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Medicinal Flora of Socotra Island as a Source of Novel Anti-Infective Agents: Diversity, Ethnopharmacology, Bioassays, and Lead Optimization

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Abstract

The concept of antimicrobial resistance (AMR) has become one of the most pressing concerns in the current public health agenda, underscoring the urgent need to find new anti-infective agents in nature. Medicinal plants have traditionally been central in the process of drug discovery, and biodiversity hotspots are untapped sources of new bioactive compounds. Of these, the Socotra Island in Yemen is a rare site of endemic plants, with close to 30 percent of the flora not found elsewhere on the planet. This unmatched endemism, along with a long tradition of ethnomedicinal activities, makes Socotra an unprecedented bioprospecting location. The current review identifies the prospect of Socotra medicinal flora as a source of anti-infective leads, extending beyond ethnopharmacological documentation toward rigorous scientific validation of traditional medicinal knowledge. Using a synthesis of available evidence on phytochemical diversity, bioassays, and mechanistic understanding, the paper evaluates antibacterial, antifungal, and antiparasitic drug-discovery evidence for key endemic species, including *Dracaena cinnabari*, *Aloe perryi*, and *Punica protopunica*, while distinguishing direct species-specific findings from indirect evidence. In addition, it highlights the significance of lead optimization methods, structure-activity relationships, semi-synthetic alterations, and computational methods in the conversion of natural compounds into drug-like molecules. Finally, the paper establishes the endemic flora of Socotra as a strategic frontier in combating infectious diseases and AMR globally.

Keywords

Antimicrobial Resistance (AMR), Socotra Island Medicinal Flora,

Ethnopharmacology, Phytochemical Diversity, Bioassay-Guided Screening, Anti-Infective Drug Discovery, Lead Compound Optimization, Conservation, Access and Benefit-Sharing (ABS)

1. Introduction

Antimicrobial resistance (AMR) is a single of the most significant 34 health challenges of the 21st century. In the 21st century, there is a risk of jeopardizing decades of infectious disease treatments [1]. 35 Effectiveness of 36 has decreased substantially because of the alarming increase in the number of multidrug-resistant pathogens. However, no new anti-infective agents have been discovered and the existing antibiotics are urgently required [2]. Natural products 37 have traditionally been a central product in the discovery of anti-infective drugs and many leading drugs are currently in use. The fact that the source of the therapeutics is natural, as in the case of artemisinin and quinine extracted from plants and 39 other medicinal plants, is a crucial point. The filamentous fungus Penicillium is the source of the antibiotic penicillin [2]-[4]. However, in spite of the importance of biodiversity, many regions with extraordinary botanical diversity in developing countries are still underutilized in the development of pharmaceutical innovations, in the development of which they played a pivotal role. insufficiently studied. **Figure 1** shows *Dracaena cinnabari*, the dragon's blood tree, one of the most iconic resin-producing endemics of the archipelago and a recurring example throughout this review.

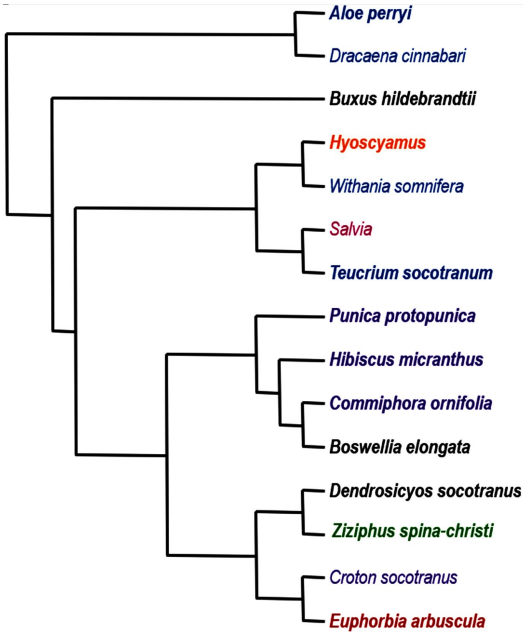
Figure 1. Dragon's blood tree, also known as *Dracaena cinnabari* [5] [6].

Figure 2 situates the Socotra Archipelago geographically, showing the main island alongside the three satellite islands of Abd al Kuri, Samha, and Darsa.

The geological history, geographic isolation and climatic conditions are key factors in shaping Socotra's biological richness [6] [7]. Insular taxa are also important for biogeographic study of colonization and speciation but do not necessarily give direct clues to medicinal-plant relationships [7] [8]. Around one-third of Socotra's flora is endemic, and native plants that have a broader range of distribution in the region's medicinal flora are also included [6] [7] [9]. **Table 1** thus differentiates Socotra-endemic, native non-endemic and native broadly distributed taxa. The accepted names and biogeographic status were mainly sourced from Eth-

noflora of the Soqotra Archipelago and were cross checked through the current taxonomic databases [9]. **Figure 3** shows a schematic phylogenetic overview of the considered medicinal taxa, self-elaborated and is a visual illustration of the broad family level comparison instead of a phylogenetic reconstruction.

