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Commentary

Shadowed by Giants: Desert Plants Versus Rainforest Plants as Targets for Novel Antibacterial Drug Discovery

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ABSTRACT

The escalating global crisis of bacterial resistance to antibiotics poses a threat to public health. Urgent measures are required to identify novel antibacterial treatments. Multidrug-resistant bacterial strains limit the effective therapeutic options available, raising concerns about a post-antibiotic era and a reduced ability to treat infections that were previously not classified as serious. Simultaneously, the threat of emerging infectious diseases, including zoonotic pathogens, underscores the need to develop effective antibiotics against these pathogens. Innovative approaches to antibiotic development, such as novel chemical scaffolds, combination therapies, antimicrobial peptides, and phage therapy, show promise but require the discovery of new antibacterial compounds. Desert and rainforest ecosystems, despite being disparate in climate and biodiversity, offer unique prospects for developing antibacterial compounds. Deserts, which are characterized by extreme aridity and temperature fluctuations, harbor plants and micro-organisms with specialized antibacterial defences honed through evolution. Conversely, rainforests, with their biodiversity and high humidity, are promising for the development of potential antibacterial compounds. To date, much natural product research aimed at discovery of new antibiotic compounds has focussed on rainforest plants due to the biodiversity of these ecosystems, and because plants develop chemical defences against microbes that are prevalent in those environments. In comparison, the search for new antimicrobial compounds from desert plants has been overshadowed, despite some noteworthy antibacterial activities in arid environment plants. This commentary discusses the comparative potential of desert and rainforest ecosystems as reservoirs of novel antibacterial agents and emphasises the importance of screening plants in both environments.

Keywords: Antibiotic resistance, Biodiversity, Traditional medicine, Bioprospecting, Ethnobotany, Natural medicine.

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INTRODUCTION

The emergence and spread of antibiotic resistance among bacterial pathogens has created a formidable challenge for global healthcare systems. Antibiotic-resistant infections not only increase morbidity and mortality rates, but also strain healthcare resources and increase treatment costs.[1] Furthermore, the alarming rise in multidrug-resistant bacterial strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant *Enterobacteriaceae* (CRE),[1,2] has left clinicians with limited therapeutic options, threatening to usher in a post-antibiotic era where even common infections may become untreatable.

The global community faces the persistent threat of emerging infectious diseases. Zoonotic pathogens including *Bacillus anthracis*, Ebola virus, *Mycobacterium tuberculosis*, *Yersinia pestis* (plague), Middle east respiratory syndrome corona virus (MERS-CoV), and the novel SARS-CoV-2 have demonstrated the potential to spark pandemics, with devastating consequences.[3] The rapid transmission of bacterial pathogens highlights the urgent need for new antibiotics that can effectively combat emerging infectious diseases. Innovative approaches to the development of new antibiotics, including the identification of new chemical scaffolds, the development of combination therapies, harnessing the potential of antimicrobial peptides, and the use of phage therapy offers potential solutions to combat antibiotic resistance. However, most of these strategies still rely on the identification of novel chemical entities with antibacterial properties and substantially more work is required in this field to ensure an adequate antibiotic pipeline is maintained. By expanding our arsenal of effective antibiotics, we can bolster our defences against resistant pathogens and emerging diseases,

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ultimately safeguarding public health and preserving the effectiveness of this life-saving class of drugs for generations to come. Thus, the discovery of new antibiotics remains not only a scientific imperative, but also a critical public health necessity in our ongoing battle against microbial threats.

The search for novel antibacterial treatments has led researchers to explore a wide range of natural sources, including plants from diverse ecosystems, to uncover novel microbial resistance-fighting compounds. Among the ecosystems that have garnered significant attention are deserts and rainforests.[4-6] These environments, despite their extreme differences in climate and biodiversity, each offer unique potential for the discovery of antibacterial compounds. Deserts, which are characterized by their arid conditions and harsh climatic extremes, are paradoxically teeming with life adapted to survive in the harshest of environments. The adaptation strategies employed by desert plants often involve the production of unique chemical compounds to fend off microbial threats,[4,5] as water scarcity and extreme temperatures necessitate robust defence mechanisms. Researchers have identified a number of antibacterial molecules from desert flora, including cacti, succulents, and even from some strains of bacteria found in arid soils.[7-9] These compounds, honed by evolution, have potential to serve as a valuable resource for developing novel antibiotics.

Conversely, rainforests have a high biodiversity of luxuriant vegetation, existing in high temperature and humidity environments. Therefore, they offer a substantially different avenue for antibiotic discovery. Within the rich and complex ecosystems of tropical rainforests, countless plant species, fungi and microorganisms engage in intricate chemical warfare, competing for resources and survival. Many of these organisms have evolved potent antibacterial compounds as a means of gaining a competitive advantage in this biologically intense environment.[6] Researchers have uncovered an array of antibacterial agents sourced from plants, tree barks, and indigenous microorganisms from rainforests globally. These compounds often have unique chemical structures and may have significant potential for addressing antibiotic resistance by providing novel druggable targets.

Despite their contrasting ecological contexts, both deserts and rainforests are vast natural sources of potentially novel antibacterial agents. Examining these ecosystems by screening their plants for antibacterial activity and isolating bioactive compounds may help address the global challenge of antibiotic resistance by identifying compounds with novel antibacterial mechanisms, which may allow them to effectively combat bacteria that are resistant to other antibiotics. This commentary aims to explore and provide insights on multiple facets concerning the utilization of desert plants in comparison to rainforest plants in the search for novel antibacterial treatments.

MATERIALS AND METHODS

The information documented in this study was obtained from peer-reviewed original research studies, reviews and books. Google Scholar, PubMed, Scopus and ScienceDirect online databases were searched using the following keywords: "rainforest", "wetland", "desert", "arid", "semi-arid", "medicinal plant", "antibiotic compounds', "antibiotic resistance", and "antibacterial". Each keyword was searched alone and in combination with the other keywords. Only publications that met the following criteria were included in this study:

- Only English language studies published prior to October 2023 were included herein to avoid misinterpretation.
- Only plant species that are specifically recorded for the treatment of bacterial infections (or those that have been studied for anti-bacterial activities) are included in this review.
- This study is not intended to be a comprehensive listing of plants in rainforests or desert ecosystems. Instead, the study was biased towards Australian plant species, particularly with regards to the rainforest plants, as a large number of plants from these environments have been documented. However, several well known plants of international origin were also included as examples.
- The study is otherwise non-biased with regards to ethnobotany. Additionally, the study had no taxonomic preferences.
- Plant species and family names were verified and updated using The WFO Plant List (https://wfoplantlist.org/plant-list).

