (Crossing Press, 2009), Green and co-author Kathi Keville write, “If essential oils are used in the proper dilutions and with the respect that they deserve, they can be both economical and environmentally sustainable.” The authors advise aromatherapists and consumers to use the least amount possible to achieve the desired effect, such as putting only 5 drops, and not 30, into a running bath. “One drop of essential oil does represent a lot of plant material, so use it with respect and an understanding of its potency and power,” they write.35

Sustainability concerns exist for some trees whose oil is usually harvested by cutting the tree down or taking it from the roots—both practices that kill the plant. Importantly, none of the current threatened species, such as sandalwood (Santalum album, Santalaceae), rosewood (Aniba rosaeodora, Meliaceae), and agarwood (Aquilaria malaccensis, A. agallocha, Thymelaeaceae), are knowingly being studied or considered for use against drug-resistant bacteria. Also, several essential oil companies offer sustainably-harvested or cultivated products. The Himalayan and Nicaragua Oregano Oil Against MRSA projects, for example, were recently created as SEED Initiatives of the International Union for the Conservation of Nature (IUCN). Both aim to provide rural Indian and Nicaraguan farmers with a sustainable income for collecting and distilling wild oregano, which will be used to make a fair trade antimicrobial product to prevent hospital-acquired infections like MRSA.36

The most glaring barrier to widespread clinical use of essential oils for drug-resistant bacteria is the low number of human studies. But, according to Dr. Halcón, an increase in this research will be possible in the years to come—“especially when there is a track record,” she noted. “We need a few more key researchers who will be relentless in submitting research grant proposals and making the scientific case. The popular interest in antiseptic and anti-infective uses for essential oils is very energizing, and I think that there are people in healthcare and in industry who are receptive to being partners.”

Dr. Schnaubelt thinks a different obstacle might prevent widespread usage of essential oils for drug-resistant bacteria: lack of interest from the pharmaceutical industries.

“I think in the culture that we live in, if it’s not coming from a corporation, it’s not considered valid,” said Dr. Schnaubelt. Though he thinks more human research on essential oils should be conducted, Dr. Schnaubelt said that this might not make much of a difference because the pharmaceutical industry will not be interested in un-patentable products. Instead, Dr. Schnaubelt said, essential oils will have a future in being a “viable underground therapy. It’s being done as we speak.”

Though Buckle recognizes the likely un-patentable nature of essential oils, she thinks that money could be made from the synergistic relationship between essential oils and antibiotics. “[Essential oils] could be hugely valuable in terms of the medicine of the future,” she said. “I think the reason that [pharmaceutical companies] would want to fund
research is that some essential oils appear to work synergistically with antibiotics. That is a hugely attractive area for everybody.”

But much remains to be done if essential oils for drug-resistant bacteria are to receive the attention that some say they deserve. While the majority of existing research articles characterize the use of essential oils against drug-resistant bacteria as an area of “great potential and hope” and “a promising alternative,” many infectious disease and antibiotic-related organizations, as well as the pharmaceutical industry, have little awareness of the possible treatment.

The Infectious Disease Society of America (IDSA), for example, is currently sponsoring a campaign to discover or develop 10 new antibiotics or antimicrobials by the year 2020. But when asked about the potential of essential oils in this area, IDSA spokesperson John Heys said, “This isn’t something IDSA necessarily has a policy or opinion on as an organization . . . This isn’t something I’ve heard discussed in the context of addressing antibiotic resistance” (e-mail, May 17, 2010).

Likewise, the National Foundation for Allergy and Infectious Disease did not have anybody who could discuss the area of essential oils and drug-resistant bacteria. Additional organizations, including the Alliance for the Prudent Use of Antibiotics, National Foundation for Infectious Disease, and Extending the Cure, a drug resistance project of the nonprofit Resources for the Future, did not respond to interview questions by press time, but a search of each group’s website did not return any results on essential oils for drug-resistant bacteria.

Most organizations and healthcare facilities focus on preventing the spread of drug-resistant bacteria and related infections through different efforts. The CDC Campaign to Prevent Antimicrobial Resistance in Healthcare Settings, for example, advises practitioners to prevent infection through immunizations and responsible use of patient catheters, to treat the infection instead of colonization, to use vancomycin only when absolutely necessary, and to keep hands clean. According to Dr. Goldhammer of PhRMA, the pharmaceutical industry is researching how resistance evolves and how to target single, specific particles of bacteria, and it is also continuing to focus on developing new classes of structurally different antibiotics in attempt to decrease the speed at which bacteria develop resistance. Dr. Goldhammer acknowledged that bacteria might eventually develop resistance to these new antibiotics, as has been the case with linezolid (Zyvox®), a novel and expensive antibiotic that carried much hope until MRSA began developing resistance to it within a year of FDA approval. But while bacteria are developing resistance to new antibiotics, they will also lose resistance toward some of the older, previously used antibiotics, he said. Dr. Goldhammer was not aware of the possible synergistic effects among antibiotics and essential oils.

Despite these efforts, the drug-resistance problem continues to grow, and many organizations and institutions are not aware of the potential that essential oils might offer if incorporated into their current activities. A recent hand-washing study, for example, found that a soap containing 5% tea tree oil and an emulsifier was as active and sometimes more active against E. coli when compared to another skin wash containing 5% tea tree oil as well as 10% alcohol. Both tea tree combination soaps were more effective than a soft soap hand wash.