Figure 2. The Socotra Archipelago "The Jewel of Arabia" is located in the Arabian sea, off the coast of the Yemeni peninsula. It includes the main island of Socotra (12˚30'36"N, 53˚55'12"E), three satellite islands (Abd al Kuri, Samha and Darsa) and some small rocky outcrops [5].



Note: Taxonomic and biogeographic classification was done mainly according to the Ethnoflora of the Soqotra Archipelago [9] with cross checking through the IUCN Red List and Kew's Plants of the World Online. The species mentioned with "Socotra-endemic" means those species that are naturally distributed only in Socotra Archipelago; "native non-endemic" means those species naturally distributed in Socotra and other geographical regions; "native broadly distributed" means species with broad natural distributions including Socotra. This entry was formerly known as "*Hyoscyamus socotranus*" but the accepted taxonomy and distribution of that species on Socotra proved difficult to confirm. The adjusted table thus has 14 species.

Figure 3. Socotra medicinal flora phylogenetic tree (Source: Self-elaborated).

Table 1. Medicinal plants recorded from the socotra archipelago: Biogeographic status, phytochemistry, pharmacological evidence, and traditional uses.

No.	Species	Common Name	Family	Biogeographic Status	Extraction Method/Material	Major Reported Constituents	Reported Biological Evidence	Traditional Medicinal Use
1	*Dracaena cinnabari Balf. f.*	Dragon's Blood Tree	Asparagaceae	Socotra-endemic [9]	Methanolic or ethanolic resin extracts prepared by maceration or Soxhlet extraction	Flavonoids, phenolic compounds, proanthocyanidins, and tannins	Antibacterial, antifungal, antioxidant, and wound-healing activities have been reported for the resin [16] [20] [22] [23]	Wounds, ulcers, bleeding, diarrhoea, and dysentery [9] [16]
2	*Aloe perryi Baker*	Socotrine Aloe	Asphodelaceae	Socotra-endemic [9]	Aqueous, ethanolic, or methanolic extracts of leaf exudate, gel, or resin	Aloin-related anthraquinones, aloe-emodin-related compounds, and polysaccharides	Phytochemical and preliminary pharmacological activities have been reported, but direct species-specific antimicrobial evidence remains limited [17] [21]	Laxative or purgative; topical treatment of wounds and some skin conditions [9]
3	*Punica protopunica Balf. f.*	Socotran Pomegranate	Lythraceae	Socotra-endemic [9] [18]	Methanolic or hydroalcoholic extracts of fruits, peels, or seeds	Phenolic compounds, flavonoids, tannins, and ellagitannin-related constituents	Species-specific antibacterial and antiprotozoal activities have been reported [15] [18]-[20]	Diarrhoea, dysentery, sores, and intestinal complaints [9] [18]
4	*Boswellia elongata Balf. f.*	Socotran Frankincense Tree	Burseraceae	Socotra-endemic [9]	Resin extracts and essential oils obtained by solvent extraction or hydrodistillation	Terpenoids, monoterpenes, and boswellic-acid-related constituents	Direct species-specific anti-infective evidence remains limited; findings from other Boswellia species should be considered indirect	Respiratory complaints, inflammation, and incense-related traditional practices [9]
5	*Commiphora ornifolia* (*Balf. f.*) *J. B. Gillett*	Socotran Myrrh Tree	Burseraceae	Socotra-endemic [9]	Resin or plant extracts prepared using organic solvents; essential oils where reported	Sesquiterpenes and other resin-associated terpenoids	Direct antimicrobial evidence for this species remains limited; findings from other Commiphora species are indirect [24]	Wound care and traditional resin-based applications [9]
6	*Dendrosicyos socotranus Balf. f.*	Cucumber Tree	Cucurbitaceae	Socotra-endemic [9]	Solvent extracts of relevant plant parts, where reported	Cucurbitacin-related compounds and flavonoids	No sufficiently verified species-specific anti-infective activity value was identified	Digestive complaints [9]
7	*Croton socotranus Balf. f.*	Socotran Croton	Euphorbiaceae	Socotra-endemic [9]	Organic-solvent extracts of leaves or other plant parts, where reported	Diterpenoid- and flavonoid-related constituents	Species-specific anti-infective evidence remains insufficient and requires confirmation from primary studies	Skin-related traditional applications [9]