RESULTS AND DISCUSSION

Biodiversity and potential

Rainforests: A treasure trove of diversity

Rainforests have rich biodiversities, containing an estimated 80% of the world's terrestrial species.[10] This incredible variety extends to plant life, with thousands of plant species co-existing in rainforest environments. The vast reservoir of botanical species harboured within rainforests increases the likelihood of discovering novel antibacterial compounds with the potential to combat antibiotic-resistant pathogens. The rich diversity of chemical compounds found in these plants (many of which have not been fully explored) increases the chances of identifying effective antibacterial agents. Thus, the diversity of rainforest plants provides a valuable resource in the quest for innovative antimicrobial agents. Additionally, as rainforest plants live in environments rich in microbial pathogens and foraging animals, they have developed phytochemical defences, and these phytochemicals may have potential for the development as antibiotic chemotherapies. Some noteworthy rainforest plant species with antibacterial activity are summarised in Table 1. Due to the high number of rainforest plants worldwide with

antibiotic activity, we have limited the discussion herein to focus on Australian rainforest plants, although a limited number of noteworthy species from other regions are also included.

Research efforts across Africa, the Americas, Asia, and Oceania have uncovered a diverse array of rainforest plants with promising medicinal properties. *Piper nigrum* L. (commonly known as black pepper), is a rainforest plant with antibacterial activity that has been verified through scientific investigation. Its antibacterial potential has been reported against multiple bacterial strains, including *Staphylococcus aureus, Escherichia coli*, and *Salmonella* spp.[11-13] The antibacterial attributes of black pepper are predominantly due to its alkaloid compounds, particularly piperine (Figure 1a) and piperlongumine (Figure 1b), which exert inhibitory effects on bacterial growth by interfering with essential cellular processes.[14,15] Notably, piperine has demonstrated robust antibacterial activity against diverse bacterial strains.[15,16]

In the Americas, the Amazon rainforest has been a focal point for research into medicinal plants, with studies into multiple plant species published, including *Cinchona officinalis* L. (cinchona tree), identifying the compound quinine (Figure 1c) as a potent antimalarial agent.[17,18] Notably, quinine also has antibacterial activity against multiple bacteria.[19] Asian rainforests have also yielded a rich pharmacopeia, with the discovery of compounds including camptothecin (Figure 1d) from *Camptotheca acuminata* Decne. (Chinese Happy Tree), which has antibacterial activity against *S. aureus, E. coli, P. aeruginosa* and *H. pylori*.[20] *Schinus molle* L. (Brazilian pepper tree), originates from wet coastal regions of the Americas. It produces relatively high levels of the compounds polygodial (Figure 1e) and drimanial (Figure 1f), which have verified antibacterial properties.[21-23] These compounds are currently under investigation for their potential pharmaceutical applications.

The forests of Oceania have also revealed numerous drug leads, including those derived from *Melaleuca alternifolia* (Maided and Betche) Cheel (Australian tea tree).[13,24] The primary active compound responsible for its antibacterial effects has been identified as terpinen-4-ol (Figure 1g). Tea tree oil is commonly used topically for its antibacterial, antifungal, and antiviral properties.[13] Similarly, *Leptospermum scoparium* J.R/Frost and G.Frost. (commonly known as Manuka, New Zealand tea-tree, broom tea-tree), is a tree that is native to the east coast rainforest regions of Australia, and to New Zealand. This species is known for its antibacterial properties.[25,26] Manuka honey, derived from the nectar of the Manuka tree's flowers, contains a unique compound called methylglyoxal (MGO), which is responsible for its strong antibacterial activity.[27] Manuka honey is used for wound healing and has been studied for its effectiveness against antibiotic-resistant bacteria.[28]

Several Asian rainforest plant species are also used for their antibacterial activity. *Azadirachta indica* A. Juss. (commonly known as neem) is native to South Asia, where it is found in coastal rainforest regions. Neem oil and neem extracts are used in traditional medicine for their antibacterial and antifungal effects,[29,30] which have been linked with the compounds azadirachtin (Figure 1h), nimbin (Figure 1i), and nimbidin (Figure 1j).[31] Similarly, *Curcuma longa* L. (commonly known as turmeric) is a South Asian plant that grows in high rainfall coastal areas. It is well-known for its antibacterial and anti-inflammatory properties.[32,33] Indeed, it is effective against multiple bacteria, including *Staphylococcus aureus* and *Escherichia coli*. These studies collectively highlight the therapeutic potential of rainforest plants and the critical importance of preserving these ecosystems for future drug discovery efforts.

The biodiversity of plant species within rainforests provides an interesting prospect for the discovery of novel antibacterial compounds. The sheer abundance of plant species in these environments amplifies the likelihood of encountering novel chemical entities with potent antibacterial properties. Importantly, a substantial portion of these chemical compounds remain unexplored, representing untapped potential for the identification of efficacious antibacterial agents. Furthermore, the intricate web of ecological relationships within rainforests has fostered the evolution of distinctive chemical defences among plants, potentially representing valuable resources for addressing bacterial infections. These defences, honed over millennia of coexistence with diverse organisms, may hold the key to combating antibiotic-resistant pathogens. The convergence of

Table 1: Selected rainforest plants with antibacterial activity, with a focus on Australian species.

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Abrophyllum ornans Hook.f.	Rousseaceae	Native hydrangea	Subtropical rainforests of Australia. Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa*, and *E.coli* (MICs 156-624 µg/mL).	Not reported in that study.	34

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Acacia aulacocarpa A.Cunn. Ex Benth.	Fabaceae	Golden flowered salwood, New Guinea wattle	Collected from Paluma rainforest, Australia. Also found in Papua New Guinea.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa*, and *E.coli* (MICs 78-624 µg/mL).	Not reported in that study.	34
Acacia melanoxylon R.Br.	Fabaceae	Australian blackwood	Collected from Paluma rainforest, Australia. Also found in other parts of Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 78-624 µg/mL).	Not reported in that study.	34
Acronychia acronychioides (F.Muell.) T.G.Hartley	Rutaceae	White aspen	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Alphitonia whitei Braid	Rhamnaceae	Red ash, red almond, sarsaparilla	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 39-312 µg/mL).	Not reported in that study.	34
Apodytes brachystylis F.Muell.	Metteniusaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 156-1250 µg/ mL).	Not reported in that study.	34
Archidendron vaillantii F.Meull.	Fabaceae	Salmon bean	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 312-2500 µg/ mL).	Not reported in that study.	34
Azadirachta indica A.Juss.	Meliaceae	Neem, UIndian lilac	Native to South-East Asia.	Inhibits the growth of *E. coli, P. aeruginosa, S. aureus, S. typhi.*	Azadirachtin compounds.	29-31
Banksia integrifolia L.f.	Proteaceae	Coastal banksia	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 78-1250 µg/mL).	Not reported in that study.	34
Beilschmiedia obtusifolia F.Muell. Ex Meissner	Lauraceae	Bush walnut, hard bolly gum, nut wood	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 78-1250 µg/mL).	Not reported in that study.	34
Buckinghamia celsissima F.Muell.	Proteaceae	Ivory curl tree, spotted silky oak	Rainforest areas of Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa*, and *E. coli* (MICs 312-624 µg/mL).	Not reported in those studies.	34,36

