Abstract
Antibiotic resistance is becoming a pivotal concern for public health that has accelerated the search for new antimicrobial molecules from nature. Numbers of human pathogens have inevitably evolved to become resistant to various currently available drugs causing considerable mortality and morbidity worldwide. It is apparent that novel antibiotics are urgently warranted to combat these life-threatening pathogens. In recent years, there have been an increasing number of studies to discover new bioactive compounds from plant origin with the hope to control antibiotic-resistant bacteria. This review attempts to focus and record the plant-derived compounds and plant extracts against multi-drug-resistant (MDR) pathogens including methicillin-resistant Staphylococcus aureus (MRSA), MDR-Mycobacterium tuberculosis and malarial parasites Plasmodium spp. reported between 2005 and 2015. During this period, a total of 110 purified compounds and 60 plant extracts were obtained from 112 different plants. The plants reviewed in this study belong to 70 different families reported from 36 countries around the world. The present review also discusses the drug resistance in bacteria and emphasizes the urge for new drugs.

Keywords
Plant metabolites · Antibiotic resistance · MRSA · Medicinal plants

Introduction
Approximately, 500,000 species of both identified and unidentified plants have been estimated on Earth. Among them, only 1–10% are being used as foods by animals and humans (Borris 1996; Cowan 1999). Plants are the key source for drugs and an alternative medicine for fighting against diseases since ancient times. Evidential specimens proved that Neanderthals living 60,000 years ago in present-day Iraq used plants such as hollyhock (Thomson 1978; Stockwell 1988; Cowan 1999) and these plants are still widely being used in ethnomedicine across the world. Interestingly, about 50% of all pharmaceutical products distributed in the United States have plant origin. Among which, very few are used as antimicrobials, since the microbial sources are widely relied upon (Cowan 1999). Nevertheless, since the arrival of antibiotics in the 1950s, the use of plant derivatives as antimicrobials has been literally non-existent. Researchers are interested in plant extracts as medicines as they are undisputable substitution for antibiotics prescribed by physicians (Cowan 1999). Besides, the public is becoming increasingly aware of problems with the overuse and misuse of antibiotics. In addition, many people are attracted in having more autonomy over their medical care (Cowan 1999). The self-medication with plant substances is common due to easy availability. The use of plant-derived natural products in medical treatments is attracting more attention due to its potential efficacy and no side effects (Cowan 1999). Indeed, plants are a rich source of valuable secondary metabolites, such as quinones, tannins, terpenoids,
alkaloids, flavonoids, and polyphenols that are used by plants as defence mechanisms against predation by microorganisms, insects, and herbivores. Some, such as terpenoids, give plants their odors; quinones and tannins are responsible for plant pigmentation. Many compounds including terpenoids are responsible for plant flavor and some of the herbs and spices, which are being used by humans to season foods, could yield useful medicinal compounds (Cowan 1999; Dixon 2001; Kyaw et al. 2012). The number of bioactive compounds derived from plants has been estimated to be at least 200,000 and it still represents only a fraction of the compounds produced by the plant species growing on Earth (Efferth and Koch 2011). Research interest on medicinal plants is being amplified in recent years, which is seen by the increase in the number of publications on plant-based pharmacological interactions and synergistic principles (van Vuuren and Viljoen 2011). This interest has led to the discovery of new/novel biologically active molecules by the researchers and pharmaceutical industries and the adoption of crude extracts of plants for self-medication by the general public. In this review, an effort is made to summarize one decade (2005–2015) of plant antimicrobials including the purified plant-based bioactive compounds, crude and partially purified plant extracts against MDR human pathogens including MRSA, MDR-M. tuberculosis and malarial parasites Plasmodium spp. This is by no means an exhaustive search of all plant-derived compounds and plant extracts during this past 10-year period. Nevertheless, the list provided in this review is impressive and illustrates the potential of plant antimicrobials against MDR human pathogens.

Drug resistance in bacteria: alarming need of new antibiotics

Antibiotic-resistant bacterial infections are already widespread on the globe (Golkar et al. 2014). In February 2017, World Health Organization (WHO) published its first ever list of antibiotic-resistant ‘priority pathogens’ that pose the greatest threat to human health. The first critical priority pathogens are carbapenem-resistant Acinetobacter baumanii, carbapenem-resistant Pseudomonas aeruginosa and carbapenem-resistant and extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae. The second level high priority pathogens are vancomycin-resistant Enterococcus faecium, methicillin-resistant Staphylococcus aureus, clarithromycin-resistant Helicobacter pylori, fluoroquinolone-resistant Campylobacter spp., fluoroquinolone-resistant Salmonellae and cephalosporin and fluoroquinolone-resistant Neisseria gonorrhoeae. These priority pathogens are resistant to multiple antibiotics and have in-built abilities to resist treatment and transfer along genetic material that leads other bacteria to become drug-resistant as well (http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/, accessed on 09/05/2017). Therefore, new/novel antibiotics are desperately needed for battling these rapidly evolving pathogens. The production of new antibiotics has diminished progressively over the past 20 years, entrusting less possibilities to treat these drug-resistant pathogens (Ventola 2015). The treatment of infections caused by MDR pathogens is complicated and limited (Kanj and Kanafani 2011). Meanwhile, clinicians are still prescribing the existing drugs with appropriate dosage and combinations of various drugs for preventing and treating these super bugs (Safavi et al. 2016). Table 1 displays some of the WHO priority drug-resistant pathogens and their current antibiotics of choice for their treatment.

Multi-drug-resistant (MDR) pathogens: a threat to public health

The underuse, overuse, and misuse of antibiotics by humans are the selective pressure, which eventually lead to the development of antibiotic resistance in microbes (Davies and Davies 2010). Globally, emerging MDR pathogens also called as ‘ESKAPE’ organisms such as Enterococcus spp., S. aureus, Klebsiella spp., A. baumannii, P. aeruginosa and Enterobacter spp. are a serious threat now-a-days to public health (Boucher et al. 2009). MDR microorganisms can survive the treatment with antimicrobial drugs, thereby standard treatments become ineffective and infections persist, increasing the risk of spread to others. In general, MDR microbes are resistant to three or more antibiotics (Styers et al. 2006); however, strains of Mycobacterium tuberculosis are extremely drug-resistant (XDR) that are virtually resistant to all classes of antimicrobials (Gandhi et al. 2006). In 2012, WHO reported a gradual increase in resistance to HIV drugs, although not reaching critical levels (WHO 2012). Since then, further increase in resistance to first-line treatment drugs was reported, which might require using more expensive drugs soon (http://www.who.int/medicentre/factsheets/fs194/en/, accessed on 18/08/2016). In addition, the Centre for Disease Control (CDC) estimates that each year, nearly 2 million people in the United States acquire an infection while in hospital, resulting in 90,000 deaths. More than 70% of the bacteria that cause these infections are resistant to at least one of the antibiotics commonly used to treat them (http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143568.htm, accessed on 18/08/2016). The globally emerging antibiotic resistance, nevertheless, makes MDR microbes substantially difficult...
to control or kill and also builds them more stronger. It is clear that the currently available antibiotics are insufficient to control these superbugs and, hence, more research and novel antimicrobial sources are highly demanded.