Continued

8	*Euphorbia arbuscula Balf. f.*	Socotran Spurge	Euphorbiaceae	Native, non-endemic [9]	Latex or plant-part extracts prepared using organic solvents, where reported	Diterpenoid-related compounds and triterpenes	Direct species-specific antimicrobial evidence remains insufficiently characterized	Traditional topical applications for skin lesions [9]
9	*Ziziphus spina-christi* (*L.*) *Desf.*	Christ's Thorn Jujube	Rhamnaceae	Native, broadly distributed [9]	Aqueous or organic-solvent extracts of leaves or fruits	Saponins, flavonoids, tannins, and other phenolic compounds	Antimicrobial activity has been reported for this broadly distributed species; the geographical origin of the tested material should be specified	Digestive complaints and wound care [9]
10	*Withania somnifera* (*L.*) *Dunal*	Ashwagandha	Solanaceae	Native, broadly distributed [9]	Organic-solvent extracts, particularly root extracts	Withanolides and alkaloids	Immunomodulatory and other pharmacological activities have been widely reported, but these findings do not constitute direct anti-infective evidence from Socotran material	General health, stress-related conditions, and immune-related traditional uses
11	*Teucrium socotranum Vierh.*	Socotran Germander	Lamiaceae	Socotra-endemic [9]	Solvent extracts of aerial plant parts, where reported	Flavonoids and terpenoids	Direct species-specific antibacterial evidence remains limited and requires primary-study confirmation	Respiratory complaints [9]
12	*Buxus hildebrandtii Baill.*	Socotran Boxwood	Buxaceae	Native, non-endemic [9]	Organic-solvent extracts of bark or other plant parts, where reported	Steroidal alkaloids and other Buxus-associated alkaloids	No sufficiently verified species-specific anti-infective evidence was identified	Traditional treatment of fever, where ethnobotanically documented [9]
13	*Hibiscus micranthus L. f.*	Wild Hibiscus	Malvaceae	Native, broadly distributed [9]	Aqueous or organic-solvent extracts, where reported	Flavonoids, anthocyanins, and other phenolic compounds	Anti-inflammatory and antimicrobial activities require confirmation using primary studies and correctly identified plant material	Digestive complaints [9]
14	*Salvia socotrana Balf. f.*	Socotran Sage	Lamiaceae	Socotra-endemic [9]	Essential oils obtained by hydrodistillation or solvent extracts of aerial parts	Essential-oil constituents and phenolic compounds	Direct species-specific antimicrobial evidence remains limited; quantitative activity values require confirmation from primary studies	Colds, coughs, and respiratory complaints [9]

Note: Taxonomic and biogeographic classification was done primarily based on the Ethnoflora of the Soqotra Archipelago by Miller and Morris [9] and was cross checked from IUCN Red List and Plants of the World Online maintained by Kew. "Socotra-endemic" means a species found naturally only on Socotra, "native non-endemic" means a species found naturally on Socotra and other geographically separate areas and "native broadly distributed" means a species with broad natural distribution including Socotra. This entry was formerly called "*Hyoscyamus socotranus*" but the taxonomic identity and occurrence on Socotra could not be confirmed. The modified table now has 14 species because the one that was eliminated from the original table appears again in the new one.

This review aims to give an introduction to the ethnopharmacological importance of Socotran plants and their current utilization in the discovery of new drugs. The 14 species selected were those that have been documented on Socotra, their traditional medicinal use and the availability of phytochemical or pharmacological evidence, as well as representative of different biogeographic categories. Therefore, the endemism of species was not the only criterion used in selecting them. They are organized generally from the ecologically and culturally significant trees, like *Dracaena cinnabari*, to shrubs to herbaceous species. This is a logical botanical and ethnopharmacological progression, which this organization offers.

Based on the adopted floristic classification, *Dracaena cinnabari*, *Aloe perryi*, *Punica protopunica*, *Boswellia elongata*, *Commiphora ornifolia*, *Dendrosicyos socotranus*, *Croton socotranus*, *Teucrium socotranum*, and *Salvia socotrana* were classified as Socotra-endemic. *Euphorbia arbuscula*, *Buxus hildebrandtii were classified as native but non-endemic*, *and Ziziphus spina-christi*, *Withania somnifera*, *and Hibiscus micranthus as native but broadly distributed. The entry for Hyoscyamus socotranus was removed due to an inability to confirm its taxonomic identity and occurrence in the Socotra Archipelago through Miller and Morris* [9] or through Kew's Plants of the World Online.

Phylogenetic and spatial approaches can help identify patterns in medicinal-plant chemistry and prioritize taxa for drug-discovery research [8] [10]-[12]. The prism perspective, which integrates plant phylogeny, chemical composition, and medicinal efficacy, provides a related framework for prioritization [13] [14].

Ethnopharmacological studies and preliminary phytochemical investigations have revealed significant medicinal potential in species like *Dracaena cinnabari*, *Aloe perryi* and *Punica protopunica* [15]-[21], but there are limited empirical evidences for their anti-infective activities. Additionally, bioassays have not frequently been combined with other modern drug design approaches, limiting the use of this unique flora for drug development. The main research gap that was identified and targeted in this review is the lack of systematic approaches for the characterization and prioritization of medicinal plants of Socotra, focusing on endemic species as potential source of novel anti-infective compounds. In accord with this, the present review critically summarises the available ethnopharmacological, phytochemical and pharmacological data and considers the application of lead-optimisation strategies in the post-genomic era of drug discovery. In doing so, it positions Socotra's medicinal flora as a promising but underdeveloped resource for combating AMR globally.