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Camptotheca acuminata Decne	Nyssaceae	Happy tree, cancer tree, tree of life	Native to China and Tibet.	Inhibits *B. subtilis, S. aureus, S. epidermidis, E. coliu, P. vulgaris, P. aeruginosa*.	Pentacyclic triterpenoids.	20
Cardwellia sublimis F. Muell.	Proteaceae	Northern sliky oak, bull oak, lacewood	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 19-2500 µg/mL).	Not reported in that study.	34
Chinchona officinalis L.	Rubiaceae	Quinine tree, red chinchona	Native to rainforests in Colombia, Ecuador and Peru.	Used traditionally to treat malaria. Also inhibits *E. coli* and *S. aureus,* although with high MIC values (≥16 mg/mL).	Quinine	17,18
Copaifera langsdorfii Desf.	Fabaceae	Desert tree	South American tropical rainforest regions	Inhibits multiple bacteria, including *Streptococcus* spp. *L. casei* (MICs as low as 2 µg/mL).	Terpenoids	37,38
Croton insularis Baill.	Euphorbiaciae	Silver croton	Rainforest regions of eastern Australia. Also found in New Caledonia and Vanuatu.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Cryptocarya corrugata C.T.White and W.D.Francis	Lauraceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-1250 µg/mL).	Not reported in that study.	34
Cryptocarya putida B.Hyland	Lauraceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa*, and *E. coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Curcuma longa L.	Zingiberaceae	Turmeric	Native to hot, wet regions of South and South-East Asia.	Inhibits the growth of multiple bacterial pathogens, including antibiotic resistant strains.	Curcumin	32,33
Darlingia darlingiana (F.Muell.) L.A.S.Johnson	Protaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 39-312 µg/mL).	Not reported in that study.	34

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Denbrobium spp.	Orchidaceae	Varies across species	Found in diverse habitats across Asia, Australia, and the Pacific. Particularly prevalent in rainforests.	Endophytes associated with this genus inhibit multiple bacteria.	Polysaccharides.	39-41
Drypetes lasiogyna (Pax and K.Hoffm.) P.S.Green	Putranjivaceae	Grey bark	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 19-2500 µg/mL).	Not reported in that study.	34
Elaeocarpus arnhemicus Blume	Elaeocarpaceae	Blue plum, bony quandong	Rainforest areas of Australia and Indonesia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Elaeocarpus largiflorens C.T.White	Elaeocarpaceae	Tropical quandong	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Endiandra discolor Benth.	Lauraceae	Rose walnut, domatia tree	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 39-1250 µg/mL).	Not reported in that study.	34
Endiandra wolfei B.Hyland	Lauraceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Flindersia pimenteliana F.Muell.	Rutaceae	Maple silkwood, red beech, rose silkwood	Rainforest areas of Australia and Papua New Guinea.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 78-624 µg/mL).	Not reported in that study.	34
Glochidion hylandii Airy Shaw	Phyllanthaceae	Buttonwood, Hyland's buttonwood, pin flower tree	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 78-624 µg/mL).	Not reported in that study.	34
Handroanthus impetiginosa (Mart. Ex DC.); synonym *Tabebuia impetiginosa*	Bignoniaceae	Trumpet tree, Pau d'arco, lapacho	South American rainforests.	Inhibited *B. cereus* growth (MIC = 45 µg/mL). Also has noteworthy immunomodulatory and anti-inflammatory activity.	Flavonoids, quinones.	42,43

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Hedycarya loxocarya (Benth.) Francis	Lauraceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 78-624 µg/mL).	Not reported in that study.	34
Heptapleurum actinophyllum (Endl.) Lowry and G.M.Plunkett	Araliaceae	Australian umbrella tree	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 78-1250 µg/mL).	Not reported in that study.	34
Khaya senegalensis (Desr.) A.Juss.	Meliaceae	African mahogany, Khaya wood	Central African rainforest regions.	Inhibits P. mirabilis, K. pneumoniae, *A. baylyi, P aeruginosa* and *S. pyogenes* growth MICs 185->1000 µg/mL). Also inhibits Giardia duodenalis parasite growth (IC_{50} = 187 µg/mL).	Not reported in that study.	44
Leptospermum amboinense Blume	Myrtaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 312-624 µg/mL).	Not reported in that study.	34
Leptospermum scoparium J.R/ Frost and G.Frost.	Myrtaceae	Manuka	Rainforest and high rainfall regions of Eastern Australia and New Zealand.	Inhibits multiple bacteria including *L. monocytogenes, S. typhimurium, S. flexneri, S. sonnei, S. intermedius, S. aureus* (MICs in the low µg/mL range).	Methylgloxal, leptospermone.	25,26,28
Litsea australis B.Hyland	Lauraceae	Brown bollywood	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Lippia sidoides Cham.	Verbenaceae	Unknown	Rainforest regions of Brazil.	Inhibited *S. mutans, S. mitis, S. salivarius* and *S. sanguis,* although with relatively high MICs (5-10 mg/mL).	Caracol, thymol and other volatile compounds.	45,46
Macaranga subdentata Benth.	Euphorbiaciae	Needle bark	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs <1-1250 µg/mL).	Not reported in that study.	34
Macaranga tanarius (L.) Müll. Arg.	Euphorbiaciae	Parasol tree, bush macaranga, nasturtium tree	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-624 µg/mL).	Not reported in that study.	34

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Mackinlaya confusa Hemsl.	Apiaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa*, and *E. coli* (MICs 156-1250 µg/mL).	Not reported in that study.	34
Melaleuca alternifolia (Maiden and Betche) Cheel	Myrtaceae	Tea trees, paperbarks, honey myrtles	Australia and Oceania region.	Inhibits the growth of multiple species of bacteria.	Terpenoids.	13,24
Melicope broadbentiana F.M.Bailey	Rutaceae	False eudia	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 31-1250 µg/mL).	Not reported in that study.	34
Melicope vitiflora (F.Muell.) T.G.Hartley	Rutaceae	Northern evodia, fishpoison wood, leatherwood	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 78-625 µg/mL).	Not reported in that study.	34
Melodinus australis (F.Muell.) Pierre	Apocyanaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 78-625 µg/mL).	Not reported in that study.	34
Mischarytera lauteriana (F.M.Bailey)	Sapindaceae	Corduroy tamarind	North-east rainforest regions of Australia.	Inhibited the growth of *K. pneumoniae* and *B. cereus* (MICs 500-950 µg/mL).	Not reported in that study.	47
Mycaria cauliflora (Mart) O.Berg	Myrtaceae	Jaboticaba	Rainforest regions of South America and the Carribean.	Inhibited the growth of a panel of bacteria. MIC values were not reported.	Not reported in that study.	48
Neolitsea dealbata (R.Br.) Merr.	Lauraceae	Whire bolly gum	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 78-625 µg/mL).	Not reported in that study.	34
Omalanthus novo-guineensis (Warb.) K.Schum.	Euphorbiaciae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Parsonsia straminea (R.Br.) F.Muell.	Apocyanaceae	Common silkpod, monkey rope	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 312-1250 µg/mL).	Not reported in that study.	34

