Are Ancient Remedies the New Answer to Fighting Infections?

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Abstract

Although modern medicine has made great strides over the past decades, there still exists a struggle in the fight against microbial infections. As microbes continue to develop antimicrobial resistance, it is imperative that new treatment options be developed to overcome this hurdle. Bacteria can develop resistance to current antimicrobial agents through several methods, some requiring cell-to-cell contact through conjugation and other mechanisms that require no contact at all. As current treatments become less toxic to microbes, the need for new treatments is intensified. Throughout the history of human existence, plant and animal products have been used for various infectious diseases. As these products have been further analyzed, the phytochemicals, or active molecules involved, have begun to be uncovered. Discovering the mechanisms of action of the active molecules in these ancient remedies may lead to the development of new drugs to help fight infection.

Keywords

Antibiotic resistance · Alternative antibiotic · Anti-infective · Ancient remedy

1 Introduction

Throughout history, humans have fought infections caused by viruses, bacteria, parasites, and fungi that cause colds, sexually transmitted diseases, digestive disorders, and many more. Today, these diseases are typically treated with synthetic drugs, including various antimicrobials, but before modern medications were

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available, humans turned to their environment to fight off infections. These remedies were often plant-based, including leaves, flowers, stems, barks, roots, as well as animal-based substances, such as honey, venom, and mucus. Civilizations from all regions of the world expended their environment to fight infections throughout history. There are records dating back thousands of years within various cultures and regions around the world describing the use of environment-based medicines. For example, China, a country well-known for its ancient remedies, has a medicinal system approximately twenty-three centuries old (Chen 2001). Chinese medicine has focused on the balance of Yin (passive) and Yang (active); however, when this balance is disrupted, it is believed to cause illness (Chen 2001). One of the earliest archives of medicine includes the use of orally and externally administered medicinal wine to ward off disease, dating as far back as 2500 BC during the Shang dynasty and Zhou dynasty (Xia 2013). In fact, it is believed that the first record of using medicinal plants is found in the text of *The Divine Husbandman's Classic of Materia Medica (ShenNong Ben Cao Jing)*, written in the late Eastern Han Dynasty (25–220 AD) (Jaiswal et al. 2016).

China isn't the only country with a rich background in ancient remedies. India, for example, also has a long history of using natural remedies to treat illness, with the first record of using plants as medicine dating back to between 6000 and 4000 BCE (Pan et al. 2014). Ancient Indian remedies are based on approximately 25,000 plant formulations that have been used for almost 30 different types of human diseases (Sharma et al. 2007). Africa, having more than 5400 known species of plants used in traditional medicine, is another region of the world with a strong history of using environmental resources as medicine (Van Wyk 2015). For example, a well-known traditional plant dating back to prehistoric times, centella (*C. asiatica*), was utilized for wound healing, tuberculosis, lupus, inflammation, syphilis, diarrhea, and many more (van Wyk 2008). In 1500 BC, traditional medicinal practices were established in Mesoamerica and continued until the 1500s when the Spaniards arrived (Pena 1999). Two documents, the *Badianus codex* and the *Sahagun codices*, provide documentation of Aztec medicine before Columbian civilization (Guerra 1966). Native American medicinal practices frequently varied from tribe to tribe, but in many instances, healing required both rituals and botanical substances, ranging from over 200 different species of plants (Hershman and Campion 1985). However, medicinal practices quickly changed to treat infectious diseases like smallpox, influenza, measles, and other infections of European origin post-Columbus arrival. The *Old English Herbarium*, *Bald's Leechbook*, and *Lacnunga* are some of the earliest recordings of medicine in Europe, dating back to the ninth century. *Bald's Leechbook*, the most prominent of the three, was written around 950 AD. The chronicles examined remedies for various human diseases starting at the head and moving down toward the toes (Watkins et al. 2011). This series of records was composed of three books, the first two describing diseases of both external and internal complaints and the third providing a list of plant names and instructions (Watkins et al. 2011).

Within the last 100 years, modern medicine has implemented new ways of warding off infection through the use of medications, including antimicrobials

(Yazdankhah et al. 2013). Near the start of the antibiotic era, the Surgeon General of the United States stated, "It is time to close the book on infectious diseases, and declare the war against pestilence won" (Spellberg and Taylor-Blake 2013). Assuming the fight against infection was over, the emphasis for discovery of new antimicrobial agents was tapered. However, the capacity for pathogens to evolve resistance to antimicrobials was soon apparent. In a 2011 national survey, 60% of infectious disease specialists had seen a microbial infection that was resistant to the first line of antibiotics within the last year, further proving the fight against microbial infections is far from over (Ventola 2015). As antimicrobial resistance continues to rise, the need for new methods of fighting infection is becoming abundantly clear. Interestingly, the answer to much-needed new forms of antimicrobial drugs might be found by looking at traditional medicine. In this review, we discuss the need for new antimicrobial agents and explore the potential of the natural remedies that have been used in different regions of the world throughout history.

2 Antimicrobial Resistance

Antimicrobial-resistant infections are an increasing problem within the medical field, and one of the major causes of mortality and morbidity (Martinez and Baquero 2014). As antimicrobial drugs continue to be overly prescribed and abused by clinicians, patients, and livestock farmers, bacteria have been pressured by their environment for survival (Ventola 2015; Michael et al. 2015; Shay and Freifeld 1999; Fiore et al. 2017; Grigoryan et al. 2007). The majority of antibiotics in use today are secondary metabolites derived from actinomycete bacteria (Mak et al. 2014) and target essential cell processes, such as protein synthesis, cell wall synthesis, and DNA synthesis (Mahajan and Balachandran 2012). However, bacteria can become resistant to these metabolites through various mechanisms. One way bacteria resist killing by antimicrobials is by pumping the drug out of the cell before it can act. Multidrug resistance efflux pumps are frequently found in clinical strains of bacteria (Alcalde-Rico et al. 2016; Sun et al. 2014). Efflux pumps provide bacteria the capability to extrude antimicrobials, as well as heavy metals, organic pollutants, quorum sensing signals, and other substances (Blanco et al. 2016). For example, many strains of *Pseudomonas aeruginosa* express an efflux pump, PA1874-1877, which can be overly expressed during infection and result in biofilm-specific resistance to antimicrobials (Alcalde-Rico et al. 2016; Zhang and Mah 2008).

Bacteria can also develop resistance to antimicrobials through mutations or the acquisition of new genes that confer resistance (Martinez and Baquero 2014). Mutations in the genes that code for targets, transporters, or proteins that pre-antibiotics use for either activation or entrance into the targeted bacteria can lead to resistance (Baquero et al. 2009). The acquisition of new resistance determinants can occur through horizontal gene transfer in multiple ways. Through conjugation, plasmids, integrons, transposons, genetic islands, and integrative conjugative elements can carry genetic information among bacteria. It has been hypothesized that these resistance genes originate from either environmental microbiota or commensal bacteria (Martinez and Baquero 2014; Sommer et al. 2009; Davies 1997). Frequently, the genetic information on these mobile genetic elements can insert themselves into the bacterial chromosomal DNA, which can be reversible or irreversible (Brown-Jaque et al. 2015). Without cell-cell contact, phages and genetic transfer agents can integrate genetic information into bacteria as well (Brown-Jaque et al. 2015).

Community-based resistance in the form of a biofilm promotes bacterial tolerance against antimicrobial agents. It is accepted that the majority of bacteria exist in a biofilm both in the environment and within the human body (Costerton et al. 1995). Biofilms are composed of a variety of microbes living in close proximity to each other and encased in a matrix that includes extracellular DNA (eDNA), exopolysaccharides, proteins, and various lipids (Donlan 2002). This matrix creates a barrier that can be exceptionally difficult for antimicrobial agents to penetrate and reach the bacteria within the biofilm. The bacteria in the biofilm generally live in an altered metabolic state in order to survive the low oxygen and nutrient-deplete environment (Penesyan et al. 2015). This slowed metabolism adversely impacts the capability of antimicrobials to enter the bacteria and work efficiently (Costerton et al. 1995). Persister cells, bacteria deep within the biofilm that have a slow or nongrowing phenotype, are highly resistant to antimicrobials (Conlon et al. 2015). Due to the mechanism of antibiotics, such as β-lactams that work by inhibiting growth factors, persister cells will oftentimes survive antimicrobial treatment, while the remaining bacterial population is killed off. This phenomenon can lead to recurring infections initiated by bacteria that have strategies for tolerating antimicrobials, producing further infections that are even more problematic (Cho et al. 2014). In conclusion, the vast variety and number of methods that bacteria can utilize to become resistant to antimicrobials further emphasize the need for new antimicrobial treatment agents.

3 Herbal Remedies

3.1 Africa

Africa, a continent of 54 countries, has one of the shortest life expectancies in the world at only 56 years (Kuate Defo 2014). One of the most virulent diseases in Africa is HIV/AIDS, with 5% of adults infected in Sub-Saharan Africa and 5.7% of adults in North Africa and the Middle East (Kilmarx 2009). Diarrheal diseases are another common infection seen in Africa, killing millions of children each year (Levine et al. 2013). Throughout the ages, people in Africa began utilizing various parts of plants and shrubs to help alleviate these diseases. Plants from the families of Guttiferae (Kuete et al. 2011), Apiaceae (El-Haci et al. 2014), Crassulaceae (Akinpelu 2000), Melastomataceae (Baba and Onanuga 2011), Bignoniaceae (Mbosso Teinkela et al. 2016), Fabaceae (Koffuor et al. 2014), Loranthaceae (Deeni and Sadiq 2002), and Balanophoraceae (Ohiri and Uzodinma 2000) were often used to treat diarrheal diseases and dysentery, and leaves from *Sutherlandia frutescens* (family: Fabaceae) were used to control HIV/AIDS (Koffuor et al. 2014). Many of these families also include plants that were used to treat various infections and signs of disease, such as tuberculosis (Baba and Onanuga 2011), colds (Sonibare et al. 2016; Selles et al. 2013), coughs (El-Haci et al. 2014; Akinpelu 2000; Baba and Onanuga 2011), headaches (Akinpelu 2000; Bisignano et al. 2000), and chest pain (Ohiri and Uzodinma 2000; Sonibare et al. 2016; Viljoen et al. 2003).