**Methicillin-resistant* S. aureus* (MRSA)**

In this decade, the fastest evolving pathogen is MRSA. There has been a continuous increase in the incidence of MRSA worldwide. In the United States, current MRSA rates exceed 50% of all *S. aureus* infections and stand close to 90% in some Asian countries (Office for National Statistics 2005). The mortality rates for deaths involving MRSA have increased over 15-fold during the period 1993 to 2002 (Office for National Statistics 2005). MRSA has developed resistance to a number of antibiotics such as oxacillin, penicillin and amoxicillin. In some countries, over 60% of *S. aureus* cases in hospital intensive care units are now resistant to these first-line antibiotics (Laxminarayan and Malani 2007). MRSA has been categorized into two groups based on their infections such as hospital-acquired and community-acquired MRSA (HA-MRSA and CA-MRSA), which marginally differ in their genetic makeup.

HA-MRSA is a deadly pathogen and often infects hospitalized patients particularly those who are immunocompromised (Sheen 2010). HA-MRSA was first appeared in the United States in 1968 and showed resistance against β-lactam antibiotics and other various types of antibiotics (Chanda et al. 2010). The National Audit Office estimated that HA-MRSA was the primary factor in 5000 deaths per annum (National Audit Office 2000). CA-MRSA emerged in the community setting recovered from a clinical culture from a patient residing in the surveillance area, who had no established risk factors usually correlated with HA-MRSA (Chanda et al. 2010). The established risk factors include the isolation of MRSA two or more days after hospitalization; a history of hospitalization, surgery, dialysis, chronic diseases, or residence in a long-term care facility within 1 year before the MRSA-culture date; the presence of a permanent indwelling catheter or percutaneous medical device at the time of culture; or previous isolation of MRSA (Fridkin et al. 2005; Chanda et al. 2010). CA-MRSA often causes skin infection and severe infection resulting in fatal on certain occasions displaying resistance to β-lactam antibiotics, nevertheless susceptible to trimethoprim/sulfamethoxazole, clindamycin and tetracyclines (Deresinski 2005; Chanda et al. 2010). *Staphylococcus aureus* is one of the most critical human pathogens causing wide range of infections from mild skin diseases to life-threatening endocarditis (Chambers 2001). After identifying the evidential occurrence of methicillin resistance among *S. aureus* strains, vancomycin and quinolones antibiotics have been used as alternative drugs of choice as staphylococcal infections therapy (Tiwari et al. 2009). Nevertheless, over a decade, most of the *S. aureus* strains including MRSA developed resistance to many commonly used fluoroquinolones by acquiring a rapid mutation in the genes encoding for target enzymes and expression of the efflux pump (Tanaka et al. 2000; Gade and Qazi 2013). Looking at the widespread development of fluoroquinolones resistance in *S. aureus* (FRSA), potential antibiotics are required and demand more awareness in public health care and community settings.

### Table 1 List of some WHO priority drug-resistant pathogens and their current antibiotics of choice for treatment

| WHO priority drug-resistant pathogen | Currently using antibiotics | References |
|--------------------------------------|-----------------------------|------------|
| Carbapenem-resistant *A. baumannii* | Colistin, carbapenems, sulbactam, rifampin and tigecycline | Viehman et al. (2014) |
| Carbapenem-resistant *P. aeruginosa* | Ticarcillin-clavulanate, ceftazidime, aztreonam, imipenem, ciprofloxacin and colistin | Kanj and Kanafani (2011) |
| Carbapenem-resistant, ESBL-producing Enterobacteriaceae | Polymyxins, fosfomycin, carbapenems, tigecycline and aminoglycosides | Morrill et al. (2015) |
| Vancomycin-resistant *E. faecium* | Streptogramin, linezolid, daptomycin, oritavancin and tigecycline | Linden (2002) |
| Methicillin-resistant *S. aureus* | Vancomycin, trimethoprim-sulfamethoxazole, clindamycin, linezolid, tetracyclines and daptomycin | Kali (2015) |
| Clarithromycin-resistant *H. pylori* | Amoxicillin, esomeprazole, rabeprazole, omeprazole, metronidazole, levofoxacin and clarithromycin | Safavi et al. (2016) |
| Fluoroquinolone-resistant *Campylobacter* spp. | Erythromycin, ciprofloxacin and fluoroquinolones | Wieczorek and Osek (2013) |
| Compound/extract | Plant | Source | Target | Reported country | References |
|------------------|-------|--------|--------|------------------|------------|
| Aqueous alkaloid, organic alkaloid and non-alkaloid | *Rhazya stricta* | Leaves | MRSA | Saudi Arabia | Khan et al. (2016) |
| Aqueous, chloroform, ethanol and hexane | *Alkanna tinctoria* | Leaves | MRSA, MDR-*Acinetobacter baumannii*, *E. coli* and *P. aeruginosa* | Pakistan | Khan et al. (2015) |
| Dehydroabietic acid | *P. elliottii* | Resin-oil | MDR-*Staphylococcus epidermidis*, *S. capitis*, *S. haemolyticus*, *E. faecium* and *E. faecalis* | Brazil | Leandro et al. (2014) |
| Dichloromethane, methanol, petroleum ether, chloroform, ethyl acetate, acetone, ethanol and water | *Lantana camara* L. | Leaves | MRSA, VRE, MDR-*A. baumannii*, *P. aeruginosa*, *Streptococcus pyogenes*, *Citrobacter freundii*, *Proteus mirabilis* and *P. vulgaris* | India | Dubey and Padhy (2013) |
| Petroleum ether, acetone, methanol, ethanol and water | *Butea monosperma* Lam. | Leaves | MRSA, VRSA | India | Sahu and Padhy (2013) |
| Ethanol and water | *Anthecephalus cadamba* and *Pterocarpus santalinus* | Leaves and bark | MDR-*Acinetobacter sp.*, *P. aeruginosa*, *C. freundii* and *Proteus sp.* | India | Dubey et al. (2012) |
| Ethanol | *Rhus coriaria* | Seeds | MDR-*P. aeruginosa* | Palestine | Advan et al. (2010) |
| (+)-Lyoniresinol-3-alpha-O-beta-p-glucopyranoside | *Lycium chinense* Mill. | Roots and bark | MRSA | China | Lee et al. (2005) |
| Baicalin | *Scutellaria baicalensis* Georgi. | NA | Synergistic effect with beta-lactam-resistant strains of *S. aureus*, synergies between baicalein, tetracycline, beta-lactams and ciprofloxacin against MRSA and inhibit MRSA-pyruvate kinase | China | Chan et al. (2011) |
| Sophoraflavanone G, 7,9,2',4'-tetrahydroxy-8-isopentenyl-5-methoxychalcone | *Sophora flavescens* | Roots | MRSA, VRE | China | Cha et al. (2009), Lee et al. (2010) |
| Chloroform and chloroform + HCl | *Andrographis paniculata* | NA | MRSA | India | Roy et al. (2010) |
| Hexane | *Sclerocarya birrea* | Seeds | MRSA | Malaysia | Mariod et al. (2010) |
| Cold and hot aqueous and ethanol | *Terminalia chebula* Retz. | Dried seedless ripe fruits | MRSA, trimethoprim-sulphamethoxazole-resistant uropathogenic *E. coli* | India | Bag et al. (2009) |
| 20-Hydroxyecdysone | *Achyranthes japonica* | Roots | MRSA | South Korea | Kim et al. (2009) |
| Aqueous and ethanol | *Fabiana bryoides*, *F. densa*, *F. punensis*, *Baccharis boliviensis*, *Chuquiraga atacamensis*, *Parastrephia lepidophylla*, *P. lucida*, *L. phyliciformis*, *Frankenia triandra*, *Chiliotrichiopsis keideli* | Aerial parts | MRSA, MSSA, MRSCN, MSSCN and MDR-*E. faecalis* | Argentina | Zampini et al. (2009) |
Vancomycin-resistant Enterococcus (VRE)