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Pilidiostigma tropicum L.S.Sm.	Myrtaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 19-312 µg/mL).	Not reported in that study.	34
Petalostigma pubescens Domin.	Picrodendraceae	Quinine bush	Rainforest regions of northern Australia and Papua New Guinea.	Inhibited the growth of *P. mirabilis, K. pneumoniae, A. baylyi, P. aeruginosa* and *S. pyogenes*, although the MIC values indicated low to moderate activity. The extracts potentiated the activity of conventional antibiotics substantially.	Not reported in that study.	49,50
Petalostigma triloculare Mull. Arg.	Picrodendraceae	Quinine bush	Rainforest regions of north-east Australia.	Inhibited the growth of *P. mirabilis, K. pneumoniae, A. baylyi, P. aeruginosa* and *S. pyogenes,* although the MIC values indicated low to moderate activity. The extracts potentiated the activity of conventional antibiotics substantially.	Not reported in that study.	49,50
Piper spp.	Piperaceae	Multiple species, collectively known as pepper plants or pepper vines	Globally, in tropical forests and rainforests.	Inhibits the growth of multiple species of bacteria.	Terpenoids, flavonoids.	11,12,51
Planchonella australis (R.Br.) Pierre	Sapotaceae	Black apple, yellow buttonwood, black plum	Rainforest along the east coast of Australia.	Inhibited a wide panel of bacteria although MIC values were not reported.	Not reported in that study.	52
Podocarpus grayae de Laub.	Podocarpaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 39-624 µg/mL).	Not reported in that study.	34
Polyscias ustraliana (F.Muell.) Philipson	Araliaceae	Unknown	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E. coli* (MICs 156-2500 µg/mL).	Not reported in that study.	34
Schinus molle L.	Anacardiaceae	Peruvian pepper	Native to wet regions of the Peruvian Andes and Southern Brazil.	Inhibits multiple bacteria including *E. coli,* and *B. cereus*, with MICs as low as 30 µg/mL.	Multiple terpenoids, including limonene, cymene, polygodial and drimanial.	21-23

Plant Species	Family	Common/ Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Schizomera ovata D.Don	Cunoniaceae	Australian white birch, crab apple, white cherry, snowberry, humbug, squeaker	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 19-624 µg/mL).	Not reported in that study.	34
Syncarpia glomulifera (Sm.) Nied.	Myrtaceae	Turpentine tree, yanderra	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa,* and *E.coli* (MICs 2-624 µg/mL).	Not reported in that study.	34
Syzygium spp.	Myrtaceae	Multiple names for different species	Tropical and subtropica regions (including rainforests) globally.	Inhibited multiple bacteria, with low MIC values.	Polyphenolics, tepenoids, flavanoids.	34,53-57
Terminalia ferdinandiana Exell.	Combretaceae	Kakadu plum, gubinge, billy goat plum	Native to "dry rainforests" (high rainfall regions with distinct wet and dry seasons) of Northern and North-West Australia.	Inhibits a wide range of bacteria, with low MIC values.	A diversity of tannins, flavonoids, terpenoids.	58-62
Tinospora cordifolia (Willd.) Miers ex Hook F. and Thoms.	Menispermaceae	Heart-leaved monsoon, gurjo or giloy	Indigenous to tropical rainforest regions of the Indian subcontinent.	Inhibits *P. aeruginosa* (MIC ~4mg/mL).	Berberine	35
Uncaria tomentosa (Willd. Ex. Schult.) DC.	Rubiaceae	Cat's claw	Rainforest regions of South and Central America.	Inhibits a broad-spectrum of bacteria including *S. mutans, Staphylococcus* spp., *P. aeruginosa*.	Polyphenolics, alkaloids, flavonoids, terpenoids.	63,64
Xanthophyllum fragrans C.T.White	Polygalaceae	Fragrant boxwood	North-eastern Australia.	Inhibits P. aeruginosa growth (MIC 1000-2500 µg/mL).	Tannins, including gallic acid and procatocatechuic acid.	65
Xanthophyllum octandrum (F.Nmuell.) Karel Domin	Polygalaceae	Macintyre's boxwood, false jitta, yellow boxwood	Collected from Paluma rainforest, Australia.	Inhibited the growth of *B. cereus, S. aureus, S. pneumoniae, P. aeruginosa*, and *E. coli* (MICs 39-624 µg/mL).	Not reported in that study.	34

biodiversity and chemical complexity in rainforest plant species highlights the potential of these ecosystems for developing innovative solutions to address the global challenge of bacterial antibiotic resistance.

This study is biased towards Australian plant species as a large number of plants from rainforest environments have been documented globally. Several well-known plants of international origin were also included.

Desert plants

Survivors with therapeutic potential

In stark contrast to rainforests, desert ecosystems are characterized by extreme aridity, low precipitation, and harsh conditions. Desert plants have evolved adaptive strategies to thrive in these challenging environments and to protect themselves from pathogens and foraging animals. These strategies include water conservation mechanisms, tolerance of high temperatures, inhibition of microbial growth, and deterrence of herbivores. Water conservation features, such as succulence and reduced leaf surface area allow desert plants to endure drought periods and reduce the risk of pathogen infections. Additionally, desert plants often have resilient cuticles and leaf structures to minimize transpiration and protect against desiccation, as well as further hindering microbial growth. Some desert plants also produce secondary metabolites with potential antimicrobial properties (summarised in Table 2). Furthermore, physical defences such as thorns and spines deter herbivores, minimizing the risk of pathogen entry.

Recent studies have explored the potential of desert plants from Africa, the American, Asia, the Middle East, and the Oceania region (summarised in Table 2). Studies conducted on desert flora within these distinct geographical regions have highlighted their adaption mechanisms, leading to the synthesis of unique chemical compounds with substantial bioactive potential. For example, species of the genera *Eremophila, Commiphora*, and *Pittosporum* spp. have attracted considerable attention due to their antibacterial properties. *Eremophila duttonii* F. Muell. (and other species of this genus) has been explored for its antibacterial activity, which has been linked to phenolic glycosides and terpenoids.[4,66-68] *Commiphora* spp., including *Commiphora molmol* (Nees) Engl., also inhibit the growth of multiple bacteria.[74,80] Additionally, the Australian species *Pittosporum angustifolium*, inhibits the growth of multiple bacteria, possibly due to its secondary metabolites, including alkaloids and flavonoids.[69,70] *Opuntia* spp. (exemplified by the prickly pear cactus), are indigenous to arid and semi-arid regions across the Americas. These species may also have antibacterial activity, although this remains to be rigorously studied. Similarly, the arid and semi-arid ecosystems of Oceania have a diversity of endemic species with antibacterial potential. *Melaleuca alternifolia* (commonly known as tea tree), has received substantial attention due its ethnobotanical uses, and studies have verified its antimicrobial properties.[13,24] Interestingly, this species has a wide distribution, and also grows in high rainfall areas, as well as in semi-arid environments.