Ethnopharmacological surveys and preliminary phytochemical investigations have confirmed significant medicinal use of species like *Dracaena cinnabari*, *Aloe perryi* and *Punica protopunica* [15] [21], but empirical studies of these plants for their anti-infective activity is limited. Furthermore, the data from bioassays have not frequently been used in conjunction with modern drug design approaches, limiting the potential of this unique flora to be translated into drug development. One of the main gaps highlighted in the review is the absence of systematic ap-

proaches for characterization and prioritization of medicinal plants of Socotra, especially endemic taxa, as a source of novel anti-infective compounds. Thus, the present review critically consolidates existing ethnopharmacological, phytochemical, and pharmacological data, as well as evaluating the potential of applying lead-optimization strategies in a contemporary drug-discovery process. It does this, putting Socotra's medicinal flora in the spotlight as a viable yet untapped potential source to combat AMR at the global level.

2. Study Design and Literature Search Methodology

The purpose of this review was to provide a structured narrative review addressing the available evidence about the medicinal flora of Socotra and its significance in the fields of antimicrobial resistance, ethnopharmacology, phytochemical diversity, anti-infective drug research, and conservation-based bioprospecting. The relevant literature was identified from major scientific databases and academic sources using various combinations of the keywords Socotra, medicinal plants, endemic flora, ethnopharmacology, phytochemistry, antimicrobial activity, anti-infective agents, natural products and drug discovery from PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. The literature cited included 73 references that were representative of the major thematic areas of the review. Records from January 2000 until July 2026 were searched using the Medline/PubMed, Scopus, Web of Science, ScienceDirect and Google Scholar databases, in English language only. Representative search strings were those involving the use of Boolean operators between Socotra-specific terms, such as "Socotra" OR "Soqotra" OR "Socotra Archipelago" and a pharmacological term, for instance: "medicinal plant*" OR "ethnopharmacology" OR "antimicrobial" OR "antibacterial" OR "antifungal" OR "antiparasitic" OR "phytochemistry" OR "natural product*", or species-specific searches, e.g., "*Dracaena cinnabari*" AND "antimicrobial", "*Aloe perryi*" AND "antibacterial" or "*Punica protopunica*" AND "activity". The titles and abstracts for all records retrieved were first screened for duplications and obviously irrelevant records, and then the full text of all potentially relevant records were evaluated based on the eligibility criteria below. A two-stage identification and eligibility screening process is summarized here to aid in the search's reproducibility, which is similar to that of a narrative (non-systematic) review design.

Research and reviews related to Socotran medicinal plants, traditional applications, phytochemical profile, bioactivity, antimicrobial activity, toxicity, phytopharmacology, drug development potential, conservation, access and benefit sharing were considered. Authentic evidence from the named species was deemed to be direct species specific evidence. The evidence that did not support species-specific activity or mechanistic claims was considered to be either congruent with the species or general review evidence, or indirect evidence, or evidence from the related taxa, and these evidence types were not used individually in the species-specific activity or mechanistic claims. If there was no information on the underlying primary study, quantitative activity values were not included. Evidence was gathered from all the manuscript tables and sections, such as the 14 medicinal

plant species represented in Table 1 and the three important species (*Dracaena cinnabari*, *Aloe perryi* and *Punica protopunica*) enlisted in Table 2.

Table 2. Comparison of three key endemic medicinal plants of socotra.

Plant Name (Scientific)	Common Name	Family	Ecological Environment	Key Chemical Composition	Key Active Compounds	Traditional Uses	Pharmacological Activity
Dracaena cinnabari	Dragon's Blood Tree	Dracaenaceae	Found on limestone plateaus and rocky cliffs; adapted to arid, high-altitude areas.	Flavonoids, proanthocyanidins, and phenolic compounds [16] [22] [23].	Dracorhodin-, loureirin-, and tannin-related constituents reported in dragon's-blood literature [22] [23].	Wounds, ulcers, bleeding, and gastrointestinal complaints [9] [16] [45] [47].	Species-specific antifungal, antibacterial, antioxidant, and toxicity evidence [16] [20] [48].
Aloe perryi	Socotrine Aloe	Asphodelaceae	Grows in dry, rocky habitats; tolerates harsh sunlight and low water availability.	Anthraquinone-related constituents and polysaccharides [17] [21] [32].	Aloin- and aloe-emodin-related constituents; evidence from isolated derivatives is indirect [17] [21] [32].	Laxative or purgative use and topical applications [9].	Phytochemical and preliminary pharmacological evidence; direct species-specific antimicrobial validation remains limited [17] [21].
Punica protopunica	Socotran Pomegranate	Lythraceae	Thrives in valleys and areas with limited water; adapted to semi-arid conditions.	Ellagitannin-related constituents, flavonoids, and phenolic compounds [18] [19].	Ellagic-acid- and tannin-related constituents [18] [19].	Diarrhoea, dysentery, sores, and intestinal complaints [9] [18].	Species-specific antibacterial and antiplasmodial activity [15] [18] [20]; anthelmintic data from *P. granatum* are indirect [49] [50].