Interestingly, the majority of the plants that have been studied from Africa are either shrubs or flowering plants. Different elements of these plants have been tested for active molecules or phytochemicals to determine their antimicrobial mechanism(s) of action (MOA). Some of the most common phytochemicals found in this region include tannins (Baba and Onanuga 2011; Koffuor et al. 2014; Chah et al. 2000), saponins (Baba and Onanuga 2011; Koffuor et al. 2014; Chah et al. 2000), and alkaloids (Baba and Onanuga 2011; Chah et al. 2000; Lohombo-Ekomba et al. 2004). It is hypothesized that tannins inhibit biofilm formation, as they are bacteriostatic, and can damage bacterial membranes and negatively impact matrix production (Trentin et al. 2013). Saponins are molecules that become “soaplike” in water. Their antimicrobial MOA is thought to be disruption of the bacterial cell membrane, which leads to cell lysis (Arabski et al. 2012). The proposed MOAs of alkaloids, on the other hand, are to inhibit cell division and/or nucleic acid synthesis or to disturb the Z-ring at the site of division (Cushnie et al. 2014; Lutkenhaus and Addinall 1997). Table 1 details 29 different species of plants, with the majority native to central, western, or southern Africa.

Along with plants, the mucus from *Achatina fulica* (giant African land snail) (Pitt et al. 2015), venom from *Androctonus amoreuxi* (African fat-tailed scorpion) (Almaaytah et al. 2012; Du et al. 2015), and propolis from bees (Suleman et al. 2015) have also been exploited in Africa for their antimicrobial properties.

3.2 Asia

For the context of this review, Asia includes Russia, China, India, the Middle East, Japan, and North and South Korea. Table 2 details 44 species of plants, royal jelly from honeybees (Fratini et al. 2016), and scorpion venom (Ahmed et al. 2012) that have been used medicinally as antimicrobials within this region of the world. Among plant-based medicines, herbs (Karuppiah and Rajaram 2012; Reiter et al. 2017; Ooi et al. 2006; Hong et al. 2014), mushrooms (Chowdhury et al. 2015), flowers (Hong et al. 2014; Ozusaglam et al. 2013; Yang et al. 2012; Sun et al. 2017), and fruits/berries (Shukla et al. 2016; Li et al. 2012; Paudel et al. 2014; Li et al. 2014) have been at the forefront. *Bletilla ochracea* (Chinese butterfly orchid), found throughout Vietnam and China, is particularly interesting due to the orchid’s history of being used to treat vampirism. It is fascinating that in parts of India and Thailand, *Heterometrus xanthopus* (giant forest scorpion) venom has been utilized as an antimicrobial agent. Meanwhile, venom from the African fat-tailed scorpion in North Africa exhibits similar antimicrobial properties. The majority of agents tested for their antimicrobial properties within this region have also served as treatments for diabetes (Ooi et al. 2006; Shukla et al. 2016; Paudel et al. 2014; Zeng et al. 2011;

Table 1 African remedies

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals (if known)	Uses	References
Plant based						
1.	Subtropical Africa	*Albertisia villosa* Root, bark	Flowering plant (Menispermaceae)	Alkaloids	Malaria, other infectious diseases, dandruff control, antimicrobial against *K. pneumoniae*, *B. subtilis*, *C. diphtheria*, *P. aeruginosa*, *S. typhi*, *S. pyogenes*, *T. longiformis*, *C. albicans*, *A. flavis*, *M. canis*, *F. solani*, *E.* spp.	Lohombo-Ekomba et al. (2004)
2.	Tropical Forest Africa	*Allanblackia floribunda Oliver* Root, bark	Tree or shrub (Guttiferae)	Phenolics	Toothache, dysentery, anticancer, antimicrobial against *M. smegmatis*, *M. tuberculosis*, *T. rubrum*	Kuete et al. (2011)
3.	Northern Africa	*Ammodaucus leucotrichus* Fruit	Flowering plant (Apiaceae)	Perilla aldehyde, monoterpenes	Stomach pain, indigestion, diarrhea, vomiting, intestinal worms, allergy symptoms, coughing, antimicrobial against *E. coli*, *S. aureus*, *E. cloacae*, *B. cereus*, *S. typhimurium*, *F. oxysporum*, *A. flavus*	El-Haci et al. (2014)
4.	Central and Southern Africa	*Anacardium occidentale* Bark	"Cashew tree" (Anacardiaceae)	–	Antibacterial against *B. cereus*, *B. stearothermophilus*, *B. subtilis*, *C. sporogenes*, *C. pyogenes*, *K. pneumoniae*, *M. luteus*, *P. vulgaris*, *P. aeruginosa*, *P. fluorescens*, *S. dysenteriae*, *S. aureus*, *S. faecalis*	Akinpelu (2001)
5.	Northern Africa	*Anacyclus pyrethrum* Floral bud	"Mount Atlas daisy" (Asteraceae)	Sesquiterpenes	Common cold, toothache, pyorrhea, antimicrobial against *S. aureus*, *C. albicans*	Selles et al. (2013)
6.	Western and Tropical Africa	*Bridelia ferruginea* Bark extracts	Woody shrub (Euphorbiaceae)	–	Gonorrhea infections, candida oral thrush, and antimicrobial against *C. albicans*, *E. coli*, *P. mirabilis*, *P. vulgaris*, *Klebsiella* sp.	Irobi et al. (1994)

7.	Tropical and Subtropical Africa	*Bryophyllum pinnatum* Leaves	"Miracle leaf plant" (Crassulaceae)	–	Ear infections, cough, dysentery, headaches, and antimicrobial against *B. subtilis*, *E. coli*, *P. vulgaris*, *S. dysenteriae*, *S. aureus*	Akinpelu (2000)
8.	Tropical Africa	*Carica papaya* Fruit	Fruit tree (Caricaceae)	–	Eczema, dermatitis, psoriasis, antimicrobial against *E. faecalis*, *S. saprophyticus*, *C. albicans*	Mbosso Teinkela et al. (2016)
9.	South Africa	*Carpobrotus muirii* Whole plant	Flowering plant (Aizoaceae)	–	Antimicrobial against *S. aureus and M. smegmatis*	Springfield et al. (2003)
10.	South Africa	*Carpobrotus quadrifidus* Whole plant	Flowering plant (Aizoaceae)	–	Antimicrobial against *S. aureus*, *M. smegmatis*	Springfield et al. (2003)
11.	Semiarid savanna regions of Africa	*Combretum apiculatum* Leaves	Flowering plant (Combretaceae)	Bibenzyls (including combretastatin)	Abdominal disorders, conjunctivitis, infertility, and venereal diseases, antimicrobial against *S. aureus*, *C. albicans*	Katerere et al. (2012)
12.	Tropical Africa	*Combretum collinum* Leaves	Flowering plant (Combretaceae)	Phenanthrenes	Antimicrobial against *M. fortuitum*, *S. aureus*	Katerere et al. (2012)
13.	Eastern and Southern Africa	*Combretum hereroense* Fruit	Shrub (Combretaceae)	Phenanthrenes	Abdominal disorders, conjunctivitis, infertility, and venereal diseases, antimicrobial against *M. fortuitum*, *S. aureus*	Katerere et al. (2012)
14.	Western Africa	*Costus lucanusianus* Herb	Herbaceous plant (Costaceae)	Glycosides, tannins, saponins	Anti-abortive, weak antimicrobial against *B. subtilis*, *S. aureus*, *P. aeruginosa*, *E. coli*, *K. pneumoniae*	Baba and Onanuga (2011)

(continued)

Table 1 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals (if known)	Uses	References
15.	Western Africa	*Dissotis rotundifolia* Herb	"Pink Lady" (Melastomataceae)	Alkaloids, glycosides, saponins	Rheumatism, painful swellings, stomachache, diarrhea, cough, conjunctivitis, venereal diseases, bilharzias (East Africa), weak antimicrobial against *B. subtilis*, *S. aureus*, *P. aeruginosa*, *E. coli*, *K. pneumoniae*	Baba and Onanuga (2011)
16.	Southern Africa	*Ficus bubu* Stem bark, leaves, latex	Terrestrial tree (Moraceae)	–	Anticancer, antimicrobial against *C. albicans*, *E. coli*, *E. faecalis*, *K. pneumoniae*, *S. saprophyticus*	Mbosso Teinkela et al. (2016)
17.	Tropical Africa	*Mitracarpus scaber* Whole plant	Flowering plant (Rubiaceae)	–	Headaches, toothache, amenorrhea, dyspepsia, hepatic disease, leprosy, antimicrobial against *S. aureus*, *C. albicans*	Bisignano et al. (2000)
18.	South Africa	*Osmitopsis asteriscoides* Essential oil	Flowering plant (Asteraceae)	Sesquiterpene, lactones	Chest complaints, cuts, swelling, antimicrobial against *S. aureus*, *B. subtilis*, *C. neoformans*, *P. aeruginosa*	Viljoen et al. (2003)
19.	Western Africa	*Pavetta crassipes* Leaves	Low shrub (Rubiaceae)	PcF3.4	Antimicrobial against *E. coli*, *C. albicans*, *T. cruzi*, *L. infantum*, *T. brucei*, *P. falciparum*	Balde et al. (2010)
20.	Africa	*Paullinia pinnata* Saponin	"African woody vine" (Sapindaceae)	Methylinositol, steroidal terpenoids, oleanane, triterpenoids	Malaria, erectile dysfunction, antimicrobial against *S. typhi*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, *E. coli*, *E. faecalis*, *E. aeroginese*, *P. smartii*, *C. albicans*, *C. guilliermondii*, *C. lusitaniae*, *C. parapsilosis*, *T. equinum*, *M. audouinii*, *T. mentagrophytes*, *M. gypseum*, *E. floccosum*	Lunga et al. (2014)
21.	Tropical and Subtropical Africa	*Phyllanthus muellerianus* Stem, bark	Evergreen shrub (Euphorbiaceae)	–	Antimicrobial against *C. sporogenes*, *S. pyogenes*	Brusotti et al. (2011)