The genus *Aloe* consists of a diversity of plant species, many of which have been used in traditional healing systems for a range of therapeutic effects, including antibacterial activities.[71] For this reason, *Aloe* spp., have been the focus of numerous investigations into their antimicrobial properties. Several species (particularly *Aloe vera, Aloe ferox* and *Aloe arborescens*) have demonstrated the ability to combat a broad spectrum of pathogens, including bacteria, fungi, and viruses.[9] The antimicrobial properties of *Aloe* spp. are attributed to the presence of multiple bioactive compounds including aloin (Figure 1k) and aloe-emodin (Figure 1l), which have significant antimicrobial activity.[9]

Similarly, *Boswellia* species, renowned for their gum resin, are also a promising source of natural antimicrobial agents. The resin obtained from *Boswellia* spp. trees (generally referred to as frankincense) possesses compounds with antibacterial and antifungal properties.[71-74] The South Asian species *Boswellia serrata* Roxb. and the Omani/Arabian species *Boswellia sacra* Flueck. have been most extensively investigated for their antimicrobial potential.[71,72] and substantially more work is required to confirm the antibacterial properties of the other species. The active compounds in *Boswellia* spp. resins, including boswellic acids, lupeol and a diversity of terpenoids, have noteworthy antimicrobial activity against various pathogenic bacteria and fungi.[71-74] This body of research highlights the valuable role that *Boswellia* spp. have played in traditional medicine, and indicates that they may have significant potential in the development of novel antimicrobial therapies, offering promising avenues for developing effective treatments against infectious diseases.

Traditional knowledge

Rainforests: Guardians of traditional medicine

Indigenous communities inhabiting rainforest regions have a rich history of utilizing local plants diversity for medicinal purposes, with traditional knowledge passed down through generations. This indigenous wisdom is deeply rooted in empirical observations and practical experience, offering a valuable resource for modern researchers exploring the therapeutic potential of rainforest flora. These communities possess a profound understanding of these plants' unique properties, including their identification, preparation methods, dosages, and applications in treating a wide range of ailments. This traditional knowledge reflects a holistic approach to healthcare, intertwined with cultural, spiritual and ecological dimensions, demonstrating the harmonious relationship between these communities and their rainforest environments.

Traditional medicine practices in rainforest regions can provide valuable insights into the antibacterial properties of local plants. Indeed, ethnobotanical studies are an invaluable resource for highlighting species for screening studies. Collaborative efforts with indigenous communities will facilitate the systematic validation of traditional practices. Such collaborations bridge the gap between traditional medicine and modern science, enabling the systematic exploration of bioactive compounds, the elucidation of pharmacological mechanisms, and the development of evidence-based pharmaceuticals derived from rainforest plants.

This interdisciplinary approach not only contributes to cultural heritage preservation, but also has potential for addressing global healthcare challenges through the discovery of novel drugs and therapies sourced from these ecologically and culturally significant ecosystems.

Ethnobotanical studies conducted within rainforest regions constitute an important interface between traditional indigenous knowledge and contemporary scientific research, particularly in the quest for antibacterial agents derived from local plant species. These studies, often undertaken through collaborative partnerships with indigenous communities, serve as an invaluable repository of centuries-old wisdom, meticulously documenting the traditional uses of plants for medicinal purposes. Indigenous societies are generally intimately connected to their environments and have profound insights into the therapeutic potential of rainforest flora, based on empirical observations and practical experience. By meticulously cataloguing these ethnomedicinal practices, ethnobotanical research not only conserves cultural heritage, but may also highlight plant candidates that exhibit antibacterial properties to focus future studies.

Several examples demonstrate the importance of ethnobotanical knowledge in directing antibacterial discovery. In the Brazilian Cerrado biome, collaborative ethnobotanical research with the Krahô community has spotlighted several plant species, including *Copaifera langsdorffii* Desf.[37,38] and *Lippia sidoides* Cham.[45,46] These species have subsequently undergone rigorous screening studies to validate their antibacterial efficacy.[37,38,45,46] Similarly, in the Amazon rainforest, ethnobotanical partnerships facilitated the identification of the Amazonian vine *Uncaria tomentosa* (Willd. Ex. Schult.) DC. (commonly known as cat's claw), which is used in traditional medicine for its wound healing and infection control properties.[63,64] Those studies investigated the antibacterial properties of this species and validated its antibacterial potential, highlighting how traditional knowledge and scientific investigation can work together to expedite the discovery of novel antibacterial agents from rainforest ecosystems.

Desert plants

Ancient healing wisdom

Indigenous communities residing in arid desert regions possess a deep reservoir of traditional knowledge concerning the therapeutic properties of desert plants. Traditional healers within these communities have historically utilized locally available desert flora to address multiple health concerns, including bacterial infections. This ancestral wisdom, rooted in empirical observations and holistic healthcare approaches, offers a valuable and time-tested resource for contemporary researchers aiming to investigate the antibacterial properties of desert plants. Collaborative efforts that respectfully engage indigenous communities facilitate the documentation and validation of traditional practices. This approach holds promise for advancing our understanding of the therapeutic potential of desert-adapted plants and addressing global healthcare challenges, whilst also preserving cultural heritage.

Traditional knowledge of desert plants as antibacterial agents presents a valuable avenue for exploration and these species should not be overlooked by drug discovery programs. Indigenous communities across arid regions have historically employed various plant species for their antimicrobial attributes. For example, the First Australians used native plants including *Melaleuca alternifolia* (Maiden and Betche) Cheel (commonly known as tea tree) for its antimicrobial properties.[13,24] Similarly, the Australian desert plant *Eremophila duttonii* F. Muell. has been traditionally utilized for its antibacterial properties by First Australians from arid inland areas.[4] Additionally, North American Indigenous communities have employed *Larrea tridentata* (DC.) Coville for its antibiotic properties.[88,89] Collaborative initiatives between indigenous knowledge holders and natural product researchers hold the promise of bridging the gap between traditional wisdom and scientific exploration, facilitating the systematic documentation and validation of these ethnobotanical practices within the context of antibacterial drug discovery.