The variability in the studies in terms of plant species, extraction method, phytochemical analysis, antimicrobial assay, and result of the outcome, were the reasons why all the evidence was processed qualitatively. The literature gathered has been classified into seven main groups: traditional use, phytochemical composition, antimicrobial and anti-infective activity, toxicity and *in vivo* evidence, optimization of lead compounds, computational potential for drug discovery, and conservation and access and benefit sharing. This approach enabled the integrated assessment of the therapeutic potential of medicinal plants of Socorro, as well as identification of gaps in standardization, safety assessment and translation of some medicinal plants.

3. Phytochemical Diversity and Classification

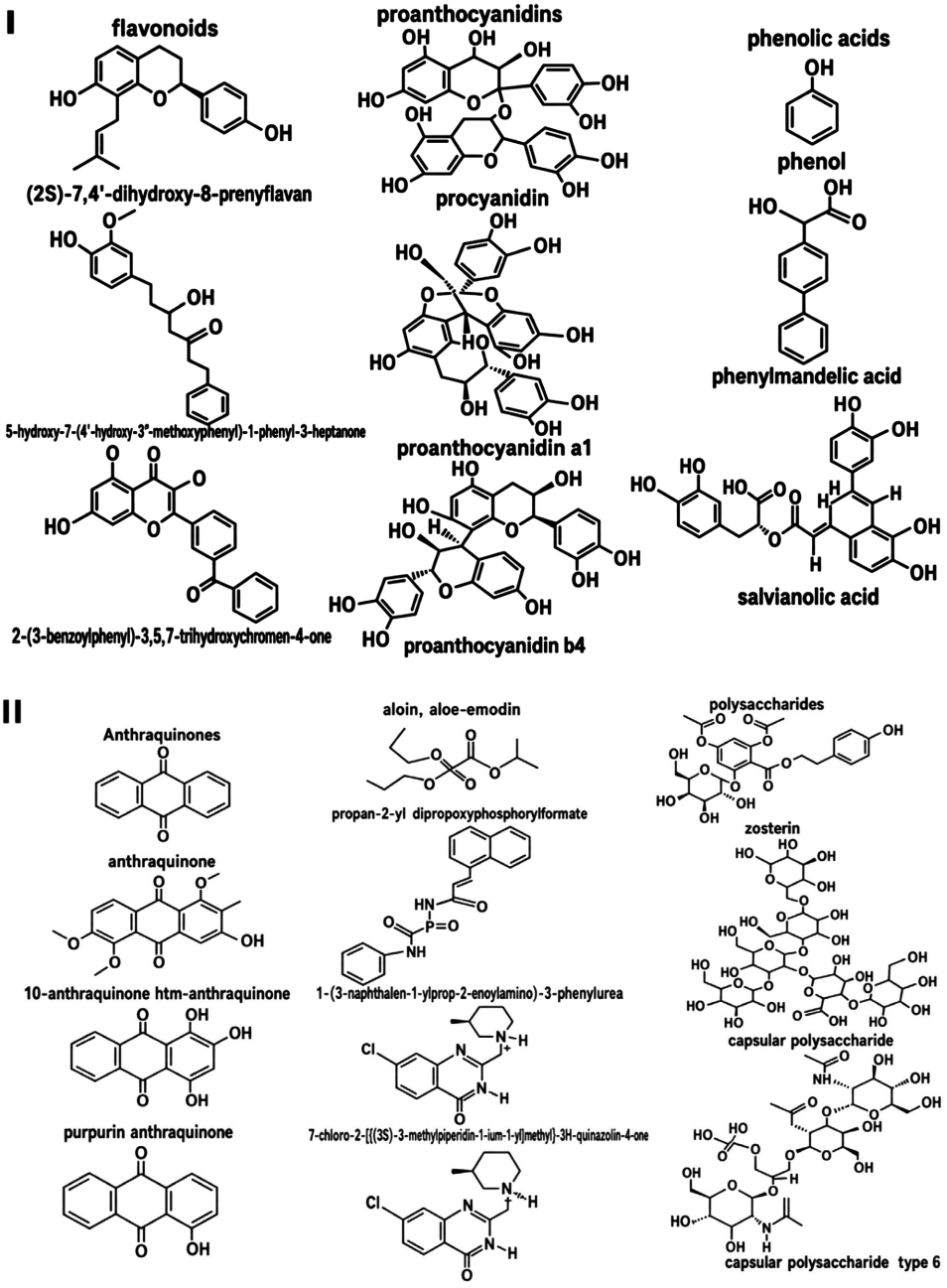
3.1. Major Compound Classes

Medicinal flora present in Socotra has a number of significant classes of specialised metabolites such as terpenoids, steroids, flavonoids, alkaloids, phenolics, qui-