22.	Tropical Africa	*Solanum torvum* Fruit	"Turkey berry shrub" (Solanaceae)	Steroidal alkaloids, tannins, saponins	Abscesses, jigger wounds, ringworm, athlete's foot, and antimicrobial against *A. pyogenes*, *B. subtilis*, *E. coli*, *K. pneumoniae*, *S. typhimurium*, *S. aureus*, *S. pyogenes*, *A. niger*, *C. albicans*	Chah et al. (2000)
23.	Western and Central Africa	*Solenostemon monostachyus* Leaves	Herbaceous plant (Lamiaceae)	Glycosides, flavonoids, tannins, saponins, anthraquinones	Type 2 diabetes, tuberculosis, anti-abortive, antimicrobial against *B. subtilis*, *S. aureus*	Baba and Onanuga (2011)
24.	Tropical dry forests of Africa	*Spathodea campanulata* Flowers	"African tulip tree" (Bignoniaceae)	–	Kidney disease, animal poisoning, wound healing, herpes, diarrhea, anticancer, antimicrobial against *E. faecalis*, *K. pneumoniae*, *S. saprophyticus*, *C. albicans*	Mbosso Teinkela et al. (2016)
25.	Southern Africa	*Sutherlandia frutescens* Leaves	"Cancer bush" (Fabaceae)	Saponins, sterols, tannins, coumarins	HIV/AIDS, fever, flu, chicken pox, rheumatism, hemorrhoids, cancer, diarrhea, antimicrobial against *E. coli*, *P. aeruginosa*, *S. typhi*, *K. pneumoniae*, *E. faecalis*, *S. aureus*, *S. pneumoniae*, *B. subtilis*, *C. albicans*	Koffuor et al. (2014)
26.	Northern Africa	*Tapinanthus dodoneifolius* Leaves	"Kauchi or African mistletoe" (Lorenthaceae)	–	Anticancer, anti-parasite, stomachache, diarrhea, dysentery, and antimicrobial against *Bacillus* sp., *E. coli*, *Proteus* sp., *Pseudomonas* sp., *Salmonella* sp., *A. tumefaciens*, *A. niger*, *Candida* sp.	Deeni and Sadiq (2002)
27.	Southern and Western Africa	*Thonningia sanguinea* Root extract	"Pineapple of the bush" (Balanophoraceae)	Phenolics	Hemorrhoids, anal lesions, bronchial asthma, dysentery, sore throat, skin diseases, antimicrobial against *C. albicans*, *B. subtilis*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. typhimurium*, *S. aureus*	Ohiri and Uzodinma (2000)

(continued)

Table 1 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals (if known)	Uses	References
28.	Western Africa	*Vernonia cinerea* Whole plant	"Ironweed" (Asteraceae)	Phenolics, flavonoids	Common cold, asthma, bronchitis, fever, filariasis, blisters, vaginal discharge, and antimicrobial against *S. aureus*, *B. subtilis*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *P. vulgaris*, *C. albicans*	Sonibare et al. (2016)
29.	Western and Tropical Africa	*Xylopia parviflora* Volatile oil	"Striped African pepper" (Annonaceae)		Anticancer, anti-inflammatory, and antimicrobial against *S. aureus*, *E. coli*, *P. aeruginosa*, *E. faecalis*, *C. albicans*	Woguem et al. (2014)
Animal based:						
30.	Mild climates in Africa	*Achatina fulica* Mucus	"Giant African land snail" (Achatinidae)		Antibacterial against *S. aureus*	Pitt et al. (2015)
31.	Northern Africa	*Androctonus amoreuxi* Venom	"African fat-tailed scorpion" (Buthidae)	AamAP1, AamAP2(Almaaytah et al. 2012) AaeAP1, AaeAP2 (Du et al. 2015)	Antimicrobial against *S. aureus*, *E. coli*, *and C. albicans*	Almaaytah et al. (2012) and Du et al. (2015)
32.	South Africa	Propolis	Bee product	Flavonoids	Antibacterial against *S. aureus*	Suleman et al. (2015)

Table 2 Asian remedies

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/phytochemicals	Uses	References
Plant based						
1.	Manchuria and Korea	*Aconitum macrorhynchus* Whole plant	"Friar's cap" (Ranunculaceae)	–	Fever, pain, anti-inflammatory, sedation, antimicrobial against *S. aureus*	Paudel et al. (2014)
2.	Central Asia	*Allium sativum* Clove	"Garlic" (Liliaceae)	Allicin	Common colds, flu, heart diseases, fever, antimicrobial against *E. coli*, *Enterobacter* sp., *P. aeruginosa*, *Proteus* sp., *Klebsiella* sp., *S. aureus*, *Bacillus* sp., *S. pneumoniae*, *K. pneumoniae*, *A. baumannii*, *S. pyogenes*	Karuppiah and Rajaram (2012) and Reiter et al. (2017)
3.	Turkey and Western Asia	*Allium scabriflorum* Flower	Flowering bulb (Liliaceae)	–	Antimicrobial against *E. coli*, *S. aureus*, *L. monocytogenes*, *B. cereus*, *P. aeruginosa*, *M. luteus*, *S. sonnei*, *Y. entercolitica*, *C. albicans*, *S. cerevisae*, *S. enteritidis*	Ozusaglam et al. (2013)
4.	Turkey and Western Asia	*Allium tchihatschewii* Flower	Flowering bulb (Liliaceae)	–	Antimicrobial against *E. coli*, *S. aureus*, *L. monocytogenes*, *B. cereus*, *P. aeruginosa*, *M. luteus*, *S. sonnei*, *Y. entercolitica*, *C. albicans*, *S. cerevisae*, *S. enteritidis*	Ozusaglam et al. (2013)
5.	Northeast Russia and Arctic	*Alopecurus roshevitzianus* Whole plant	"Foxtail grass" (Poaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)

(continued)

Table 2 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/phytochemicals	Uses	References
6.	Northern Asia and Europe	*Aquilegia oxysepala* Whole plant	"Granny's bonnet" (Ranunculaceae)	Genkwanin, apigenin, magnoflorine, berberine	Gynopathy, antimicrobial against *S. aureus*	Yu et al. (2007)
7.	China	*Aristolochia delavayi* Aerial parts	"Birthwort" (Aristolochiaceae)	Dodecanal, heptanal, decanal, (E)-dec-2-enal, (E)-dodec-2-enal	Gout, eczema, arthritis, pain, digestive disorder, snakebite, antimicrobial against *P. aeruginosa*, *E. coli*, *E. aerogenes*, *P. stuartii*, *S. typhi*, *E. faecalis*, *S. aureus*, *C. albicans*, *C. glabrata*, *C. guilliermondii*, *C. neoformans*	Li et al. (2013a)
8.	China and Russia	*Artemisia lagocephala* Whole plant	Flowering plant (Compositae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
9.	Japan and Korea	*Astragalus schelichovii* Whole plant	Legume (Fabaceae)	–	Diabetes, nausea, vomiting, diarrhea, antimicrobial against *S. aureus*	Paudel et al. (2014)
10.	China and Southwest Asia	*Betula alba* Leaves	"European white birch" (Betulaceae)	Saponins, coumarins	HIV/AIDS, eczema, gout, rheumatism, edema, antimicrobial against *E. coli*, *P. aeruginosa*, *S. typhi*, *K. pneumoniae*, *E. faecalis*, *S. aureus*, *S. pneumoniae*, *B. subtilis*, *C. albicans*	Koffuor et al. (2014)
11.	Vietnam and China	*Bletilla ochracea* Roots	"Chinese butterfly orchid" (Orchidaeceae)	Phenanthrenes	Vampirism disease, antimicrobial against *S. aureus*, *S. epidermidis*, *B. subtilis*	Yang et al. (2012)

12.	Western Himalayas and India	*Cedrus deodara* Pine needle	"Deodar cedar" (Pinaceae)	Phenols, flavonoids, tyrosinase	Fevers, diarrhea, dysentery, tuberculosis, diabetes, insomnia, antimicrobial against *E. coli*, *P. vulgaris*, *S. aureus*, *B. subtilis*, *B. cereus*, *S. thermophilus*, *S. lutea*, *P. citrinum*, *A. niger*, *A. flavus*, *C. krusei*	Zeng et al. (2011)
13.	Korea and Eastern Russia	*Chosenia arbutifolia* Whole plant	Flowering plant (Salicaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
14.	Southern China	*Cinnamomum cassia* Bark	"Chinese cinnamon" (Lauraceae)	–	Erectile dysfunction, diabetes, high blood pressure, digestive disorders, cramps, menstrual problems, cancer, abortion inducing, depression, antimicrobial against *S. aureus*, *E. coli*, *E. aerogenes*, *P. vulgaris*, *P. aeruginosa*, *V. cholerae*, *S. typhimurium*, *V. parahaemolyticus*, *Candida* spp., *Aspergillus* spp.	Ooi et al. (2006)
15.	Northern Russia and Arctic	*Cladonia stellaris* Whole plant	"Star reindeer lichen" (Cladoniaceae)	Usnic acid	Antimicrobial against *S. aureus*	Paudel et al. (2014)
16.	Southwestern Asia and Europe	*Daucus carota* Root juice	"Wild carrot" (Apiaceae)	Carotol, sabinene, B-caryophyllene, a-pinene	Eyesight, digestive disorders, contraceptive, tonsillitis, mouth infections, anthelmintic, antimicrobial against *L. monocytogenes*, *S. aureus*, *S. enteritidis*, *S. typhimurium*, *E. coli*, *S. dysenteriae*, *A. niger*	Ma et al. (2015)