Vancomycin-resistant Enterococcus (VRE) is another current threat in emerging drug-resistant pathogens in hospitals worldwide (Johnstone et al. 2017). Approximately, 66,000 healthcare-associated enterococcal infections are reported in the United States every year. Out of them, approx. 20,000 are vancomycin-resistant infections with about 1300 deaths attributes to VRE infections (Centre for Disease Control 2013). Hospital incurred Enterococci infections are resistant to several drugs including daptomycin, linezolid, penicillin and cephalosporins, and their progressive resistance has been
| Compound/extract                          | Plant                                | Source                  | Reported country | References                        |
|------------------------------------------|--------------------------------------|-------------------------|------------------|------------------------------------|
| 20% Ethanol                              | *Prunella vulgaris* L.                | Whole plant             | China            | Lu et al. (2011)                   |
| Dihydro-β-agarofuran sesquiterpenes      | *Celastrus vulcanicola*              | Dried leaves            | Spain            | Torres-Romero et al. (2011)        |
| 6% hexane, ethanol, ethyl acetate, 6%-butanol, and methanol extracts | *Flourensia cernua*                 | Whole plant             | Mexico           | Molina-Salinas et al. (2011)       |
| 70% ethanol                              | *Allium sativum*                     | Cloves                  | Pakistan         | Hannan et al. (2011), Dini et al. (2011) |
| Bisbenzylisoquinoline alkaloids          | *Tilia triandra*                     | Roots                   | Thailand         | Sureram et al. (2012)              |
| Alcohol                                  | *Humulus lupulus*                    | Whole plant (stems, leaves and roots) | Iran            | Serkani et al. (2012)              |
| Essential oil                            | *Citrus* sp.                         | NA                      | USA              | Crandall et al. (2012)             |
| Obtusifoliol                             | *Struthanthus marginatus*            | Aerial parts            | Brazil           | Leitao et al. (2013)               |
| 3-O-n-acil-lup-20(29)-en-3β,7β,1 5α-triol | *Struthanthus sconcinus*            | Leaves                  | Brazil           | Leon-Diaz et al. (2013)            |
| (-) Licarin A                            | *Aristolochia taliscana*             | Roots                   | Mexico           | Nogueira et al. (2013)             |
| Ethanol extract                          | *Hypericum* sp.                      | Aerial parts            | Portugal         | Jimenez-Arellanes et al. (2013)    |
| Ursolic and oleanolic acids              | *Chamaedorea tepejilote*            | Aerial parts            | Mexico           | Uc-Cachon et al. (2014)            |
| Maritinine and 3,3′-biplumbagin          | *Diospyros anisandra*                | Stem and bark           | Mexico           | Zhang et al. (2015)                |
| 70% Ethanol and water eluted part of ethanol extract | *Ranunculus ternati* Radix          | Whole plant             | China            | Radji et al. (2015)                |
| Water, methylene chloride, ethanol, 6-hexane and ethyl acetate extracts | *Andrographis paniculata, Annona muricata, Centella asiatica, Pluchea indica and Rheo spathacea* | Whole plant and dried leaves | Indonesia | Jang et al. (2016), Gupta et al. (2010) |
| Diterpenoids including ent-kaurane, kaurnate and grayanane | *Croton tonkinensis*                | Whole plants or leaves  | South Korea      | Jang et al. (2016), Gupta et al. (2010) |
| Water extract                            | *Acalypha indica* L.                 | Leaves                  | India            | Lakshmanan et al. (2011)           |
|                                        | *Acalypha vasica*                     | Leaves                  | India            | Birk et al. (2012)                 |
|                                        | *Allium cepa*                         | Bulbs                   | India            | Gupta et al. (2012)                |
|                                        | *Allium sativum*                      | Cloves                  | India            | Singh et al. (2013)                |
| Pure gel of *Aloe vera*                  | *Aloe vera* L.                        | Pure gel                | India            | Gupta et al. (2012)                |
| Ethyl p-methoxycinnamate                 | *Kaempferia galanga*                 | Rhizome                 | India            | Singh et al. (2013)                |
| Piperine                                 | *Piper nigrum* L.                     | Seeds                   | India            | Singh et al. (2013)                |
| 5,10-Pentadecadiyn-1-ol, a-curcumen, hydroxyjunipene, cycloisosativene, valencine and selino 3,7 (11)-diene | *Vetiveria zizanioides*             | Fresh roots           | India            | Gupta et al. (2012)                |
| Alkaloids, flavonoids                    | *Urtica dioica*                      | Leaves                  | India            | Singh et al. (2013)                |
discovered across the world posing an alarming concern (Simeon et al. 2006; Johnstone et al. 2017).

Table 2 summarizes 15 plant-derived compounds and 40 plant extracts reported during 2005–2015 against MDR pathogens including MRSA, VRE, Trimethoprim–sulphamethoxazole-resistant uropathogenic *Escherichia coli* and various MDR Gram-negative and MDR Gram-positive human pathogens. This list clearly demonstrates the substantive and ongoing role of plant-derived compounds against MRSA and other MDR pathogens. A total of 43 plants are reviewed in Table 2; they are belonging to 23 different families. Interestingly, out of the 43 plants, 42 are angiosperms excluding the Brazilian *Pinus elliottii* (Leandro et al. 2014). Results show that both angiosperms and gymnosperms harboring potential antimicrobials against MDR pathogens; nevertheless, angiosperms are widely studied against MDR pathogens.

**Table 3 continued**

| Compound/extract | Plant | Source | Reported country | References |
|------------------|-------|--------|------------------|------------|
| Plumericin and iso-Plumericin | *Plumeria bicolor* | Bark | India | Kumar et al. (2013) |
| Emodin | *Ventilago madraspatana* | Stem and bark | India | Basu et al. (2005) |
| Diospyrin | *Diospyros montana* | Stem and bark | India | Dey et al. (2014) |
| Andrographolide | *Andrographis paniculata* | Whole plant | India | Prabu et al. (2015) |
| Aqueous, boiling water and methanol extracts | *Punica granatum* | Fruit | India | Dey et al. (2015) |

Multi-drug-resistant tuberculosis (MDR-TB)