nones and anthraquinones [10] [11] [25]. The literature on Boswellia and Commiphora describes terpenoid rich resins and related pharmacological activities, but there is indirect evidence for the activity of *Boswellia elongata* and *Commiphora ornifolia* [24] [26] [27]. A number of natural compounds can have both antimicrobial and anti-inflammatory properties [28]. *Dracaena cinnabari* resin has been reported to possess polyphenolic compounds like flavonoids and proanthocyanidins and exhibit antioxidant and antimicrobial properties [16] [20] [22] [23] [29]. Species-specific evidence for constituents related to phenolics and ellagitannins has been found in *Punica protopunica* [18] [19], while common pomegranate, *Punica granatum* is congener, but the findings should be considered as such [30]. The bioactive constituents of Direct phytochemical studies conducted on *Aloe perryi* have identified [17] [21] but the results of antimicrobial or safety studies from other Aloe species and isolated hydroxyanthracene derivatives remain indirect [31]-[33]. When considering the connection between phytochemical composition and traditional use and drug-development potential, plant-specific evidence is important. *Dracaena cinnabari* resin has been reported with flavonoids, phenolic compounds and proanthocyanidins [16] [22] [23] and specific studies show antifungal, antibacterial and antioxidant properties [16] [20]. In a broader survey of anti-skin and anti-wound medicinal plants, it was found that they had beneficial effects, but not those of a particular medicinal plant, Dracaena [34]. Preliminary pharmacological properties and phytochemical profile have been characterized from direct analyses of *Aloe perryi* [17] [21]. Persons claiming with *Aloe vera*, aloe-emodin (isoflavone), aloin or other species of Aloe should make indirect claims and/or claims based on aloe-emodin, aloin or other species of Aloe. The plant traditionally known as Socotrine aloe is still *Aloe perryi* [9]. The *Aloe perryi* is illustrated in **Figure 4**.

Figure 4. Perry's aloe (*Aloe perryi*).

Phenolic and other bioactive components have been reported in species-specific *Punica protopunica* material using phytochemical investigation [19]. The antibacterial activity of extracts from *P. protopunica* was confirmed in a primary survey of medicinal plants collected from Socotra [20] and an *in vitro* antiplasmodial activity against *Plasmodium falciparum* was reported in a separate study of the species [15]. A species-specific review of traditional uses and general medicinal properties has been provided [18]. There is no direct information on terpenoid and pharmacological activity for *B. elongata* and *C. ornifolia*, based on the other Boswellia and Commiphora species [24] [26] [27]. **Figure 5** summarizes some representative representatives of the three important endemic species.