Dr. Warnke, the stem cell researcher and plastic surgeon who studied tea tree- and eucalyptus-containing Polytoxinol, thinks aromatherapists’ and herbal scientists “should not stop trying” to convince the “old-school” physicians and researchers to study essential oils’ activity against drug-resistant bacteria.

“It is very important to put this research on a level where everybody believes it is right,” he said. “This urgently needs to be brought into a pathway where everybody can utilize it for the wellbeing of their patients.”

Perhaps all it will take is more time and effort. “If you find that something works for you, and you tell somebody else, that’s the way it spreads,” said Dr. Buckle. “We need to get our act together, because this is where it begins.”
References


**Sidebar: Essential Oils and Food-Borne Bacteria**

In the ongoing worldwide effort to prevent, control, and treat drug resistance, experts have called for a decrease in the massive amount of antibiotics used in agriculture, widely thought to contribute to drug resistance among humans. Essential oils are being used and researched within this area and the results suggest that they could replace some of the antibiotics used in food production.

The most recent estimate from the Union of Concerned Scientists (UCS) in 2001 puts the weight of all antibiotics used in food animal production in the United States at 13 million pounds. The largescale, industrial, and crowded nature of the meat and dairy industries increases the chance that infection and illness will spread quickly, so it is common for many animals, or even a whole herd or flock, to be given antibiotics when only one animal is sick in order to prevent disease. Even more common, 80% of antimicrobials given to animals are for reasons unrelated to sickness, such as growth promotion. But these conditions make it particularly likely that bacteria will quickly develop resistance to drugs.

Laboratory and epidemiologic research has shown that drug-resistant bacteria from animals can enter a person’s body...
when that person consumes animal products, handles colonized animals, or comes into contact with someone who has. Additionally, bacteria can be absorbed by produce and transferred to people who eat it, an increasingly common cause of food-borne illness in humans.\textsuperscript{2} The European Union banned the use of antibiotics in animals for growth promotion in 2006, while the US government has yet to implement any regulations on the use of antibiotics in the livestock industry.\textsuperscript{3}

Though some still consider antibiotics to be the industry’s only hope for adequate livestock health and weight at slaughter, several techniques could decrease antibiotic dependency, including replacing some antibiotics with certain antimicrobial essential oils.\textsuperscript{4,5}

The essential oils in orange (\textit{Citrus sinensis}, Rutaceae) peel and pulp, for example, were recently found to be effective at killing \textit{Salmonella} in the intestinal tract of sheep,\textsuperscript{6} and an essential oil blend has proven to reduce intestinal bacteria and increase weight gain in thousands of chickens.\textsuperscript{7} The essential oil constituents capsaicin (from hot peppers [\textit{Capsicum} spp., Solanaceae]), cinnamaldehyde, and carvacrol (from thyme and oregano) have been shown to improve feed conversion weight in chickens; enhance their breast muscle proportion; reduce \textit{E. coli}, \textit{Clostridium perfringens}, and fungi; and increase beneficial \textit{Lactobacillus}.\textsuperscript{8} In 2001, the journal \textit{World Poultry} wrote that essential oil blends “should be regarded as one of the tools available to animal nutritionists in formulating diets for poultry.”

Additional research has found that the essential oils of horseradish (\textit{Armoracia rusticana}, Brassicaceae), mustard (\textit{Brassica juncea}, Brassicaceae), oregano, and cassia (Chinese cinnamon [\textit{Cinnamomum aromaticum}, Lauraceae]) would be a good replacement for the antimicrobial growth promoter Mecadox\textsuperscript{®} (Pfizer Animal Health) in nursery pigs, as the oils increased the amount of food the piglets ate and oregano reduced the numbers of intestinal pathogens.\textsuperscript{9} Furthermore, the US Meat Animal Research Center reported in 2002 that essential oils containing a thymol and carvacrol combination were found to reduce or inhibit coliforms, \textit{E. coli}, and nitrogenic and odorous excrements in waste from livestock feedlots.\textsuperscript{10} Seven reports on essential oil usage in dairy cows found that thymol, eugenol, vanillin, guaiacol, and limonene, as well as garlic (\textit{Allium sativum}, Alliaceae) and juniper oils, increased feed efficiency, milk yields, digestion, and fat and protein percentages of milk.\textsuperscript{11}

Some studies, however, have found that the essential oils studied did not affect growth performance or milk production as expected, and that they reduced counts of beneficial bacteria\textsuperscript{12,13} The authors of a recent literature review on essential oil use in livestock nutrition state that most studies have been short-term and the results vary because each study used different essential oils, dosages, and diets.\textsuperscript{13}

This research and various regulatory environments have contributed to the growing use of essential oils in livestock and agricultural products. A survey of livestock feed manufacturers in 7 EU countries, for example, found that plant extract and essential oil use increased from 55% to 75% after the EU banned growth-promoting antibiotics.\textsuperscript{14}

Essential oils’ potential for use in the food system expands into other areas. Candles containing essential oils from orange, thyme, and eucalyptus have been found to be effective at killing several surface bacterial strains. Researchers conclude that plug-in devices combining essential oils and ions generated by an electrical discharge might offer the same benefits for large scale food production.\textsuperscript{15} Additionally, some essential oils and their components are currently being used in food packaging to kill pathogens on meat, fish, and vegetables, and to decrease food spoilage, which allows the use of fewer preservatives like salt and potentially carcinogenic synthetic antioxidants.\textsuperscript{16,17,18,19}

— \textit{Lindsay Stafford}

\textbf{References}


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