Adaptations and survival

Rainforests: Chemical warfare in a biodiversity hotspot

The high competition for resources in rainforests has driven the evolution of complex chemical defences in plants, which serve multifaceted purposes, including deterring herbivores, and attracting pollinators. Some of these chemical defences also display potent antibacterial properties. For example, *U. tomentosa* produces oxindole alkaloids with antibacterial activity.[63,64] Similarly, the herbaceous vine *Tinospora cordifolia* (Willd.) Miers ex Hook F. and Thoms. (commonly known as heart-leaved monsoon, gurjo or giloy) produces the bioactive compound berberine (Figure 1m).[35] Berberine is recognized as an effective antibacterial agent due to its wide-ranging antibacterial properties.[102] This antibacterial efficacy arises from several key mechanisms, including the disruption of bacterial cell membranes through its integration into the lipid bilayer, leading to alterations in membrane permeability and subsequent leakage of vital intracellular components, resulting in bacterial cell death. Additionally, berberine binds to bacterial DNA, hindering DNA replication and transcription, thereby impeding critical processes in bacterial growth and division.[102,103] Furthermore, berberine inhibits bacterial efflux pumps, rendering the bacteria more susceptible to conventional antibiotics and diminishing the likelihood of antibiotic resistance development.[104] Berberine also disrupts bacterial biofilm, which confer antibiotic resistance to bacteria, thus augmenting the effectiveness of antibacterial treatments.[102] Additionally, berberine immunomodulatory effects have the potential to enhance the host's immune response.

The "chemical warfare" that occurs in rainforests may yield valuable antibacterial compounds. The competition for resources prompts plants to evolve an array of chemical defences against herbivores and pathogens, resulting in a reservoir of compounds with antibacterial potential. The intricate dynamics between plants and microorganisms in rainforest ecosystems provide a unique opportunity for researchers to delve into nature's own antibacterial strategies. The biodiversity of rainforests provides a diversity of natural antibacterial compounds across multiple plant species. Rainforest orchids of the genus *Dendrobium* have been found to produce dendrobine (Figure 1n) and dendrobium alkaloids,[39-41] potentially contributing to their resistance against microbial infections. *Chinchona officinalis* L., native to South American rainforests, yields quinine from its bark.[17,18] Quinine is an antimicrobial alkaloid, which is traditionally used in the treatment of malaria. The sap of the *Dracaena cinnabari* Balf. f. (commonly known as dragon's blood tree, or catuaba tree)[81,82] is another example of rainforest flora that harbor bioactive compounds with antibacterial properties.

Desert plants: Surviving the elements with chemistry

Desert plants, confronted with water scarcity and extreme temperature fluctuations, have evolved a distinctive suite of adaptations, including the synthesis of secondary metabolites that confer protective attributes. These metabolites encompass a wide range of chemical compounds including alkaloids, terpenoids, and phenolics. Some of these compounds have antibacterial activities. For example, the desert succulent *Agave americana* L. (commonly known as century plant) produces saponins and phenolic acids, which exhibit antibacterial

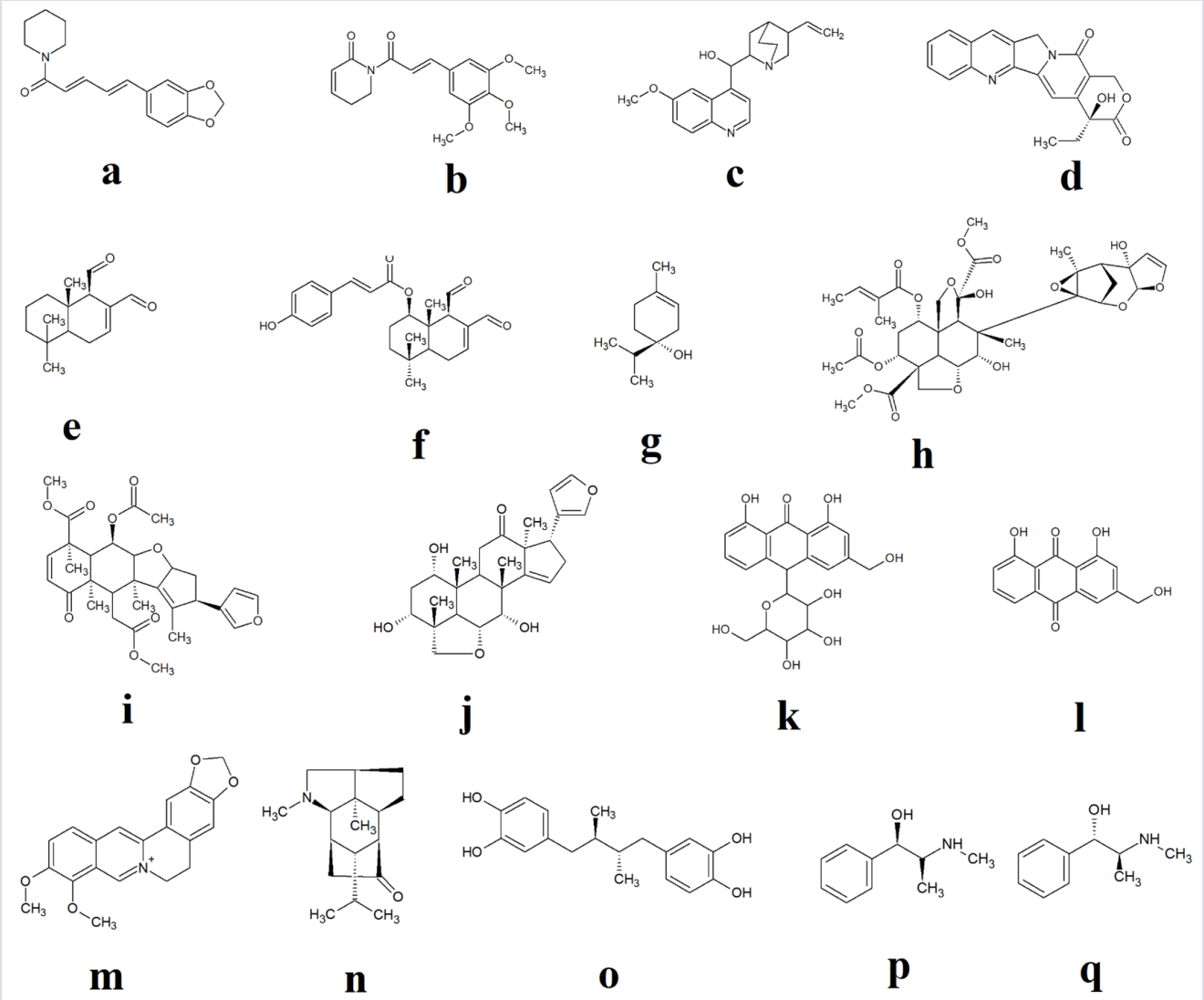

Figure 1: Noteworthy compounds from rainforest and desert plants: (a) piperine, (b) piperlongumine, (c) quinine, (d) camptothecin, (e) polygodial, (f) drimanial, (g) terpinen-4-ol, (h) azadirachtin, (i) nimbin, (j) nimbidin, (k) aloin, (l) aloe-emodin, (m) berberine, (n) dendrobine, (o) nordihydroguaiaretic acid, (p) ephedrine, and (q) pseudoephedrine.