(continued)

Table 2 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/phytochemicals	Uses	References
17.	Eastern Russia	*Dracocephalum palmatum* Whole plant	Flowering plant (Lamiaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
18.	Asia	*Dryopteris fragrans* Whole plant	"Fragrant fern" (Aspidiaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
19.	Southern China	*Ecdysanthera rosea* Stem		–	Sore throat, chronic nephritis, antimicrobial against *S. aureus*, *E. faecalis*, *P. smartii*, *C. albicans*, *C. neoformans*, *C. guilliermondii*	Song et al. (2014)
20.	China, Korea, and Japan	*Edgeworthia tomentosa* Flower	"Nakai flower" (Thymelaeaceae)	Monoterpenes, sesquiterpenes, terpenoids	Anti-inflammatory, analgesic, antimicrobial against *D. pneumonia*	Sun et al. (2017)
21.	Central Asia	*Ephedra sinica* Stem	"Ephedrae herba" (Ephedraceae)	Ephedrine, pseudoephedrine, N-methylephedrine, N-methylpseudoephedrine, norephedrine, norpseudoephedrine	Asthma, cough, diaphoretic, antimicrobial against *P. aeruginosa*, *MRSA*, *C. albicans*, *B. subtilis*, *S. aureus*, *E. coli*	Zang et al. (2013)
22.	Asia and Europe	*Galium verum* Whole plant	"Lady's bedstraw" (Rubiaceae)	Terpenoid, benzopyrone	Urinary disease, epilepsy, anti-inflammatory, antimicrobial against *S. aureus*	Paudel et al. (2014)
23.	India	*Grewia asiatica* Fruit	"Falsa" (Grewioideae)	Phenols, saponins, flavonoids, tannins	Anti-inflammatory, urological disorders, diabetes	Shukla et al. (2016)

24.	Bangladesh and Southern Asia	*Hypsizygus tessulatus* Mushroom	"Shimeji mushroom" (Lyophyllaceae)	Glucans, niacin, vitamin B, vitamin D, sterols, ergosterol, phenols, flavonoids, ascorbic acid	Immunity, weight loss, osteoporosis, antiaging, antimicrobial against *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. typhi*, *K. pneumoniae*, *C. albicans*, *S. cerevisiae*	Chowdhury et al. (2015)
25.	Southern Asia, India, and Bangladesh	*Impatiens balsamina* Stem	"Rose balsam" (Balsaminaceae)	Quinones, flavonoids, coumarins	Anticancer, rheumatoid arthritis, bruises, antimicrobial against *P. italicum*, *P. digitatum*, *A. niger*, *A. oryzae*, *S. cerevisiae*, *C. utilis*, *B. subtilis*, *S. aureus*, *E. coli*, *S. boydii*	Su et al. (2012)
26.	Bangladesh and Southern Asia	*Lentinula edodes* Mushroom	"Shiitake mushroom" (Marasmiaceae)	Lentinan, phenols, flavonoids, ascorbic acid	Longevity, gastric cancer, antimicrobial against *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. typhi*, *K. pneumoniae*, *C. albicans*, *S. cerevisiae*	Chowdhury et al. (2015)
27.	Eastern Asia and South-Central China	*Myrica rubra* Fruit	"Chinese bayberry" (Myricaceae)	–	Digestive disorders, cholera, cardiovascular disease, arsenic poisoning, antimicrobial against *S. marcescens*, *P. aeruginosa*, *S. aureus*, *E. coli*, *M. luteus*, *H. anomala*	Li et al. (2012)
28.	China, India, Japan, and Vietnam	*Ophiopogon japonicas* Stem, roots	"Mai Men Dong" (Asparagaceae)	–	Digestive disorders, cardiovascular disease, sedative, fever, cough, diabetes, antimicrobial against *S. aureus*, *C. neoformans*	Liang et al. (2012)

(continued)

Table 2 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/phytochemicals	Uses	References
29.	Northeastern Asia	*Oxytropis adamsiana* Whole plant	Flowering plant (Leguminosae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
30.	China	*Panax notoginseng* Flower	"Chinese ginseng" (Araliaceae)	Flavonoids	Arthritis, liver disease, cardiovascular disease, energy, anti-inflammatory, antimicrobial against *S. aureus*, *A. hydrophila*, *P. aeruginosa*	Hong et al. (2014)
31.	Northern and Central Asia and Northern Europe	*Pentaphylloides fruticosa* Whole plant	"Shrubby cinquefoil" (Rosaceae)	Flavonoids	Digestive disorders, astringent, antimicrobial against *S. aureus*	Paudel et al. (2014)
32.	Northeastern Asia and Japan	*Pinus pumila* Whole plant	"Dwarf Siberian pine" (Pinaceae)	–	Rheumatoid arthritis, diuretic, urogenital infections, respiratory infections, sores, burns, boils, colds, coughs, influenza, antimicrobial against *S. aureus*	Paudel et al. (2014)
33.	Bangladesh and South Asia	*Pleurotus ostreatus* Mushroom	"Oyster mushroom" (Pleurotaceae)	Statins, phenols, flavonoids, ascorbic acid	Cardiovascular, antimicrobial against *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. typhi*, *K. pneumoniae*, *C. albicans*, *S. cerevisiae*	Chowdhury et al. (2015)
34.	Central Asia and Eastern Europe	*Ptarmica salicifolia* Whole plant	"Bloodwort" (Compositae)	–	Cardiovascular disease, diaphoretic, digestive disorder, antimicrobial against *S. aureus*	Paudel et al. (2014)

35.	Eastern Asia	*Ribes fragrans* Whole plant	Wildflower (Grossulariaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
36.	Eastern Russia, Northern China, Japan, and Korea	*Sorbaria sorbifolia* Whole plant	"False goat's beard" (Rosaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
37.	Asia	*Thymus pavlovii* Whole plant	Flowering plant (Lamiaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
38.	Iran	*Tragopogon graminifolius* Aerial parts	"Sheng" (Compositae)	–	Gastrointestinal and hepatic ailments, antimicrobial against *S. dysenteriae*, *P. vulgaris*	Farzaei et al. (2014)
39.	Russia	*Vaccinium vitis-idaea* Whole plant	"Lingonberry" (Ericaceae)	–	Astringent, diuretic, gonorrhea, arthritis, diabetes, diarrhea, antimicrobial against *S. aureus*	Paudel et al. (2014)
40.	Western Asia and Europe	*Veratrum lobelianum* Whole plant	Flowering herb (Melanthiaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
41.	Russia and Eastern Europe	*Veronica incana* Leaves	"Silver speedwell" (Plantaginaceae)	Flavonoids, iridoids, tannins	Astringent, antimicrobial against *S. aureus*, *E. coli*	Paudel et al. (2014) and Nemereshina et al. (2015)
42.	Tropical and temperate areas of East Asia	*Zanthoxylum myriacanthum* Fruit	"Maqian" (Rutaceae)	Sabinene, limonene, 1,8-cineole	Digestive disorders, detoxification, swelling, pain, antimicrobial against *S. aureus*, *A. baumannii*, *K. pneumoniae*, *P. aeruginosa*, *A. fumigatus*, *C. albicans*	Li R. et al. 2014 (Li et al. 2014)

(continued)

Table 2 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/phytochemicals	Uses	References
43.	Tropical and temperate areas of East Asia	*Zanthoxylum schinifolium* Fruit	"Huajiao" Chinese prickly ash (Rutaceae)	Linalool, limonene, sabinene	Detoxification, vomiting, stomachache, antimicrobial against *S. aureus*, *A. baumannii*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. fumigatus*, *C. albicans*	Li et al. (2014)
44.	Southern Asia	*Zingiber officinale* Root	"Ginger" (Zingiberaceae)		Nausea, asthma, cough, colic, heart palpitation, swelling, loss of appetite, rheumatism, antimicrobial against *E. coli*, *Enterobacter* sp., *P. aeruginosa*, *Proteus* sp., *Klebsiella* sp., *S. aureus*, *Bacillus* sp.	Karuppiah and Rajaram (2012)
Animal based						
45.	India, Thailand, and Indonesia	*Heterometrus xanthopus* Venom	"Giant forest scorpion" (Scorpionidae)	Hadrurin, scorpine, pandinin 1, pandinin 2	Antimicrobial against *B. subtilis*, *E. faecalis*, *P. aeruginosa*, *S. typhimurium*	Ahmed et al. (2012)
46.	China	Royal Jelly	"Ambrosia" Honeybee hypopharyngeal gland secretion		Longevity, overall health, and antimicrobial against *P. aeruginosa*, *K. pneumoniae*, *E. coli*, *S. aureus*	Fratini et al. (2016)

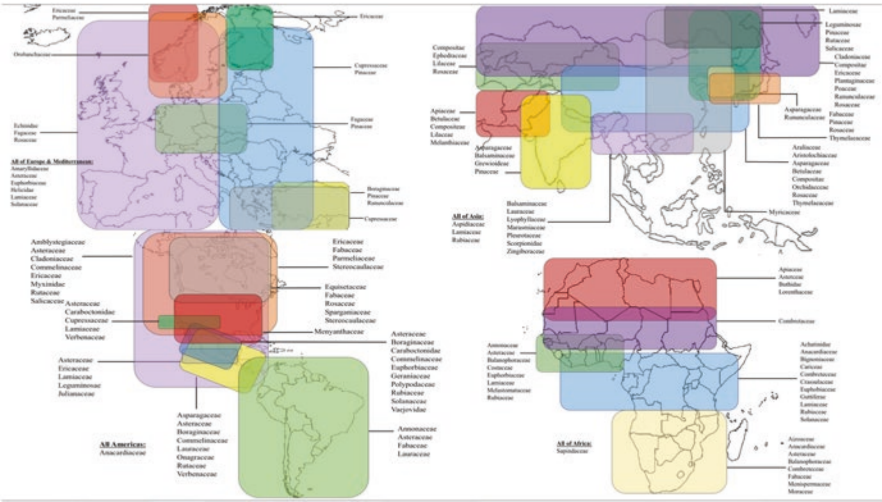

Fig. 1 Geographical distribution of ancient remedies by family classification focusing on Africa, Asia, Americas, and European and Mediterranean regions

Liang et al. 2012) and digestive disorders (Ooi et al. 2006; Li et al. 2012; Paudel et al. 2014; Li et al. 2014; Zeng et al. 2011; Liang et al. 2012; Li et al. 2013a; Ma et al. 2015; Farzaei et al. 2014). Asian herbal remedies are depicted by their geographic location of use in the western, eastern, southern, or northern regions of Asia or as being exclusive to regions in India, Russia, or East Asian countries as seen in Fig. 1. Similar to the African traditional remedies, the most common phytochemicals found in Asia include tannins (Shukla et al. 2016; Paudel et al. 2014; Nemereshina et al. 2015), flavonoids (Hong et al. 2014; Chowdhury et al. 2015; Shukla et al. 2016; Zeng et al. 2011; Nemereshina et al. 2015; Su et al. 2012), and saponins (Koffuor et al. 2014; Shukla et al. 2016). Flavonoids can be found in vegetables, nuts, seeds, tea, wine, honey, stems, and flowers and have a long history of use for their antimicrobial effects. They have the ability to inhibit fungal spore germination and prevent infection and replication of viruses; however, the mechanism of their antibacterial properties is yet to be understood (Cushnie and Lamb 2005).