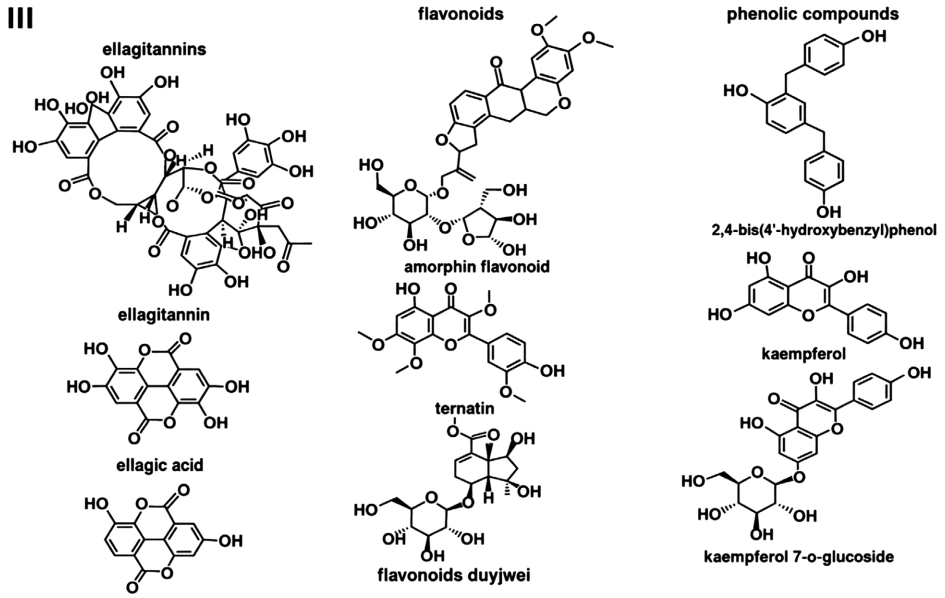


Figure 5. Representative phytochemical constituents of three key endemic medicinal plants of Socotra Island [19]-[21]. Panel I: Major bioactive compounds of *Dracaena cinnabari* resin, comprising flavonoids (flavones((2S)-7,4'-Dihydroxy-8-Prenylflavan (CAS: 271770-94-6), 5-Hydroxy-7-(4'-hydroxy-3'-methoxyphenyl)-1-phenyl-3-heptanone (CAS: 79559-61-8), 2-(3-Benzoylphenyl)-3,5,7-trihydroxychromen-4-one (CAS: 832-83-7)), proanthocyanidins (Procyanidin (CAS: 4852-22-6), Proanthocyanidin A1 (CAS: 103883-03-0), Proanthocyanidin B4 (CAS: 51196-38-4)), and phenolic acids (Phenol (CAS: 108-95-2), Phenylmandelic acid (CAS: 450-52-2), Salvianolic acid (CAS: 96574-01-5)). Panel II: Principal constituents of *Aloe perryi*, including Anthraquinones (Anthraquinone (CAS: 84-65-1), 10-anthraquinone HTM-anthraquinone (CAS: 872360-77-5), Purpurin anthraquinone (CAS: 81-54-9)), aloin, aloe-emodin (Propan-2-yl dipropoxyphosphorylformate, 1-(3-Naphthalen-1-ylprop-2-enoylamino)-3-phenylurea, 7-chloro-2-[[(3S)-3-methylpiperidin-1-ium-1-yl]methyl]-3H-quinazolin-4-one, and polysaccharides (Zosterin (CAS: 11113-95-4), Capsular polysaccharide(CAS: 133957-16-1), Capsular polysaccharide type 6 (CAS: 119903-55-8)). Panel III: Key phytochemicals of *Punica protopunica*, including ellagitannins (Ellagitannin (CAS: 133145-19-4), ellagic acid (CAS: 476-66-4)), flavonoids (Amorphin Flavonoid (CAS: 4207-90-3), Ternatin (CAS: 571-71-1), Flavonoids Duyiwei (CAS: 64421-28-9)), and phenolic compounds (2,4-Bis(4'-hydroxybenzyl) phenol (CAS: 34826-64-7), Kaempferol (CAS: 520-18-3), kaempferol 7-O-glucoside (CAS: 16290-07-6)).

3.2. Chemodiversity and Drug Discovery Potential

Socotra's floral chemodiversity is related to the unique island habitat of the island and consists of structurally diverse constituents, such as those of Dracaena, Aloe and Punica species [19] [22] [32]. The diversity results in hypotheses for drug discovery, but novelty and efficacy against infectious diseases must be proven experimentally and not just on the basis of endemism [2] [4] [10]. The compounds isolated from *D. cinnabari* and *A. perryi* can be used as potential lead compounds for future studies [16] [17] [21]-[23] [32]. However, the combined effects of multicomponent preparations and biomaterial combinations may be observed; this does not prove that there is synergy between the components unless quantitative testing is undertaken [35] [36]. Bioactivity guided fractionation and pharmacological profiling, followed by structure-activity analysis is suitable next step [37]

[38] and structure-activity analysis [39] [40]. The anti-infective effect of extracts of combined *D. cinnabari* and *A. perryi* is not supported by a recent study that reported anticancer activity [41]. A review of aloe-emodin likewise provides constituent-level evidence on pharmacological activity, safety, and formulation, but it does not establish species-specific activity for the plant extract [42]. In general, Socotra's chemical diversity is an interesting pool of hypothesized antimicrobials that could be tested.

4. Ethnopharmacological Heritage of Socotra

4.1. Traditional Healing Practices

The Socotra has a long ethnopharmacological history that can be found in social and ethnopharmacological sources including floristic, island-specific ethnopharmacological and Yemeni herbal-medicine literature [9] [43]-[45]. Traditional healers use decoctions, powders, resin and paste and a lot of knowledge is passed down orally [43]-[45]. There is a principal floristic and ethnobotanical reference for the medicinal taxa recorded from the archipelago by Miller and Morris [9]. There are factors, such as geographic isolation, and local ecological practices, that have played a role in developing this knowledge system [6] [7] [43]. However, traditional use should not be equated with experimental antimicrobial data, as in the case of species testing reported in selected Socotran plants [20] [46]. **Table 2** compares three well-known medicinal plants which are found only in certain regions of the world and the evidentiary boundaries of each profile.