Tuberculosis (TB) is an extremely notorious and infectious disease caused by *Mycobacterium* spp., particularly *M. tuberculosis*. TB is the second most fatal disease after HIV, accountable for human deaths across the globe according to the World Health Organization (WHO 2014). Around 6.1 million TB patients have been reported in the year 2013, of these, about 5.7 million (93%) cases were new (WHO 2014). About 9.6 million people were reported ill due to TB in 2014, of which approximately 1.5 million died (WHO 2014; Pandit et al. 2015). This disease is highly progressive in Asia and Africa, and more than 80% of all TB cases were reported from these two continents (Zager and McNerney 2008). Evidently, the *M. tuberculosis* is acquiring resistance against conventional drugs, thus frightening the global health community (Zignol et al. 2006). MDR-*M. tuberculosis* requires treatment courses that are much longer and less effective than those for non-resistant *M. tuberculosis*. Extensively drug-resistant TB (XDR-TB, defined as MDR-TB plus resistance to any fluoroquinolone and any second-line injectable drugs) has been identified in 100 countries, in all regions of the world (http://www.who.int/mediacentre/factsheets/fs194/en/, accessed on 18/08/2016). In this review, we have outlined plant-derived compounds and plant derivatives having significant anti-mycobacterial activity against MDR-TB reported during 2005–2015 (Table 3). Table 3 covers a total of 34 plants belonging to 26 different families and all are angiosperms. A total of 36 purified compounds and 20 plant extracts were reported during 2005–2015 against MDR-*M. tuberculosis*. These data obviously revealed that the plant-derived antimicrobials have a unique competence, as well as alternative and novel solutions to control these deadly MDR- and XDR-TB.

Malaria: a current public health concern

Malaria is a complex deadly blood disease with ravaging effects in the world (Onguéné et al. 2013). Approximately, half of the world’s population is at risk of malaria and that 1–2 million annual deaths can be attributed to malaria alone (Vogel 2010; WHO 2012; Onguéné et al. 2013). There were approximately 245 million cases of malaria in 2006 and 3.3 billion people were at risk of the disease. Among them, about 1 million deaths were mostly of children under the age of five (Oliviera et al. 2009). Currently, there are 109 malarious countries and territories, of which, 45 are within the African region (WHO 2008). A total of four protozoan species of the genus *Plasmodium* (*P. falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*) are the causative agents for this infection, although majority of fatal cases are caused by *P. falciparum* (Nogueira and Lopes 2011). Currently, malaria has been treated with
| Compound                                                                 | Plant                                      | Source          | Reported country | References                                         |
|-------------------------------------------------------------------------|--------------------------------------------|-----------------|------------------|----------------------------------------------------|
| 17-O-acetyl,10-hydroxycorynantheol                                       | *Strychnos usambarensis*                   | Leaves          | Belgium          | Cao et al. (2011)                                  |
| Alstonine                                                               | *Picralima nitida*                         | Fruits          | USA              | Okunji et al. (2005)                               |
| Methyl uguenenoate, furoquinoline and maculosidine                       | *Vepris uguenensis*                        | Roots           | South Africa     | Cheplgoi et al. (2008), Kiplimo (2012)             |
| Evoxine, arborinine and xanthoxiline                                     | *Tecla gerrardii*                          | Roots and fruits| South Africa     | Waffo et al. (2007), Tchinda et al. (2009)         |
| N-isobutyldeca-2,4-dienamide                                            | *Hugonia castaneifolia*                   | Root and bark   | Tanzania         | Baraza et al. (2008)                               |
| Pipiphyrine                                                             | *Beilschmiedia zenkeri*                    | Bark            | France           | Lenta et al. (2009)                                |
| Cryptoquindoline                                                         | *Cryptolepis sanguinolenta*                | Stems           | Ghana            | Barku et al. (2012)                                |
| Clerodane and labdane diterpenoids                                       | *Nuxia sphaerocephala*                    | Leaves          | Sudan            | Mambu et al. (2006)                                |
| 16-Oxolabda-8(17),12(E)-dien-15-oic acid, methyl-14,15-epoxyldab-8(17), 12(E)-Diene-16-oate and Turraein A | *Turreanthus africanus*                   | Seeds           | Cameroon         | Ngemenya et al. (2006)                             |
| 3-Deoxyaulacarpin A, Zambesiacolactones A and B, aulacarpin A            | *Aframomum zambesiacum*                   | Seeds           | Cameroon         | Kenmegnog et al. (2006)                            |
| Galanal B, galanolactone, (E)-8,17-epoxyldab-12-ene-5,16 dial and (E) Laba-8,12-diene-15,16 dial | *Aframomum arundinaceum*                  | Seeds           | Cameroon         | Wabo et al. (2006)                                |
| 7α-Obacunylacetate, 7α-acetoxydihyronomilin, 22-hydroxyhopen-3-one and 24-methylene cycloartenol | *Entandrophragma angolense*                | Stem and bark   | Cameroon         | Bickii et al. (2007)                               |
| 7-Deacetoxy-7-oxogedunin, Ekeberin C1–C3 and acyclic triterpenes         | *Ekebergia capensis*                       | Stem and bark   | Japan            | Murata et al. (2008)                               |
| Bisnorterpenes                                                          | *Salacia madagascariensis*                 | Roots           | USA              | Thiem et al. (2005)                                |
| Cassane furanoditerpenes                                                | *Caesalpinia volkensii*                    | Root and bark   | Kenya            | Ochieng et al. (2012)                              |
| Abietane diterpenes                                                     | *Plectranthus spp.*                        | Leaves          | South Africa     | Van Zyla et al. (2008)                             |
| Ferruginol                                                              | *Fuerstia africana*                        | Aerial parts    | USA              | Koch et al. (2006)                                 |
| 13-Epi-dioxiabiet-8(14)-en-18-ol                                        | *Hyptis suaveolens*                       | Leaves          | South Africa     | Chukwujekwu et al. (2005)                          |
| Sesquiterpenes                                                          | *Acanthospermum hispidum*                  | Flowers, leaves and stems | Belgium         | Ganfon et al. (2012)                               |
| Vernangulides A, B, Vernodalol and Vernodalin                            | *Vernonia angulifolia*                     | Aerial parts    | Denmark          | Pedersen et al. (2009)                             |
| Urosperral A-15-O-acetate                                                | *Dicoma tomentosa*                        | Whole plant     | Belgium          | Jansen et al. (2012)                               |
| Artemisinin                                                             | *Artemisia annua*                          | Seeds           | Italy            | Reale et al. (2008)                                |
| Dehydrobrachylaenolide                                                  | *Dicoma anomala subsp. gerrardii*          | Roots stocks    | South Africa     | Becker et al. (2011)                               |
| Okundoperoxide                                                          | *Scleria striatinus*                       | Roots           | Cameroon         | Efange et al. (2009)                               |
| Coloratane sesquiterpenes                                               | *Warburgia ugandensis*                     | Stem and bark   | Austria          | Wube et al. (2010)                                 |
| Beilshmiedic acid derivatives                                           | *Beilschmiedia cryptocaryoides*            | Bark            | Germany          | Talontsi et al. (2013)                             |
| 3-Hydroxy-20(29)-lupen-28-ol                                            | *Schefflera unbellifera*                   | Leaves          | South Africa     | Mthembu (2007)                                    |
| Pristimerin                                                             | *Maytenus senegalensis*                    | Root and bark   | Sudan            | Khalid et al. (2007)                               |
quinine, chloroquine, mefloquine and artemisinin among other drugs (Onguéné et al. 2013). However, the protozoans have developed resistance in many countries of the world over time towards the influential factors: poor hygienic conditions, poorly managed vector control programmes and no approved vaccines so far (White 2004). Researchers currently put their research efforts on new antimalarial agents, mainly focusing on natural origin and the development of phytomedicines (Onguéné et al. 2013). Table 4 reviews the plant-derived compounds including alkaloids, terpenoids and triterpenoids for antimalarial properties. A total of 59 anti-plasmodial compounds including a potent antimalarial drug artemisinin were reported from different plants documented during 2005–2015 (Table 4). Notably, Table 4 displays a total of 35 plants belonging to 21 families under angiosperms showing antimalarial activity. The data summarized in the Table 4 highlight the rich diversity of plant natural products that manifest to be a promising source for the development of antimalarial agents.