3.3 Americas

Within the Americas, ancient remedies can be further subdivided by either Canada/the USA, Mexico, Central America, or South America. Table 3 details 48 plant-based remedies and 3 animal-based remedies originating from these regions. Two of the animal-based remedies include venom from *Hadrurus aztecus* (Torres-Larios et al. 2000) and *Vaejovis punctatus* (Ramirez-Carreto et al. 2015), both scorpions found in Mexico. Intriguingly, Asia and northern Africa have also utilized venom from scorpions (*Heterometrus xanthopus* and *Androctonus amoreuxi*). *H.*

Table 3 Americas

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
Plant based						
1.	Mexico and Central America	*Ague* ssp. Sap	"Maguey sap" (Asparagaceae)	Saponins, polysaccharides	Digestive disorders, anti-inflammatory, tuberculosis, jaundice, syphilis, menstrual problems, antimicrobial against *P. aeruginosa*, *E. coli*, *S. paratyphi*, *S. sonnei*, *S. lutea*, *S. aureus*	Davidson and Ortiz de Montellano (1983)
2.	Canada, USA, Sweden, and Norway	*Alectoria ochroleuca* Whole plant	"Witch's hair lichen" (Parmeliaceae)	–	Antimicrobial against *S. aureus*, *E. coli*	Paudel et al. (2014)
3.	Central and Southern Mexico	*Amphipterygium adstringens* Bark	"Cuachalalate" (Julianaceae)	–	Digestive disorders, fever, hypocholesterolemia, antifungal, antiprotozoal, anticancer, antimicrobial against *S. mutans*, *P. gingivalis*, *A. actinomycetemcomitans*, *C. albicans*, *C. dubliniensis*, *E. coli*	Rodriguez-Garcia et al. (2015)
4.	Canada and USA	*Astragalus frigidus* Whole plant	"American milk-vetch" (Fabaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
5.	Latin America and Brazil	*Bowdichia virgilioides* Stem bark	"Alcornoco" (Fabaceae)	Alkaloid	Anti-hematic, astringent, antimicrobial against *S. aureus*	Agra et al. (2013)
6.	Mexico	*Callisia fragrans* Leaves	"Basket plant" (Commelinaceae)	Flavonoids, phytosteroids	Burns, arthritis, skin diseases, tuberculosis, asthma, antimicrobial against *B. cereus*, *B. subtilis*, *M. luteus*, *MRSA*, *S. epidermidis*, *E. faecalis*, *A. hydrophila*, *P. vulgaris*	Tan et al. (2014)

7.	North America	*Cassiope ericoides* Whole plant	Flowering plant (Ericaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
8.	North America	*Cladonia arbuscula* Whole plant	"Reindeer lichen" (Cladoniaceae)	–	Anti-diarrheic, scurvy, chest pains, antimicrobial against *S. aureus*	Paudel et al. (2014)
9.	Mexico	*Cnidoscolus tehuacanensis* Whole plant	Flowering plant (Euphorbiaceae)	–	Antimicrobial against *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
10.	Central America and Caribbean Islands	*Cordia curassavica* Aerial parts	"Barredor" (Boraginaceae)	–	Gastrointestinal disorders, respiratory infections, dermatological disorders, malaria, antimicrobial against *A. salina*, *S. aureus*, *S. epidermidis*, *B. subtilis*, *S. lutea*, *V. cholerae*, *A. niger*, *T. mentagrophytes*, *F. sporotrichum*, *F. moniliforme*	Hernandez et al. (2007)
11.	Southwestern North America	*Cupressus macrocarpa* Leaves	"Monterey cypress" (Cupressaceae)	–	Rheumatism, abortion inducing, antifungal against *T. rubrum*, *T. mentagrophytes*, *T. soudanense*, *T. violaceum*, *T. tonsurans*	Fahed et al. (2017)
12.	Mexico	*Datura lanosa* Leaves	Flowering plant (Solanaceae)	–	Antimicrobial against *S. aureus*, *B. subtilis*, *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
13.	USA, Mexico, and South America	*Dyssodia papposa* Whole plant	"Fetid marigold, dogweed" (Asteraceae)	Flavonoids, acetylenic thiophenes, monoterpenes	Digestive disorders, upset babies, indigestion, antimicrobial against *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
15.	Northern North America	*Equisetum fluviatile* Whole plant	"Water horsetail" (Equisetaceae)	Silica, nicotine	Arthritis, kidney infections, repair broken bones, antimicrobial against *S. aureus*	Paudel et al. (2014)

(continued)

Table 3 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
16.	Mexico	*Galium mexicanum* Aerial parts	"Mexican bedstraw" (Rubiaceae)	Triterpenes, saponins, flavonoids, sesquiterpene, lactones, glucosides	Digestive disorders, chest pain, skin diseases, antimicrobial *B. subtilis*, *MRSA*, *S. aureus*, *S pyogenes*, *C. albicans*, *C. neoformans*, *T. rubrum*	Bolivar et al. (2011)
17.	Mexico	*Geranium niveum* Flower	Flowering plant (Geraniaceae)	Proanthocyanidins, phenolics	Anticancer, epilepsy, digestive disorders, hormonal disorders, kidney dysfunction, antimicrobial against *S. aureus*, *T. mentagrophytes*	Gutierrez-Lugo et al. (1996) and Maldonado et al. (2005)
18.	Mexico and Southwestern USA	*Hadrurus aztecus* Venom	"Mexican scorpion" (Caraboctonidae)	Hadrurin	Antimicrobial against *S. typhi*, *K. pneumoniae*, *E. cloacae*, *P. aeruginosa*, *E. coli*, *S. marcescens*	Torres-Larios et al. (2000)
19.	SoutheasternMexico	*Haematoxylon brasiletto* Bark	"Palo de brasil" (Leguminosae)	Caffeic acid, methyl gallate, gallic acid, phloroglucinol	Hypertension, digestive disorders, diabetes, antimicrobial against *S. aureus*, *E. faecium*, *B. subtilis*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *C. albicans*, *S. mutans*, *P. gingivalis*	Rivero-Cruz (2008)
20.	Northern USA and Canada	*Hedysarum alpinum* Whole plant	"Alpine sweetvetch" (Fabaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
21.	Western USA and Northern Mexico	*Helianthella quinquenervis* Root	"Little sunflower" (Asteraceae)	–	Antimicrobial against *T. mentagrophytes*, *C. albicans*	Gutierrez-Lugo et al. (1996)
22.	North-Central Mexico	*Heliopsis longipes* Root	"Chilcuague" (Asteraceae)	–	Anesthetic, pain, dry mouth, cough suppressant, antimicrobial against *S. aureus*, *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
23.	Mexico	*Hofmeisteria schaffneri* Essential oil	Flowering plant (Asteraceae)	Thymol	Skin infections, antimicrobial against *S. aureus*, *B. subtilis*, *C. albicans*	Perez-Vasquez et al. (2011)

24.	Northern USA	*Juncus alpinoarticulatus* Whole plant	"Northern Green Rush" (Juncaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
25.	Mexico	*Laennecia confusa* Aerial parts	"Horseweed" (Asteraceae)	Flavonoids, cyanogenic glycosides, saponins, sesquiterpene, lactones, triterpenes	Sedative, alcoholism, antimicrobial against *E. coli*, *K. pneumoniae*, *MRSA*, *P. aeruginosa*, *S. aureus*, *C. albicans*, *C. neoformans*, *T. rubrum*	Martinez Ruiz et al. (2012)
26.	Southwestern USA, Mexico, and Central America	*Lippia graveolens* Leaves, flower	"Oregano" (Verbenaceae)	2-Methyl-butanoic acid ethyl ester, benzaldehyde, B-pinene, D-limonene, eugenol, copaene, B-bisabolene	Respiratory infections, menstruation problems, diabetes, digestive disorders, antimicrobial against *Salmonella* sp., *P. fragi*, *L. plantarum*, *M. luteus*, *B. subtilis*, *S. aureus*, *E. coli*, *S. typhi*	Hernandez-Hernandez et al. (2014) and Rivero-Cruz et al. (2011)
27.	Mexico, El Salvador, and Guatemala	*Lopezia racemosa* Aerial parts	"Mosquito flower" (Onagraceae)	Oenothein B, flavonoids, sterols	Digestive disorders, anginas, infection, stomach cancer, urinary tract infection, incontinence, antimicrobial against *B. subtilis*, *A. baumannii*, *MRSA*, *M. smegmatis*, *S. aureus*, *S. pyogenes*, *C. albicans*, *C. neoformans*, *T. rubrum*	Cruz Paredes et al. (2013)
28.	Latin America	*Malmea depressa* Wood	"Elemuy" (Annonaceae)	–	Fever, digestive disorders, insomnia, pain, diabetes, antimicrobial against *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
29.	USA	*Menyanthes trifoliata* Whole plant	"Bog Bean" (Menyanthaceae)	Coumarin derivatives, aucubin	Rheumatism, rheumatoid arthritis, digestive disorders, loss of appetite, antimicrobial against *S. aureus*, *S. epidermidis*, *S. lugdunensis*, *S. pyogenes*, *M. morganii*, *P. maltophilia*, *C. amycolatum*, *C. pseudodiphteriticum*	Weckesser et al. (2007)