Table 2: Selected arid region plants with antibacterial activity.

Plant Species	Family	Common/Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Agave americana L.	Aspoaragaceae	Century plant, American aloe	Native to arid regions of Mexico and USA.	Inhibits the growth of *S. aureus, P. aeruginosa, S. typhi*, and *E. coli* although with relatively high MIC values (2.5-10 mg/mL.	Alkaloids, tannins, flavonoids.	75
Aloe spp.	Asphpdelaceae	Multiple species. *Aloe vera* L. (true aloe) and *A. ferox* Mill. (bitter aloe) are the best known and most widely used.	Distributed in Africa and Middle East. Aso naturalised widely.	Inhibits the growth of multiple species of bacteria.	Anthraquinones, flavonoids, terpenoids, polysaccharides.	9,76,77
Baileya multiradiata Harvey and A.Gray	Asteraceae	Desert marigold	North America desert regions	Inhibits bacterial growth, although MIC values were not reported.	Sesquiterpenlactones.	78
Boswellia sacra Flueck.	Burseraceae	Frankincense	Middle East and northern Africa	Inhibits the growth of multiple bacteria. Potentiates the activity of conventional antibiotics.	Boswellic acids, flavonoids, terpenoids.	71-73
Boswellia serrata Roxb. ex Colebr.	Burseraceae	Frankincense	South Asia	Inhibits the growth of multiple bacteria. Potentiates the activity of conventional antibiotics.	Boswellic acids, flavonoids, terpenoids.	71
Commiphora molmol (Nees) Engl.; Synonym *Commiphora myrrha*	Burseraceae	Myrrh, common myrrh, African myrrh	Middle East and northern Africa	Inhibits *P. mirabilis, P. vulgaris, A. baylyi,* and *S. pyogenes* growth (MIC = 460-3000 µg/mL).	Terpenoids	73,79
Dracaena cinnabari Balf.f.	Asparagaceae	Dragon's blood tree.	Arid regions of Yemen and the Arabian Peninsula	Inhibits the growth of *S. aureus, E. coli, K. pneumonia*, with MICs 1.25-2.5 mg/mL.	Flavonoids, sterols, triterpenoids.	80,81
Eremophila spp.	Scrophulariaceae	Multiple species, commonly known as emu bush or poverty bush	Arid inland regions of Australia	Inhibits the growth of multiple species of bacteria.	Polyphenols, flavonoids, terpenoids.	4,66-68
Eucalyptus spp.	Myrtaceae	Multiple species	Australia	Inhibits the growth of multiple species of bacteria.	Terpenoids	24,82-86

Plant Species	Family	Common/Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Harpagophytum procumbens (Burch.) DC. ex Meisn.	Pedaliaceae	Devil's claw, grapple plant, wood spider	Arid inland regions of southern Africa	Inhibited the growth of an extended panel of bacteria, with MIC values as low as 125 µg/mL. Also has good anti-inflammatory activity.	Harpagoside	87
Larrea tridentata (DC.) Coville	Zygophyllaceae	Chaparral, creosote bush, greasewood	Mojave, Sonoran and Chihuahuan deserts of North America	Bactericidal activity against *S. aureus, S. pyogenes, B. cereus*, and *P. aeruginosa* (MBCs 1-1000 µg/mL).	Lignans and flavonoids.	88,89
Leptospermum spp	Myrtaceae	Multiple species, commonly known as tea trees	Australia and Oceania region	Inhibits the growth of multiple species of bacteria.	Terpenoids	24,90
Melaleuca spp.	Myrtaceae	Multiple species, commonly known as tea trees, paperbarks, honey myrtles	Australia and Oceania region	Inhibits the growth of multiple species of bacteria.	Terpenoids	13,24
Optunia spp.	Cactaceae	Prickly pear cactus	Distributed widely throughout arid regions of the Americas		Several lipophilic compounds.	7,91
Pittosporum angustifolium Lodd.; formerly *Pittosporum phylliraeoides*	Pittosporaceae	Gumby gumby, gumbi, gumbi, cumbi cumbi, native apricot	Australia	Inhibits *P. mirabilis* and *K. pneumoniae* growth (MIC = 26 and 52 µg/mL).	Polyphenolics, flavonoids, saponins, terpenoids.	69,78
Plantago squarrosa Murray	Plantaginaceae	Unknown	Northern Africa and the Middle East	Inhibits *P. mirabilis, P. vulgaris, A. baylyi,* and *S. pyogenes* growth (MIC = 484-3700 µg/mL).	Polyphenolics, flavonoids, saponins, terpenoids.	92
Scaevola spinescens R.Br.	Goodeniaceae	Currant bush, maroon bush, prickly fan flower	Arid inland regions of Australia	Inhibits the growth of multiple bacteria and potentiates the activity of conventional antibiotics.	n-Tetradecane, α-amyrin, stigmasterol, luteolin derivatives, flavonoid glycosides.	93-97
Simmondsia chinensis (Link) C.K.	Simmondsiaceae	Jojoba, goat nut, deer nut, pignut, wild hazel, quinine nut, coffeeberry	Desert regions of North America	In combination with other plant preparations, inhibits the growth of multiple species of bacteria.	Not reported	98,99

Plant Species	Family	Common/Local name	Origin Region	Therapeutic Uses/ Antimicrobial Bioactivities	Known Phytoconstituents	References
Solanum incanum L.	Solanaceae	Thorn apple, bitter apple, butter tomato	Sub-Saharan Africa, Middle East	Inhibits growth of *S. aureus, E. coli, P. aeruginosa, Acinetobacter* spp. (MICs >4000 µg/mL).	Phenolic acids, cinnamic acid, coumaric acid.	100
Swainsona formosa (G.Don) Joy Thomp.	Fabaceae	Sturts desert pea	Arid inland regions of Australia	Inhibits the growth of an extended panel of bacterial pathogens, with MICs as low as 150 µg/mL.	Swainsonsine, N,N-dimethyltryptamine.	101

properties by disrupting bacterial cell membranes and interfering with their metabolic processes.[75] Similarly, the resinous exudates of the desert shrub *Larrea tridentata* (DC.) Coville (commonly known as creosote bush), contain a rich assortment of secondary metabolites including flavonoids and lignans, which have antibacterial effects via enzyme inhibition and the disruption of bacterial cell walls.[88,89] These examples underscore how the arid desert environment has driven the evolution of desert plants to synthesise secondary metabolites with antibacterial potential, and provides insights into their biochemistry and potential applications in combating bacterial infections.