### Drug discovery from plants

The concept of ‘the active principle’ in medicine first reported in the fifteenth century; however, pure compounds isolated from the plant extracts were reported in the late eighteenth and earlier nineteenth century (Houghton 2001). It is important to note that plant-derived pure compounds had the similar effect as the plant extract and thus been promptly substituted in many cases as the important ingredient in medicines (Houghton 2001). Codeine and narcotine were the first natural compounds isolated from *Papaver somniferum*. Since then, numbers of compounds have been isolated from plants and many of these remain in extensive use in medicine as drugs (Houghton 2001; Lahlou 2013). Some of the prominent plant-derived commercially proven drugs, sources, brand names and their medicinal uses are shown in Table 5. Plant-derived molecules including secondary metabolites that demonstrate medicinal properties may act by similar or different mechanisms. The mode of antimicrobial action is similar between plant-derived quinones (bind to adhesions, inactivate enzymes and complex with cell wall) and flavonoids (bind to adhesions and complex with cell wall). However, polyphenols and tannins (enzyme inhibition, substrate deprivation, membrane disruption and metal ion complexation), terpenoids and essential oils (membrane disruption) and alkaloids (intercalate into cell wall) antimicrobial actions are varied in their mode of action (Pandey and Kumar 2013).

A total of 112 plants were studied during the period 2005–2015 of which, 110 purified bioactive compounds and 60 plant-derived extracts were reported and displayed significant antibacterial, antitubercular, and antimalarial activities (Tables 2, 3, 4). Totally, 40 and 20 plant extracts were reported for antibacterial and antitubercular activities, respectively, during this period (Tables 2, 3, 4). Although these plant extracts showed same therapeutic effects as pure compounds, further investigation of structural elucidation would afford novel chemical structures and new drugs. Plants reviewed in this study are reported from 36 countries around the world. Out of 112 plants, 41.96, 25.00, 10.71, 11.60, 8.90 and 1.78% were reported from Asia, Africa, Europe, North America, South America and Oceania, respectively (Fig. 1). Asia, the highest number (20) of plants, is reported for India for antibacterial and antitubercular activities in the period 2005–2015. Besides, the 112 plants revised in this study belong to 70 different plant families and 99% of them are angiosperms, which is displaying the

| Compound | Plant                                       | Source     | Reported country | References                  |
|----------|---------------------------------------------|------------|------------------|-----------------------------|
| Pentacyclic triterpenes | *Nuxia sphaerocephala* | Leaves     | Sudan            | Mambu et al. (2006)         |
| Lupeol and Lupeyl docosanoate | *Hymenocardia acida* | Bark and stems | Nigeria          | Mahmout et al. (2008), Ajaiyeoba et al. (2008) |
| Betulinic acid | *Hypericum lanceolatum* | Stem and bark | Cameroon         | Zofou et al. (2011)         |
| 3-Friedelanone | *Psorospermum glaberrimum* | Stem and bark | Germany          | Lenta et al. (2008)         |
| 3-O-betulinic acid p-coumarate | *Baillonella toxisperma* | Stem and bark | Cameroon         | Mbah et al. (2011)          |
| 2β,3β,19α-Trihydroxy-urs-12-20-en-28-oic acid | *Kigelia africana* | Stem and bark | Cameroon         | Zofou et al. (2012)         |
| Cucurbitacins B, D and 20-epibryonolic acid | *Cogniauxia podolaena* | Stem and bark | Congo            | Banzouzi et al. (2008)      |
therapeutic potential. Houghton (2001) reported that 25% of the drugs prescribed by physicians in the developed countries are obtained from flowering plants, angiosperms. Among the 70 families recorded, plants from Apocynaceae, Lamiaceae and Asteraceae showed antibacterial, antitubercular, and antimalarial activities, while plants from Acanthaceae, Lythraceae, and Euphorbiaceae disclosed antibacterial and antitubercular activities. However, plants from Fabaceae and Meliaceae exhibited antibacterial and antimalarial activities, but plants belonging to Celastraceae, Rutaceae, Hypericaceae and Zingiberaceae demonstrated antitubercular and antimalarial activities. The plant-derived extracts mentioned in this review were from various organic solvent extracts including aqueous extracts (Tables 2, 3).

Furthermore, the total number of purified compounds given in this review is not an exact number reported in the mentioned period because we also have provided the class of compounds which may contain number of derivatives. Nevertheless, the data collected in this review impose and focus the value of plant antimicrobials against the lethal MDR pathogens including malarial parasites.

**Future perspectives**

Plants are the renowned natural laboratories for producing structurally unique, diverse and complex natural products. Besides the plants, extensive efforts are also being
undertaken on microorganisms and other organisms from another living world, such as the oceans (Subramani and Aalbersberg 2013; Malve 2016) for pharmaceutically important biomolecules. However, in plants particularly angiosperms, only less than 10% have been screened for natural products discovery (Houghton 2001). Therefore, there is an immense scope for more fascinating bioactive compounds from flowering plants that will yield new/novel drugs. To access this hidden treasure, more integrative approach with various natural product discovery tools will be the key for success in discovery of phytomedicines. The complex and rich chemical diversity in plants pave to the isolation of natural products which is tough and laborious. Therefore, the significant application of tools such as high-performance liquid chromatography coupled to mass spectrometry (HPLC–MS), liquid chromatography–mass spectrometry (LC–MS), liquid chromatography–nuclear magnetic resonance–mass spectrometry (LC–NMR–MS), capillary NMR (cap-NMR) spectroscopy, LC–solid phase extraction (SPE)–NMR along with bioassay-guided fractionation and high-throughput bioassays will accelerate the access of plant-derived natural products. However, the substantial use of medicinal plants for drug discovery programme endangers their existence, so farming of medicinal plants must be instigated for assuring the future accountability (Lahlou 2013).

**Conclusion**

The use of herbs and herbal products has widely been accepted in our modern way of life and it is estimated that about 80% of the world’s population still rely on traditional medicines for their primary health care. The significance of plant-derived natural products and their extracts used by the lay community has been realized and documented since ancient time. Interestingly, researchers and clinicians pay great attention to plant-derived secondary metabolites because of their antibiotic activity without conferring any antibiotic resistance. Hence, plant-based antimicrobials have widely been used as preventative and curative solutions against multi-drug-resistant pathogens. Globally emerging MDR and XDR pathogens are a serious concern. On the other hand, most of the chemically synthesised antibiotics can cause adverse side effects and are very expensive. Therefore, these days, there is an increasing inclination towards the use of an alternative source of medicines, particularly the medicinal plants. Several plant species have already been widely reported showing potential medicinal properties. However, the emerging new infections, diseases and rapid evolution of pathogens urge the researchers for further exploration into nature for novel natural products. Plants are certainly playing a dynamic role to control antibiotic-resistant bacterial infections. However, these plant-derived active principles should be taken for further research to translate this knowledge into potential therapeutic drugs.