(continued)

Table 3 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
30.	North America, South America, and Caribbean	*Metopium brownei* Wood	"Black poisonwood" (Anacardiaceae)	–	Healing/recovery, antimicrobial against *S. aureus*	Gutierrez-Lugo et al. (1996)
31.	Central America, South America, and Southern China	*Mikania micrantha* Leaves	"Mile-a-minute weed" (Asteraceae)	Mikanolide, dihydromikanolide, sesquiterpene lactone	Dermatitis, wound dressings, digestive disorder, malarial fever, antimicrobial against *S. aureus*, *B. subtilis*, *M. luteus*, *B. cereus*, *R. dolaanacearum*, *X. oryzae*, *F. solani*, *R. solani*, *P. aphanidermatum*, *P. parasitica*	Li et al. (2013b)
32.	Mexico, Central America, and South America	*Persea Americana* Seeds	"Avocado" (Lauraceae)	–	Diarrhea, dysentery, rheumatism, asthma, antimicrobial against *M. tuberculosis*	Jimenez-Arellanes et al. (2013)
33.	Mexico	*Pleopeltis polylepis* Aerial parts	"Redscale scaly polypody" (Polypodiaceae)	–	Fever, typhoid, cough, pertussis, chest pain, hepatic diseases, antimicrobial against *A. baumannii*, *B. subtilis*, *E. coli*, *MRSA*, *P. aeruginosa*, *S. aureus*, *C. albicans*, *C. neoformans*, *T. mentagrophytes*	Contreras Cardenas et al. (2016)
34.	Southwestern USA and Northern Mexico	*Poliomintha longiflora* Aerial parts	"Mexican Oregano" (Lamiaceae)	a-Pinene, B-phellandrene, B-caryophyllene, thymol, eugenol	Respiratory disease, digestive disorders, liver obstruction, menstruation, diabetes, infections, antimicrobial against *B. subtilis*, *S. aureus*, *E. coli*, *S. typhi*, *P. aeruginosa*	Rivero-Cruz et al. (2011)

35.	Northern and Central America	*Ptelea trifoliata* Stem bark	"Common hoptree" (Rutaceae)	–	Anthelmintic, digestive disorders, fever, antimicrobial against *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
36.	Mexico	*Rhoeo bermudensis* Leaves	"Boat lily" (Commelinaceae)	Phenol, tannin, flavonoid	Anticancer, whooping cough, dysentery, tuberculosis, cough, bronchitis, pain, antimicrobial against *B. cereus*, *B. subtilis*, *M. luteus*, *MRSA*, *S. epidermidis*, *E. faecalis*, *A. hydrophila*, *P. vulgaris*	Tan et al. (2014)
37.	Southern Mexico, Guatemala, and Belize	*Rhoeo spathacea* Leaves	"Hawaiian dwarf" (Commelinaceae)	Phenol, tannin, flavonoid	Cancer treatment, anti-inflammatory, gonorrhea, diabetes mellitus, rheumatic arthritis, cardiovascular disease, antimicrobial against *B. cereus*, *B. subtilis*, *M. luteus*, *MRSA*, *S. epidermidis*, *E. faecalis*, *A. hydrophila*, *P. vulgaris*	Tan et al. (2014, 2015)
38.	New England and Canada	*Rubus chamaemorus* Leaves	"Cloudberry" (Rosaceae)	Flavonoids, ellagic acid, gallic acid	Antidiuretic, antimicrobial against *S. aureus*, *S. epidermidis*, *E. coli*, *B. subtilis*, *C. albicans*, *M. luteus*	Thiem and Goslinska (2004)
39.	North America and Canada	*Salix pulchra* Whole plant	"Tealeaf willow" (Salicaceae)	Salicin	Anesthetic, dry eyes, antimicrobial against *S. aureus*	Paudel et al. (2014)
51.	North America	*Scorpidium scorpioides* Whole plant	"Hooked scorpion-moss" (Amblystegiaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
40.	Canada	*Sparganium hyperboreum* Whole plant	"Northern bur-reed" (Sparganiaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)

(continued)

Table 3 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
41.	Canada	*Stereocaulon botryosum* Whole plant	"Cauliflower foam lichen" (Stereocaulaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
42.	Canada and USA	*Stereocaulon paschale* Whole plant	"Cottontail foam lichen" (Stereocaulaceae)	–	Rheumatism/arthritis, diabetes, bleeding, dizziness, antimicrobial activity	Paudel et al. (2014)
43.	Mexico	*Tournefortia hirsutissima* Stem bark	"Chigger bush" (Boraginaceae)	–	Fever, diabetes, hypertension, urinary problems, antimicrobial against *T. mentagrophytes*	Gutierrez-Lugo et al. (1996)
44.	Mexico	*Tradescantia pallida* Leaves	"Purple-heart" (Commelinaceae)	Phenol, tannin, flavonoid	Sore eyes, circulation, antimicrobial against *B. cereus*, *B. subtilis*, *M. luteus*, *MRSA*, *S. epidermidis*, *E. faecalis*, *A. hydrophila*, *P. vulgaris*	Tan et al. (2014)
45.	Mexico, Central America, and Columbia	*Tradescantia zebrina* Leaves	"Wandering jew" (Commelinaceae)	Phenol, tannin, flavonoid	Anticancer, antiarrhythmic, kidney disease, digestive disorders, antimicrobial against *B. cereus*, *B. subtilis*, *M. luteus*, *MRSA*, *S. epidermidis*, *E. faecalis*, *A. hydrophila*, *P. vulgaris*	Tan et al. (2014)
46.	North America	*Vaccinium corymbosum* Berry	"Northern highbush blueberry" (Ericaceae)	Anthocyanin	Digestive disorders, circulation, anti-inflammatory, cardiovascular diseases, antimicrobial against *S. aureus*, *MRSA*, *Methicillin-sensitive Staphylococcus aureus MSSA*, *E. coli*, *P. aeruginosa*, *P. mirabilis*, *A. baumannii*	Silva et al. (2016)

47.	Eastern North America	*Vaccinium macrocarpon* Berry	"Cranberry" (Ericaceae)	Anthocyanins, proanthocyanidins, phenolics	Bladder infections, antimicrobial against *E. coli*	Lacombe et al. (2010)
48.	North America	*Vaccinium uliginosum* Whole plant	"Bog blueberry" (Ericaceae)	–	Hypnotic, hypoglycemic, carminative, astringent, antimicrobial against *S. aureus*	Paudel et al. (2014)
Animal based:						
49.	Pacific Ocean from Canada to Mexico	*Eptatretus stoutii* Mucus	"Hagfish" (Myxinidae)	–	Antimicrobial against *E. coli*, *S. enterica*, *S. epidermidis*, *P. aeruginosa*, *C. albicans*	Subramanian et al. (2008)
50.	Mexico and Southwestern USA	*Hadrurus aztecus* Venom	"Mexican scorpion" (Caraboctonidae)	Hadrurin	Antimicrobial against *S. typhi*, *K. pneumoniae*, *E. cloacae*, *P. aeruginosa*, *E. coli*, *S. marcescens*	Torres-Larios et al. (2000)
52.	Mexico	*Vaejovis punctatus* Venom	Scorpion Venom (Vaejovidae)	VpAmp1.0, VpAmp2.0	Antimicrobial against *S. aureus*, *S. agalactiae*, *E. coli*, *P. aeruginosa*, *C. albicans*, *C. glabrata*, *M. tuberculosis*	Ramirez-Carreto et al. (2015)

xanthopus and *H. aztecus* both have the phytochemical hadrurin in common. Hadrurin is a known antimicrobial peptide that disrupts membrane organization in prokaryotic cells, leading to cell lysis, and it has been suggested that this peptide would be beneficial in treating Gram-negative bacterial infections (Sanchez-Vasquez et al. 2013). Although there are no other active molecules in common between the four venoms, there is overlap when looking at the microbial species that they have antimicrobial properties against. For example, *A. amoreuxi* and *V. punctatus* have an antifungal property active against *C. albicans*, *and A. amoreuxi*, *H. aztecus*, and *V. punctatus* exhibit antibacterial activity against *E. coli*, while *H. xanthopus*, *H. aztecus*, and *V. punctatus* are effective against *P. aeruginosa (*Sanchez-Vasquez et al. 2013*)*.

Another animal-based remedy found within the Americas is mucus from *Eptatretus stoutii* (hagfish) (Subramanian et al. 2008). *E. stoutii* mucus has been shown to have antimicrobial properties against *E. coli*, *P. aeruginosa*, *C. albicans*, *Staphylococcus epidermidis*, and *Salmonella enterica*, but the active molecules responsible have yet to be determined. Remedies from the northern hemisphere also contain mucus from two fish, haddock and brook trout, suggesting the interesting possibility that fish mucus could have similar active compounds.