Numerous plants growing in arid environments have evolved defensive mechanisms against microbial threats. Chemical constituents, including alkaloids, and phenolic compounds produced by desert plants have evolved as defences against both herbivores and bacteria. Notable among these compounds are the sesquiterpene lactones, including those found in *Baileya multiradiata* Harvey and A.Gray (desert marigold),[78] and nordihydroguaiaretic acid (NDGA; Figure 1o), present in *Larrea tridentata* (DC.) Coville,[88,89] the wax esters in *Simmondsia chinensis* (Link) C.K. (commonly known as Jojoba) seeds.[98,99] and the alkaloids ephedrine (Figure 1p) and pseudoephedrine (Figure 1q), found in some *Ephedra* spp.[105] These chemical defences serve not only to safeguard these plants, but also hold significant promise in the quest for novel antibacterial agents, highlighting the importance of exploring desert flora's chemical adaptations for potential applications in antibacterial drug development.

Challenges and considerations

Ethical and sustainable practices

In the pursuit of antibacterial treatments from both desert and rainforest plants, the integration of ethical and sustainable practices is of paramount importance. The utilization of plant resources for medicinal purposes, while promising for drug discovery, carries the potential risks of overharvesting, habitat degradation, and the loss of biodiversity. This is particularly concerning for desert plants as they live in particularly harsh conditions and human intervention can significantly affect their survival. To mitigate these concerns, research endeavours must be underpinned by robust ethical guidelines and sustainable principles that prioritize the conservation and preservation of these ecologically sensitive environments.

One of the primary ethical considerations is the responsible harvesting of medicinal plants from these regions. Sustainable collection practices, guided by an understanding of plant biology and population dynamics, are essential to prevent the depletion of valuable plant species. Additionally, the involvement and engagement of local indigenous communities in the research process is crucial, as their traditional knowledge and practices can provide invaluable insights into sustainable harvesting and conservation strategies. Furthermore, the ethical procurement of plant materials should adhere to national and international regulations and conventions to prevent illegal trade through biopiracy and protect endangered species. This holistic approach to ethical sourcing and sustainable utilization of plant resources is indispensable in ensuring that the exploration of antibacterial treatments from desert and rainforest plants contributes not only to scientific advancements, but also to the preservation of the natural ecosystems that harbour these invaluable resources.

Research and clinical trials

The potential of desert and rainforest plants as reservoirs of antibacterial compounds presents a promising avenue for drug discovery. However, it is crucial to prioritize rigorous scientific research to maximise discovery outputs. The initial phase of investigation involves the isolation of bioactive compounds from these botanical sources. This process requires meticulous extraction and purification procedures, often guided by sophisticated chromatographic techniques, to obtain pure and chemically well-defined compounds. Subsequent characterization, employing state-of-the-art analytical tools,

including mass spectroscopy and nuclear magnetic resonance spectroscopy, is valuable for elucidating chemical structures and confirming the identity of isolated compounds.

To determine the true therapeutic potential of these natural compounds, they must be subjected to a battery of preclinical and clinical trials, akin to the rigorous standards applied to synthetic antibacterial drugs. Preclinical studies encompass a spectrum of *in vitro* and *in vivo* assessments, aimed at elucidating the antibacterial mechanism of action, toxicity profile, and pharmacokinetic properties of the compounds. Where relevant, clinical trials involving human subjects are required to assess safety, efficacy, and dosage regimens. Adherence to established protocols and rigorous regulatory oversight is paramount to ensure the credibility and reliability of the findings. By navigating the rigorous scientific path from compound isolation and characterization through preclinical and clinical evaluations, researchers can evaluate the true potential of desert and rainforest plants as sources of antibacterial agents and contribute to the advancement of evidence-based natural products-based therapies. However, toxicity evaluation is a critical aspect of determining the suitability of natural products as antibacterial agents, as therapeutic utility hinges not only on efficacy, but also on an acceptable safety profile. This rigorous assessment seeks to elucidate any adverse effects or potential risks associated with these compounds, thereby providing a holistic understanding of their therapeutic potential. Consequently, the integration of both antibacterial efficacy and safety assessment is pivotal in harnessing the full pharmacological potential of natural products for combating bacterial infections.

Standardization and dosage

The standardization of natural remedies, including desert and rainforest plant extracts, is a complex challenge. Central to this challenge is the inherent variability in plant chemistry, which may be influenced by a multitude of factors, including environmental conditions, genetic diversity, and geographical location.[106] This variability underscores the need for meticulous attention to standardization protocols to ensure consistency and reliability in the composition and potency of natural remedies. Standardization efforts typically involve the development of rigorous quality control measures that encompass the selection of specific plant parts, the extraction processes employed, and the quantification of key bioactive constituents. For example, in the case of rainforest plants where diverse species coexist, establishing protocols to authenticate the source species and monitor batch-to-batch consistency is essential. These standardization procedures help maintain the reliability and reproducibility of natural remedies, aligning them with the rigorous standards expected in the pharmaceutical industry.

Furthermore, the determination of optimal dosages for natural remedies derived from desert and rainforest plants is a critical consideration for their safe and effective use. Identifying the right dosage regimen is contingent on a thorough understanding of the therapeutic index of these remedies to strike a balance between their efficacy and potential side effects. This requires comprehensive pharmacological investigations and clinical trials to establish appropriate dosage ranges. Factors such as the mode of administration, bioavailability, and individual patient variability further compound the complexity of this endeavour. Achieving the correct dosage is essential, not only to maximise therapeutic efficacy, but also for the safety of patients and consumers.

CONCLUSION

This comparative examination of desert and rainforest plants as potential sources of antibacterial agents encompasses a multifaceted exploration, considering multiple factors including biodiversity, traditional ethnomedicinal knowledge, ecological adaptations, and ethical implications. Rainforests, renowned for their biodiversity are a fertile ground for the investigation of potential antibacterial compounds. The intricate chemical interplay between rainforest flora and microorganisms within these lush ecosystems provides insights into nature's own strategies for bacterial defence, highlighting the wealth of bioactive compounds within this ecosystem. In contrast, desert plants, have evolved unique adaptations to survive the harsh conditions in which they live. These adaptations may have given rise to antibacterial compounds that are yet to be fully explored. Indigenous knowledge and traditional medicine play important roles in guiding research in both ecosystems, fostering collaborative and culturally sensitive approaches that respect the accumulated wisdom of generations. Ultimately, this multifaceted approach highlights the importance of evidence-based research and ethical considerations in unlocking the potential of desert and rainforest plants for antibacterial treatments.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

CRE: Carbapenem-resistant enterococcus; **MERS:** Middle East respiratory virus; **MGO:** Methylglyoxal; **MIC:** Minimum inhibitory concentration; **MRSA:** Methicillin resistant Staphylococcus aureus; **NDGA:** Nordihydroguaiaretic acid.

SUMMARY

- The development of antibiotic-resistant bacteria has highlighted the need for new antibiotics.
- Desert and rainforest plants live in harsh conditions and produce chemical protectants.
- Rainforest plants have received substantially greater attention than desert plants.
- This commentary summarises and compares the potential of these ecosystems for antibiotic discovery.

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