**Compliance with ethical standards**

**Conflict of interest** No conflict of interest was declared.

**References**

Abu-Shanab B, Adwan G, Jarran N, Abu-Hijleh A, Adwan K (2006) Antibacterial activity of four plant extracts used in Palestine in folkloric medicine against methicillin-resistant *Staphylococcus aureus*. Turk J Biol 30:195–198

Adwan G, Abu-Shanab B, Adwan K (2010) Antibacterial activities of some plant extracts alone and in combination with different antimicrobials against multidrug resistant *Pseudomonas aeruginosa* strains. Asian Pac J Trop Med 3:266–269

Ajaiyeoba EO, Ashidi JS, Okpako LC, Houghton PJ, Wright CW (2008) Antiplasmodial compounds from *Cassia siamea* stem bark extract. Phytother Res 22:254–255

Akinwumi KO, Oladapo O, Okware CE, Ifie CC, Fasure KA (2005) Screening of crude extracts of six medicinal plants used in South-West Nigerian unorthodox medicine for anti-methicillin resistant *Staphylococcus aureus* activity. BMC Complement Altern Med 5:6–12

Bag A, Bhattacharyya SK, Bharati P, Pal NK, Chattopadhyay RR (2009) Evaluation of antibacterial properties of Chebulic myrobalan (fruit of *Terminalia chebula* Retz.) extracts against methicillin resistant *Staphylococcus aureus* and trimethoprim-sulphamethoxazole resistant urapathogenic *Escherichia coli*. Afr J Plant Sci 3:25–29

Banzouzi JT, Soh PN, Mbatchi B, Caven A, Ramos S, Retailleau P, Rakotomandrahana O, Berry A, Benoît-Vical F (2008) Cogniauxia podolaena: bioassay-guided fractionation of defoliated stems, isolation of active compounds, antiplasmodial activity and cytotoxicity. Planta Med 74:1453–1456

Baraza LD, Joseph CC, Munis JJE, Nkunya MHH, Arnold N, Porzel A, Wessjohann L (2006) Antifungal rosane diterpenes and other constituents of *Hugonia castaneifolia*. Phytochemistry 69:200–205
Barku VYA, Opeko-Boahen Y, Dzotsi EY (2012) Isolation and pharmacological activities of alkaloids from Cryptolepis san-guinaolenta (Lindl) schlt. Int Res J Biochem Bioinform 2:58–61
Basu S, Ghosh A, Hazra B (2005) Evaluation of the antibacterial activity of Ventilago Madraspatana Gaertn., Rubia cordifolia Linn. and Lantana camara Linn.: isolation of emodin and physcion as active antibacterial agents. Phytother Res 19:888–894
Becker JVW, Van der Merwe M, Van Brummelen AC, Pillay P, Crampton BG, Mmutlane EM, Parkinson C, Van Heerden FR, Crouch NR, Smith PJ, Mancama DT, Maharaj VJ (2011) In vitro anti-plasmodial activity of Dicoma anomala subsp. gerrardii (Asteraceae): identification of its main active constituent, structure-activity relationship studies and gene expression profiling, Malar J 10:295
Bickii J, Tchouya GR, Tchouanque JC, Tamo E (2007) The pharmacological activities of alkaloids from Lantana camara Linn. and activity of Ventilago madraspatana Linn.: isolation of emodin and physcion as active antibacterial agents. Phytother Res 23:1326–1331
Birdbi T, D’Souza D, Tolani M, Dassani P, Heerden FR, Crouch NR, Smith PJ, Mancama DT, Maharaj VJ (2011) In vitro anti-plasmodial activity of Dicoma anomala subsp. gerrardii (Asteraceae): identification of its main active constituent, structure-activity relationship studies and gene expression profiling, Malar J 10:295
Birdi T, D’Souza D, Tolani M, Daswani P, Vaghasiya Y, Patel H (2010) Global resistance topics in applied microbiology and microbial biotechnology. Mendez-Vilas A (ed) Current research, technology, and educational odyssey. J Ethnopharmacol 51:29–38
Beck J, Tchouya GR, Tchouanque JC, Tamo E (2007) The pharmacological activities of alkaloids from Lantana camara Linn. and activity of Ventilago madraspatana Linn.: isolation of emodin and physcion as active antibacterial agents. Phytother Res 23:1326–1331
Cao MR, Tits M, Angenot LM, Frédéric M (2011) 17α-hydroxycorynantheol, a selective antiplasmodial alkaloid isolated from Sophora flavescens. Planta Med 77:2050–2053
Chambers HF (2001) The changing epidemiology of Staphylococcus aureus. Emerg Infect Dis 7:178–182
Chan BC, Ip M, Lau CB, Lui SL, Jalovilat C, Ganem-Elbaz C, Itaoudon M, Reiner NE, Gong H, See RH, Fung KP, Leung PC (2011) Synergistic effects of baicalein with ciprofloxacin against Nor A over-expressed methicillin-resistant Staphylococcus aureus (MRSA) and inhibition of MRSA pyruvate kinase. J Ethnopharmacol 137:767–773
Chanda S, Vyas BRM, Vaghasiya Y, Patel H (2010) Global resistance trends and the potential impact of methicillin resistant Staphylococcus aureus (MRSA) and its solutions, 2nd Series. In: Mendez-Vilas A (ed) Current research, technology, and education topics in applied microbiology and microbial biotechnology. Formatex, Spain, pp 529–536
Cheplologi PK, Mulholland DA, Coombes PH, Randianarivoelosia M (2008) An azole, an amide and a limonoid from Vepris uguensis (Rutaceae). Phytochemistry 69:1384–1388
Chakwujekwu JC, Smith P, Coombes PH, Mulholland DA, Van Staden J (2005) Antiplasmodial diterpenoid from the leaves of Hyptis suaveolens. J Ethnopharmacol 102:295–297
Cowan MM (1999) Plant products as antimicrobial agents. Clin Microbiol Rev 12:564–582
Crandall PG, Riche SC, O’Brian CA, Parrish NM (2012) In vitro effects of citrus oils against Mycobacterium tuberculosis and non-tuberculous Mycobacteria of clinical importance. J Environ Sci Health B 47:736–741
Davies J, Davies D (2010) Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev 74:417–433
Deresinski S (2005) Methicillin-resistant Staphylococcus aureus: an evolutionary, epidemiologic, and therapeutic odyssey. Clin Infect Dis 40:562–573
Dey D, Ray R, Hazra B (2014) Antibacterial and antibacterial activity of quinonoid natural products against multi-drug resistant clinical isolates. Phytother Res 28:1014–1021
Dey D, Ray R, Hazra B (2015) Antimicrobial activity of pomegranate fruit constituents against drug-resistant Mycobacterium tuberculosis and β-lactamase producing Klebsiella pneumoniae. Pharm Biol 53:1474–1480
Dini C, Fabbrini A, Geraci A (2011) The potential role of garlic (Allium sativum) against the multi-drug resistant tuberculosis pandemic: a review. Annali dell’Istituto Superiore di Sanita 47:465–473
Dixon RA (2001) Natural products and plant disease resistance. Nature 411:843–847
Dubey D, Padhy RN (2013) Antimicrobial activity of Lantana camara L., against multidrug resistant pathogens from ICU patients of a teaching hospital. J Herb Med 3:65–75
Dubey D, Sahu MC, Rath S, Paty BP, Debata NK, Padhy RN (2012) Antimicrobial activity of medicinal plants used by aborigines of Kalahandi, Orissa, India against multidrug resistant bacteria. Asian Pac J Trop Biomed 2:5846–5854
Efange SMN, Brun R, Wittlin S, Connolly JD, Hoye TR, Makolo FL, Mbah JA, Nelson DP, Nyongbela KD, Wirmuk C (2009) Okundoperoxide, a bicyclic cyclofarnesylsesquiterpene endoperoxide from Scleria stratioux with antiplasmodial activity. J Nat Prod 72:280–283
Elffter T, Koch E (2011) Complex interactions between photochemic- cals. The multi-target therapeutic concept of phytotherapy. Curr Drug Targets 12:122–132
Fridkin SK, Hageman JC, Morrison M, Sanza LT, Como-Sabetti K, Jernigan JA, Harriman K, Harrison LH, Lynfield RM, Farley M (2005) Methicillin-resistant Staphylococcus aureus disease in three communities. N Engl J Med 352:1436–1444
Gade ND, Qazi MS (2013) Fluoroquinolone therapy in Staphylococ- cus aureus infections: where do we stand? J Lab Physicians 5:109–112
Gandhi NR, Moll A, Sturm AW, Pawiinski R, Govender T, Laloo U, Zeller K, Andrews J, Friedland G (2006) Extensively drug resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. Lancet Infect Dis 6:1575–1580
Gafon H, Bero J, Tchinda AT, Gbaguidi F, Gbenou J, Moudachiou M, Frédéric M, Quetin-Leclercq J (2012) Antiparasitic activities of two sesquiterpenic lactones isolated from Callistemon rigidus DC. J Ethnopharmacol 141:411–417
Giang PM, Son PT, Matsunami K, Otsuka H (2006) Anti-staphylo- coccal activity of sophoraflavanone G isolated from the roots of Sophora flavescens against methicillin-resistant Staphylococcus aureus. Phytother Res 20:1326–1331
Goknar Z, Bagazra O, Pace DG (2014) Bacteriophage therapy: a potential solution for the antibiotic resistance crisis. J Infect Dev Ctries 8:129–136
Gomber C, Saxena S (2007) Anti-staphylococcal potential of Callistemon rigidus. Central Eur J Med 2:79–88
Gould SWJ, Fielder MD, Kelly AF, Naughton DP (2009) Anti- microbial activities of pomegranate rind extracts: enhancement by cupric sulphate against clinical isolates of S. aureus, MRSA
and PVL positive CA-MSSA. BMC Complement Altern Med 9:23–28