Within the Americas, there is a large overlap between remedies that have antimicrobial activity and those that were historically used for digestive disorders (Paudel et al. 2014; Davidson and Ortiz de Montellano 1983; Rodriguez-Garcia et al. 2015; Hernandez et al. 2007; Gutierrez-Lugo et al. 1996; Bolivar et al. 2011; Maldonado et al. 2005; Rivero-Cruz 2008; Hernandez-Hernandez et al. 2014; Cruz Paredes et al. 2013; Weckesser et al. 2007; Li et al. 2013b; Jimenez-Arellanes et al. 2013; Rivero-Cruz et al. 2011; Tan et al. 2014; Silva et al. 2016), rheumatism (Paudel et al. 2014; Weckesser et al. 2007; Jimenez-Arellanes et al. 2013; Tan et al. 2014; Fahed et al. 2017; Tan et al. 2015), and diabetes (Paudel et al. 2014; Gutierrez-Lugo et al. 1996; Rivero-Cruz 2008; Hernandez-Hernandez et al. 2014; Rivero-Cruz et al. 2011; Tan et al. 2014; Tan et al. 2015). Interestingly, there were also remedies commonly used for tuberculosis (Davidson and Ortiz de Montellano 1983; Rivero-Cruz et al. 2011; Tan et al. 2014). Tuberculosis was the leading cause of death in the early twentieth century; therefore, it is not surprising that herbal remedies were sought after to find a treatment for this disease (Abrams 2013). The most common phytochemicals utilized in the Americas include flavonoids (Gutierrez-Lugo et al. 1996; Bolivar et al. 2011; Cruz Paredes et al. 2013; Tan et al. 2014; Tan et al. 2015; Martinez Ruiz et al. 2012; Thiem and Goslinska 2004) and saponins (Davidson and Ortiz de Montellano 1983; Bolivar et al. 2011; Martinez Ruiz et al. 2012), which have already been discussed.

3.4 Northern Hemisphere

Throughout our review of the literature, there was a noticeable overlap of remedies between continents located in the northern hemisphere, including Asia, Europe, and North America. Table 4 details 22 plant-based remedies, as well as mucus from two

Table 4 Northern Hemisphere (Europe, Asia, North America)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
Plant based						
1.	Asia, Europe, and North America	*Achillea millefolium* Whole plant	"Yarrow" (Asteraceae)	–	Dysmenorrhea, oral mucositis, kidney disease, antimicrobial against *S. aureus*	Paudel et al. (2014)
2.	Canada, Alaska, Russia, Finland, and Sweden	*Arctophila fulva* Whole plant	"Pendant Grass" (Poaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
3.	Asia, Europe, and North America	*Artemisia jacutica* Whole plant	"Wormwoods" (Compositae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
4.	Asia, Europe, and North America	*Beckmannia syzigachne* Whole plant	"Slough grass" (Poaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
5.	Russia, Northern Europe, and Canada	*Cladonia amaurocraea* Whole plant	"Quill pixie lichen" (Cladoniaceae)	–	Headaches, dizziness, antimicrobial against *S. aureus*, *E. coli*	Paudel et al. (2014)
6.	Norway, North America, and Arctic	*Cladonia stygia* Whole plant	"Reindeer moss" (Cladoniaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
7.	Russia, Alaska, British Columbia, and Canada	*Cnidium cnidiifolium* Whole plant	"Hemlock-parsley" (Apiaceae)	–	Skin conditions, anticancer, infertility, erectile dysfunction, antimicrobial against *S. aureus*	Paudel et al. (2014)
8.	Asia, North America, and Europe	*Comarum palustre* Whole plant	"Purple marshlocks" (Rosaceae)	Proanthocyanidins	Antidiabetic, anti-arthritic, antimicrobial against *S. aureus*	Paudel et al. (2014)
9.	Eastern Russia, China, Europe, and Alaska	*Dianthus repens* Whole plant	"Northern pink" (Caryophyllaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)

(continued)

Table 4 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
10.	Asia, Europe, North America, and Northeastern South America	*Eleocharis acicularis* Whole plant	"Needle spikerush" (Cyperaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
11.	Asia, North America, and Europe	*Empetrum nigrum* Whole plant	"Crowberry" (Ericaceae)	–	Urine problems, diarrhea, cough, cold, antimicrobial against *S. aureus*, *C. albicans*	Paudel et al. (2014)
12.	Northern hemisphere	*Equisetum arvense* Whole plant	"Horsetail" (Equisetaceae)	–	Edema, kidney and bladder stones, urinary tract infections, incontinence, antimicrobial against *S. aureus*	Paudel et al. (2014)
13.	Northern Asia, Europe, and USA	*Juniperus communis* Berry, branch	"Common juniper" (Cupressaceae)	Phenolics, flavonoids, tannins	Diuretic, antiseptic, gastrointestinal issues, antimicrobial against *S. aureus*, *S. epidermidis*, *E. hirae*	Paudel et al. (2014) and Taviano et al. (2011)
14.	Northern Asia, Northern Europe, and Northern North America	*Oxycoccus microcarpus* Berry	"Small cranberry" (Ericaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
15.	Northern and Central Asia, North America, Europe, and Northern Africa	*Parnassia palustris* Herb	"Flowering plant" (Saxifragaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
16.	Asia, Canada, and Northern USA	*Ribes triste* Berry	"Swamp red currant" (Grossulariaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
17.	Asia, Europe, and North America	*Rosa acicularis* Whole plant	"Prickly wild rose" (Rosaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)

18.	Europe and North America	*Rubus fruticosus* Fruit, Leaves, Root, Stem	"European blackberry" (Rosaceae)	Tannins, gallic acid, villosin, iron, niacin, pectin, anthocyanins	Anticancer, digestive disorders, antidiabetic, antimicrobial against *E. coli*, *S. typhi*, *S. aureus*, *P. mirabilis*, *M. luteus*, *Citrobacter*, *B. subtilis*, *P. aeruginosa*	Verma et al. (2014)
19.	Asia, Europe, and North America	*Rubus matsumuranus* Berry	"Ku ye xuan gou zi" (Rosaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
20.	Asia, Europe, and North America	*Sanguisorba officinalis* Whole plant	"Great burnet" (Rosaceae)	–	Antimicrobial against *S. aureus*, *MRSA*	Paudel et al. (2014) and Chen et al. (2015)
21.	North America	*Vaccinium microcarpon* Berry	"European cranberry" (Ericaceae)	Proanthocyanidins, anthocyanins, hydroxycinnamic acid, hydroxybenzoic acid, flavonols	Digestive disorders, scurvy, urinary tract infections, *H. pylori* infections, antimicrobial against *S. aureus*	Kylli et al. (2011)
22.	Boreal forest and Arctic tundra	*Vaccinium vitis-idaea* Berry	"Lingonberry" (Ericaceae)	Proanthocyanidins, anthocyanins, hydroxycinnamic acid, hydroxybenzoic acid, flavonols	Arthritis, diabetes, diarrhea, gonorrhea, fever, antimicrobial against *S. aureus*	Kylli et al. (2011)
Animal based						
23.	North Atlantic Ocean	*Melanogrammus aeglefinus* Mucus	"Haddock" (Gadidae)	–	Antimicrobial against *E. coli*, *S. enterica*, *S. epidermis*, *P. aeruginosa*, *C. albicans*	Subramanian et al. (2008)
24.	Iceland, Europe, Asia, and North America	*Salvelinus fontinalis* Mucus	"Brook trout" (Salmonidae)	–	Antimicrobial against *E. coli*, *S. enterica*, *S. epidermis*, *P. aeruginosa*, *C. albicans*	S. Subramanian et al. (2008)

fish, *Salvelinus fontinalis* (brook trout) found in freshwater and *Melanogrammus aeglefinus* (haddock) inhabiting saltwater. As a result of the cold climate in the northern latitudes, the majority of herbal remedies were derived from berries (Paudel et al. 2014; Taviano et al. 2011; Verma et al. 2014; Kylli et al. 2011), grass (Paudel et al. 2014), lichen (Paudel et al. 2014), or moss (Paudel et al. 2014), all of which can withstand the extreme temperatures in this region. The most common dual purpose for these herbal remedies overlaps between treatments for infection and urinary disorders, such as kidney and bladder stones, urinary tract infections, and incontinence (Paudel et al. 2014; Taviano et al. 2011; Kylli et al. 2011). The two most common phytochemicals from the northern hemisphere are tannins (Paudel et al. 2014; Taviano et al. 2011; Verma et al. 2014), similarly to those found in African and Asian remedies, and proanthocyanidins (Paudel et al. 2014; Kylli et al. 2011), condensed tannins that, as mentioned earlier, can impact biofilm formation.

3.5 Other

Other regions include the European, Mediterranean, and Arctic regions. Table 5 includes 21 plant-based remedies from the European and Mediterranean regions, along with 2 animal-based remedies. One animal-based remedy is coelomic fluid from *Echinus esculentus*, the European edible sea urchin, that exhibits antimicrobial effects on a variety of microorganisms including *E. coli*, *S. aureus*, *P. aeruginosa*, and others (Solstad et al. 2016). Another animal-based remedy is mucus from *Helix aspersa*, the brown garden snail. This mucus has been used for skin regeneration and exhibited an antimicrobial effect against *S. aureus* and *P. aeruginosa (*Pitt et al. 2015*)*. Allantoin, a compound found in the mucus, is valuable for healing as it promotes keratolysis and impacts cell proliferation (Tsoutsos et al. 2009). The mucus from the giant African land snail also exhibits similar antimicrobial properties (Pitt et al. 2015). The majority of plant-based remedies were derived from the leaves (Hernandez-Hernandez et al. 2014; Fahed et al. 2017; Pavlovic et al. 2017; Quave et al. 2015; Antunes Viegas et al. 2014; Bouyahyaoui et al. 2016) or the bark/twigs (Fahed et al. 2017; Taviano et al. 2011; Apetrei et al. 2011). The most common phytochemicals within this region are flavonoids (Taviano et al. 2011; Pavlovic et al. 2017; Antunes Viegas et al. 2014; Apetrei et al. 2011; Tadic et al. 2008), also one of Asia's top active molecules. Only three antimicrobial remedies, as seen in Table 6, were found in the Arctic regions of the world, all of which were classified as a lichen (Paudel et al. 2014), but there have been no published studies analyzing the phytochemicals of these plants. In fact, there is lack of reports on the history of lichens being used for any form of ancient remedy.