Gupta R, Thakur B, Singh P, Singh HB, Sharma VM, Katoch VM, Chauhan SV (2010) Anti-tuberculosis activity of selected medicinal plants against multi-drug resistant Mycobacterium tuberculosis isolates. Indian J Med Res 131:809–813

Gupta S, Dwivedi GR, Darokar MP, Srivastava SK (2012) Anti-typhoidal activity of fractions and isolated compounds from Vernonia galensis flowers growing in Tunisia. World J Microbiol Biotechnol 28:2933–2940

Houghton PJ (2001) Old yet new—properties of products from plants. J Chem Educ 78:175–184

Jang WS, Jyoti MA, Kim S, Nam KH, Ha TK, Oh WK, Song HY (2016) In vitro antituberculosis activity of diterpenoids from the Ethiopian medicinal plant Croton tonkinensis. J Nat Med 70:127–132

Jansen O, Tits M, Angenot L, Nicolas JP, De Mol P, Nikiema JB, Jang WS, Jyoti MA, Kim S, Nam KW, Ha TK, Oh WK, Song HY (2001) Old yet new—pharmaceuticals from plants. Lancet Infect Dis 1:47–58

Kenmogne M, Prost E, Harakat D, Jacquier MJ, Frederich M, Kim ES, Jeong SI, Kim JH, Park C, Kim SM, Kim JK, Lee KM, Lee SH, So H, Park SH, Jeong SI, Kim JH (2010) Antibacterial and synergistic activity of prenylated chalcone isolated from the roots of Sophora flavescens. Arch Pharm Res 33:962–967

Khan Z, Anees M, Adnan M (2015) Anti-infective activity of Alkanna tinctoria leaves. Exell Arkivoc 9:129–134

Korhonen M (2013) A review of the use of medicinal plants in the treatment of multidrug-resistant Staphylococcus aureus. Phytother Res 27:821–829

Kiehl L, Beier S, Wimsatt WC (1996) A meta-analytical study of the efficacy of supervised home-based antibiotic therapy against resistant Gram-negative blood cultures positive for vancomycin-resistant Enterococcus. J Infect Dis 173:230–236

Kiplimo JJ (2012) The phytochemical and biological activity of Alkanna tinctoria (Asteraceae) and identification of urospermal A-15-O- beta-D-glucopyranoside isolated from the seed of Vernonia galensis. J Nat Prod 75:1576–1581

Koch TCEFA, Orjala J, Mutiso PC, Soejarto DD (2006) An antimarial abietane diterpene from Fuersia africana. Biochem Syst Ecol 34:270–272

Kumar P, Singh A, Sharma U, Singh D, Dobbal MP, Singh S (2013) Anti-mycobacterial activity of plumericin and isoplumericin against MDR Mycobacterium tuberculosis. Palm Pharmacol Ther 2:332–335

Kuwahara H, Douda Y, Hoshino S, Goto M, Mundysoor A, Hoffner S, Kumar RA (2011) Ethyl p-methoxycinnamate isolated from a traditional anti-tuberculosis medicinal herb inhibits drug-resistant strains of Mycobacterium tuberculosis in vitro. J Med Microbiol 60:127–132

Lahmou M (2013) The success of natural products in drug discovery. Pharmcol Pharm 4:17–31

Lakshmanan D, Werngren J, Jose L, Suja K, Nair MS, Varma RL, Mondayoor A, Hoffner S, Kumar RA (2011) Ethyl p-methoxycinnamate isolated from a traditional anti-tuberculosis medicinal herb inhibits drug-resistant strains of Mycobacterium tuberculosis in vitro. J Med Microbiol 60:127–132

Laxminarayan R, Malani A (2007) Extending the cure: policy responses to the growing threat of antibiotic resistance. Resources for the Future, Washington, DC, p c2007

Leandro LF, Cardoso MJ, Silva SD, Souza MG, Veneziani RC, Ambrosio SR, Martins CH (2014) Antibacterial activity of Pseudomonas aeruginosa. Mayo Clin Proc 86:250–259

Lenta BN, Devkota PK, Wansi JD, Chouna JR, Soh RC, Neumann B, Stammers HG, Tsemo E, Rosenthal PJ, Sewald N (2008) Anti-plasmodial and cholinesterase inhibiting activities of some constituents of Psorospermum glaberrimum. Chem Pharm Bull 56:222–226