Table 5 European and Mediterranean remedies

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
Plant based						
1.	Lebanon, Syria, and Turkey	*Abies cilicica* Leaves	"Cilician fir" (Pinaceae)	α-pinene, camphene, δ-3-carene, β-phellandrene, bornyl acetate, α-longipinene, β-caryophyllene, himachala-2,4-diene	Diuretic, anti-helminthic, hair growth, antimicrobial against *T. rubrum*, *T. mentagrophytes*, *T. soudanense*, *T. violaceum*, *T. tonsurans*	Fahed et al. (2017)
2.	Europe and Northern Asia	*Allium ursinum* Leaves	"European wild garlic" (Amaryllidaceae)	Organosulfur, polyphenols, tannins, flavonoids	Cardiovascular disease, respiratory disorders, gastrointestinal disorders, skin diseases, antimicrobial against *E. coli*, *P. aeruginosa*, *E. aerogenes*, *P. mirabilis*, *S. enteritidis*, *S. aureus*, *E. faecalis*, *C. albicans*	Pavlovic et al. (2017)
3.	Persia	*Arnebia* spp. Roots	Wildflower (Boraginaceae)	Naphthoquinones such as alkannins, shikonins	Diarrhea, amenorrhea, gout, kidney stone, jaundice, chronic fever, burn wound, antimicrobial against *S. aureus*, *E. faecalis*, *C. krusei*, *S. cerevisiae*, *C. glabrata*	Hosseini et al. (2018)
4.	Norway	*Asahina chrysantha* Whole plant	"Golden asahinea lichen" (Parmeliaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
5.	Norway and Arctic	*Cassiope tetragona* Whole plant	"Arctic bell-heather" (Ericaceae)	–	Antimicrobial against *S. aureus*, *C. albicans*	Paudel et al. (2014)
6.	Western and Central Europe and Northern Iran	*Castanea sativa* Leaves	"European chestnut" (Fagaceae)	–	Respiratory infections, digestive disorders, fever, pain, sclerosis, tuberculosis, sore throat, antimicrobial against *S. aureus*, *MRSA*	Quave et al. (2015)

(continued)

Table 5 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
7.	Eastern Mediterranean basin	*Cedrus libani* Cones	"Cedar of Lebanon" (Pinaceae)	α-Pinene, β-pinene, sclarene, abieta-8,11,13-triene, abieta-7,13-diene	Skin diseases, allergies, rash, respiratory infections, antimicrobial against *S. aureus*, *T. rubrum*	Fahed et al. (2017)
8.	Europe, Western Asia, and Northern Africa	*Crataegus monogyna and Crataegus oxyacantha (1:1)* Berry	"Hawthorn" (Rosaceae)	Flavonoids, procyanidins, flavone, flavonol, Phenolics	Heart failure, high blood pressure, digestive disorders, antimicrobial against *E. coli*, *S. aureus*, *S. epidermidis*, *B. subtilis*, *M. luteus*, *M. flavus*, *P. aeruginosa*, *L. monocytogenes*, *C. albicans*	Tadic et al. (2008)
9.	Europe, Asia, and Northern Africa	*Euphorbia helioscopia* Whole plant	"Madwoman's milk" (Euphorbiaceae)	–	Anthelmintic, anticancer, cholera, dermatitis, antimicrobial against *S. aureus*, *E. coli*, *A. flavus*	Lone et al. (2013)
10.	Norway and Sweden	*Euphrasia hyperborea* Whole plant	Parasitic plant (Orobanchaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
11.	Europe, Mediterranean, and Northern Africa	*Helichrysum italicum* Flowers, leaves	"Strawflower, immortelle" (Asteraceae)	Flavonoids, terpenes, acetophenones, phloroglucinols, terpenoids	Allergies, colds, cough, liver disorders, sleeplessness, antimicrobial against *S. aureus*, *C. albicans*, *HSV*, *HIV*	Antunes Viegas et al. (2014)
12.	Southern Greece, Southern Turkey, Western Syria, and Lebanon	*Juniperus drupacea* Branch	"Syrian juniper" (Cupressaceae)	Phenolics, flavonoids, tannins	Anthelmintic, antimicrobial against *S. aureus*, *S. epidermidis*, *E. hirae*	Taviano et al. (2011)
13.	Eastern Mediterranean	*Juniperus excelsa* Twigs	"Greek juniper" (Cupressaceae)	α-Pinene, δ-3-carene, α-cedrol	Antimicrobial against *S. aureus*, *T. rubrum*	Fahed et al. (2017)

14.	Morocco, Portugal, France, Iran, Lebanon, and Israel	*Juniperus oxycedrus* Branch	"Cade juniper" (Cupressaceae)	α-Pinene, α-cubebene, germacrene D, τ-cadinol	Hyperglycemia, obesity, tuberculosis, bronchitis, pneumonia, parasitic disease, antimicrobial against *S. aureus*, *S. epidermidis*, *E. hirae*, *T. rubrum*	Taviano et al. (2011) and Fahed et al. (2017)
15.	Morocco, Portugal, Italy, Turkey, Egypt, Lebanon, Israel, Jordan, Saudi Arabia, and Algeria	*Juniperus phoenicea* Leaves	"Phoenician juniper" (Cupressaceae)	a-Pinene, sesquiterpenes B-caryophyllene, germacrene	Antimicrobial against *P. aeruginosa*, *E. coli*, *C. albicans*	Bouyahyaoui et al. (2016)
16.	Mediterranean and Eurasia	*Origanum vulgare* Leaves	"Oregano" (Lamiaceae)	a-Pinene, thymol, carvacrol, germacrene D, alloaromadendrene	Digestive disorders, fever, respiratory infections, anthelmintic, antimicrobial against *Salmonella* sp., *B. thermosphacta*, *P. fragi*, *L. plantarum*, *M. luteus*	Hernandez-Hernandez et al. (2014)
17.	Europe and Northern Asia	*Physalis alkekengi* Aerial parts	"Winter cherry" (Solanaceae)	Alkaloids, glucocorticoids, lycopene, ethanolic compounds, vitamin C	Gout, urinary diseases, rheumatism, digestive disorders, malaria, antimicrobial against *S. aureus*, *S. epidermidis*, *E. faecalis*, *B. subtilis*, *B. cereus*, *E. coli*, *P. aeruginosa*, *E. cloacae*, *K. pneumoniae*, *P. vulgaris*, *C. albicans*, *C. krusei*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis*	Helvaci et al. (2010)
18.	Northern and Central Europe	*Picea abies* Rosin	"Norway spruce" (Pinaceae)	–	Cough, asthma, gout, bronchitis, whooping cough, antimicrobial against *S. aureus*, *MRSA*, *E. coli*, *P. aeruginosa*, *B. subtilis*, *C. albicans*	Sipponen and Laitinen (2011)

(continued)

Table 5 (continued)

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
19.	Central Europe	*Pinus cembra L.* Bark, needles	"Swiss stone pine" (Pinaceae)	Phenol, flavonoid, proanthocyanidin	Antimicrobial against *S. aureus*, *S. lutea*, *B. cereus*, *E. coli*, *P. aeruginosa*, *C. albicans*	Apetrei et al. (2011)
20.	Finland	*Rhododendron lapponicum* Whole plant	Flowering plant (Ericaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
21.	Grasslands in Europe	*Thalictrum foetidum* Whole plant	"Yellow meadow rue" (Ranunculaceae)	Alkaloids	Hypertension, antimicrobial against *S. aureus*	Paudel et al. (2014)
Animal based:						
22.	Western Europe	*Echinus esculentus* Coelomic fluid	"European edible sea urchin" (Echinidae)	EeCentrocins 1,2, EeStrongylocin 2 peptides	Food, antimicrobial against *B. subtilis*, *C. glutamicum*, *S. aureus*, *S. epidermidis*, *E. coli*, *P. aeruginosa*, *A. pullulans*, *C. albicans*, *Cladosporium* sp., *Rhodotorula* sp., *S. cerevisiae*	Solstad et al. (2016)
23.	Europe and Mediterranean	*Helix aspersa* Mucus	"Brown garden snail" (Helicidae)	–	Skin regeneration, antibacterial against *P. aeruginosa and S. aureus*	Pitt et al. (2015)

Table 6 Arctic

#	Region	*Scientific name* Element	Laymen name (family)	Active molecule/ phytochemicals	Uses	References
1.	Antarctic	*Cladonia verticillata* Whole plant	"British lichens" (Cladoniaceae)	–	Antimicrobial against *S. aureus*, *E. coli*	Paudel et al. (2014)
2.	Arctic-alpine	*Flavocetraria cucullata* Whole plant	"Curled snow lichen" (Parmeliaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)
3.	Arctic-alpine	*Flavocetraria nivalis* Whole plant	"Crinkled snow lichen" (Parmeliaceae)	–	Antimicrobial against *S. aureus*	Paudel et al. (2014)

4 Conclusions

Various segments of plants and animal products have been used by humans for thousands of years to ward off disease and infection. In some instances, concentrated oils and topical application of various plant and animal agents have shown enhanced antimicrobial effects in comparison to the current marketed antimicrobials and wound dressings. Although phytochemicals within these agents need to be further identified and understood, these active molecules could potentially increase our armamentarium of agents to combat antimicrobial-resistant infections. As these compounds continue to be studied, they could be of therapeutic value, and as modern medicine continues to lose the battle against antimicrobial resistance, the answer to fight back could be discovered by looking into the past. A notable example of this was a recent study that sought to reconstruct a recipe that was used in medieval times by Anglo-Saxons to treat eye infections. The recipe from *Bald's Leechbook* was translated, made in the laboratory using medieval techniques, and then tested in mice with methicillin-resistant *S. aureus* (MRSA) infections (Harrison et al. 2015). The investigators demonstrated that the medieval recipe was more efficacious at treating this modern-day, drug-resistant infection than the current last line therapy, vancomycin. Thus, with the combination of ancient antimicrobial agents and a modern understanding of medicine, new remedies could impact our battle against persistent microbial infections.

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