Lenta BN, Tantamgo D, Devkota KP, Wansi JD, Chouna JR, Soh RC, Neumann B, Stammers HG, Tsemo E, Sewald N (2009) Bioactive constituents of the stem bark of Beilschmiedia zenkeri. J Nat Prod 72:2130–2134

Leon-Diaz R, Meckes-Fischer M, Valdivinos-Martinez L, Campos MG, Hernandez-Pando R, Jimenez-Arellanes MA (2013) Antitubercular activity and the subacute toxicity of (-)-Limarin A in BALB/c mice: a neoglucosan isolated from Aristolochia taliscana. Arch Med Res 44:99–104

Linden PK (2002) Treatment options for vancomycin-resistant enterococcal infections. Drugs 62:425–441

Lu J, Qin R, Ye S, Yang M (2011) Prunella vulgaris L. extract improves cellular immunity in MDR-TB challenged rats. J Med Coll PLA 26:230–237

Mahmout Y, Mianpeurrem T, Dolmazon R, Bouchu D, Fenet B (2008) 15ème colloque sur la Pharmacopée et la Médecine Traditionnelles Africaines. Conseil Africain et Malgache pour l’Enseignement Supérieur (CAMES) 1, Libreville

Malve H (2016) Exploring the ocean for new drug developments: marine pharmacology. J Pharm Bioallied Sci 8:83–91
Oleae europaea (olive) leaf extract. Int J Antimicrob Agents 33:461–463

Sureram S, Senadeera SP, Hongmane P, Mahidol C, Ruchirawat S, Kittakaop P (2012) Antimycobacterial activity of bisbenzylisoquinoline alkaloids from Tillicora triandra against multidrug-resistant isolates of Mycobacterium tuberculosis. Bioorg Med Chem Lett 22:2902–2905

Talontsi FM, Lamshöft M, Bauer JO, Razakarivony AA, Andriamihaja B, Strohmann C, Spiteller M (2013) Antibacterial and antiplasmodial constituents of Beilschmiedia cryptoparadoxa. J Nat Prod 76:97–102

Tanaka M, Wang T, Onodera Y, Uchida Y, Sato K (2000) Mechanism of quinolone resistance in Staphylococcus aureus. J Infect Chemother 6:131–139

Tchinda AT, Fuendjiep V, Sajjad A, Matchawe C, Wafo P, Khan S, Tane P, Choudhary MI (2009) Bioactive compounds from the fruits of Zanthoxylum leprieurii. Pharmacol Online 1:406–415

Thiem DA, Sneden AT, Khan SI, Tekwani LB (2005) Bisnortriterpenes from Salacia madagascariensis. J Nat Prod 68:251–254

Thomson WAR (1978) Medicines from the Earth. McGraw-Hill Book Co., Maidenhead

Tiwari HK, Das AK, Sapkota D, Sivarajan K, Palha VK (2009) Methicillin resistant Staphylococcus aureus: prevalence and antibiogram in a tertiary care hospital in western Nepal. J Infect Dev Ctries 3:681–684

Torres-Romero D, Jimenez IA, Rojas R, Gilman RH, Lopez M, Bazzocchi IL (2011) Dihydro-Beta-Agarofuran sesquiterpenes isolated from Celastus vulcanicola as potential anti-Mycobacterium tuberculosis multidrug-resistant agents. Bioorg Med Chem Lett 19:2182–2189

Uc-Cachon AH, Borges-Argaz R, Said-Fernandez S, Vargas-Villarreal J, Gonzalez-Salazar F, Méndez-González M, Cárceces-Farfán M, Molina-Salinas GM (2014) Naphthoquinones isolated from Diospyros anisandra exhibit potent activity against pan-resistant first-line drugs Mycobacterium tuberculosis strains. Pulm Pharmacol Ther 27:114–120

van Vuuren S, Viljoen A (2011) Plant-based antimicrobial studies—methods and approaches to study the interaction between natural products. Planta Med 77:1168–1182

Van Zyla RL, Khanb F, Edwardsc TJ, Drewesc SE (2008) Antiplasmodial activities of some abietane diterpenes from the leaves of five Plectranthus species. S Afr J Sci 104:62–65

Ventola CL (2015) The antibiotic resistance crisis. Part 1: causes and threats. P T 40:277–283

Viehn MA, Nguyen MH, Doi Y (2014) Treatment options for carbapenem-resistant and extensively drug-resistant Acinetobacter baumannii infections. Drugs 74:1315–1333

Vogel G (2010) Infectious disease—new map illustrates risk from the other malaria. Science 329:618

Wabo HK, Tane P, Connolly JD (2006) Diterpenoids and sesquiterpenoids from Aframomum arundinaceum. Biochem Syst Ecol 34:603–605

Waffo AFK, Coombs PH, Crouch NR, Mulholland DA, El Amin SMM, Smith PJ (2007) Acridone and furoquinoline alkaloids from Telea serrata (Rutaceae: Toddaliaioideae) of southern Africa. Phytochemistry 68:663–667

White NJ (2004) Antimalarial drug resistance. J Clin Invest 113:1084–1092

Wieczorek K, Osek J (2013) Antimicrobial resistance mechanisms among Campylobacter. Biomed Res Int 2013:340605

World Health Organization (2008) World Malaria Report. WHO, Geneva

World Health Organization (2012) World Malaria Report. WHO, Geneva

World Health Organization (2014) Organization WH Global Tuberculosis Report, Geneva

Wube AA, Bucar F, Gibbons S, Asres K, Rattray L, Croft SL (2010) Antiprotozoal activity of drimane and coloratane sesquiterpenes towards Trypanosoma brucei rhodesiens and Plasmodium falciparum in vitro. Phytother Res 24:1468–1472

Zager EM, McNerney R (2008) Multidrug-resistant tuberculosis. BMC Infect Dis 8:10

Zampini IC, Cuello S, Alberto MR, Ordonez RM, Almeida RD, Solorzano E, Isla MI (2009) Antimicrobial activity of selected plant species from “the Argentine Puna” against sensitive and multi-resistant bacteria. J Ethnopharmacol 124:499–505

Zhang L, Li R, Li M, Qi Z, Tian J (2015) In vitro and In vivo study of anti-tuberculosis effect of extracts isolated from Rumunculi ternati radial. Sarcoidosis vasculitis and diffuse lung diseases. Off J WASOG 31:336–342

Zignol M, Hosseini MS, Wright A, Lambregts-van Wezenbeek C, Nunn P, Watt CJ, Williams BG, Dye C (2006) Global incidence of multidrug-resistant tuberculosis. J Infect Dis 194:479–485

Zofou D, Kowa TK, Wabo HK, Ngemenya MN, Tane P, Titanji VPK (2011) Hypericum lanceolatum (Hypericaceae) as a potential source of new anti-malarial agents: a bioassay-guided fractionation of the stem bark. Malar J 10:167

Zofou D, Tene M, Tane P, Titanji VPK (2012) Antimalarial drug interactions of compounds isolated from Kigelia africana (Bignoniaceae) and their synergy with artemether, against the multidrug-resistant W2met Plasmodium falciparum strain. Parasitol Res 110:539–544