4.2. Plants Used for Infections

Traditional use of Socotran plants for infections is significant part of the ethnopharmacological record of the island and traditional use is different from experimentally proven activity. The use of *Dracaena cinnabari* resin has been well documented ethnobotanically [9] [16] [45] [47] and in species-specific studies, antibacterial and antifungal activity has been reported [16] [20]. The Ag/Ag_2O study is an example of extract-assisted synthesis of the silver containing nanomaterial and not proof of the intrinsic activity of the resin [51]. Although there are direct phytochemical and preliminary pharmacological evidences supporting the use of *Aloe perryi* as a traditional medicinal species, the evidence for use of *Aloe vera*, isolated aloe-emodin, aloin or other Aloe taxa remains indirect [9] [17] [21]. Traditional uses of *Boswellia elongata* are reported from Socotra [9] [45] while indirect reports concerning the pharmacological properties of *Boswellia serrata* and general Boswellia literature are reported for *B. elongata* [26] [27]. A genus-level review of Commiphora provides indirect phytochemical and pharmacological context, but it does not establish species-specific evidence for the Socotran taxon [52]. The traditional uses documented for *Punica protopunica* [9] [18] [45] and the antibacterial and antiplasmodial evidences found in *Punica granatum* should not be automatically transferred to *Punica protopunica* [30] [49] [50].

These differences are crucial for the application of ethnomedicinal knowledge in controlled bioassays, elucidation of mechanisms [3] [53].

4.3. Broader Therapeutic Applications

Medicinal plants of Socotra are used for infections and health concerns at a broader level as mentioned in the sources from various regions and islands [9] [43]-[45]. In general reviews, the broader therapeutic use or effectiveness of medicinal plants is described, but these data can be relevant to any specific Socotran use or effect. The gastrointestinal and respiratory applications are mainly due to the ethnobotanical records of Yemenites and Socotrians [9] [44] [45]. Gastrointestinal and anthelmintic uses have been reported for *Punica protopunica* [9] [18] and the anthelmintic data of *Punica granatum* has been indirect *in vivo* [49] [50]. A more extensive literature on the antibacterial properties of plant compounds is available, but does not offer evidence of a local practice [54]. Similarly, the evidence derived from Ayurveda around inflammatory joint disorders is comparative and should not be used as evidence of Socotran use [55]. More broadly, reviews of natural products summarize antimicrobial and anti-infective activity across diverse compounds but do not replace species-specific validation of Socotran materials [56]. The importance of direct validation of local materials is evident from the species-specific phytochemical and antimicrobial screening of *Vernonia amygdalina* collected in Socotra [46].

5. Pharmacological Validation

5.1. *In Vitro* Antibacterial, Antifungal, and Antiparasitic Activities

The findings obtained *in vitro* must be confirmed and evaluated *in vivo* for therapeutic translation and safety [52] [57]. Traditional uses and biological activity have been reported for *Dracaena cinnabari* [16] [22] [23] and its direct acute and sub-acute oral toxicity has been assessed in rats [48]. More comprehensive studies of wound infection can be used to make decisions about models, but should not be confused with studies of *D. cinnabari* [34] [58]. There is no species-specific metabolite evidence for *Aloe perryi* and only constituent level evidence exists for safety and formulation of isolated aloe-emodin [33]. It was not found any *in vivo* anthelmintic study in *Punica protopunica*, and the available *in vivo* data is available in animal studies, which is indirect [49] [50]. In the same way, *in vivo* anti-inflammatory activity of other Boswellia and Commiphora species cannot be directly attributed to *Boswellia elongata* or *Commiphora ornifolia* [24] [27]. The restrictions facilitate dose standardization and authentic materials and systematic follow-up studies.

5.2. *In Vivo* Studies and Toxicity Data

In vitro findings require *in vivo* confirmation and safety assessment before therapeutic translation [52] [57]. For *Dracaena cinnabari*, the literature reports traditional use and biological activity [16] [22] [23], while direct acute and sub-acute

oral toxicity has been evaluated in rats [48]. Broader wound-infection studies can inform model selection but should not be misattributed to *D. cinnabari* [34] [58]. *Aloe perryi* has species-specific metabolite, *in vitro*, *in vivo*, and computational profiling [21]; safety and formulation evidence for isolated aloe-emodin remains constituent-level evidence [33]. No direct *in vivo* anthelmintic study of *Punica protopunica* was identified among the cited sources; available animal evidence concerns *Punica granatum* and is therefore indirect [49] [50]. Similarly, *in vivo* anti-inflammatory findings from other Boswellia and Commiphora taxa cannot be assigned directly to *Boswellia elongata* or *Commiphora ornifolia* [24] [27]. These limitations support dose standardization, authenticated materials, and systematic follow-up studies.

5.3. Mechanistic Insights into Bioactivity

Mechanistic explanation of medicinal activity of plants demands supporting evidence associated with an accepted species or the isolated compound [3] [42] [52] [54] [59] [60]. The species-specific antimicrobial evidence reported for *D. cinnabari* resin [16] [20] is based on inhibitory effects on membranes, nucleic-acid processes, adhesion, biofilms or fungal sterols, which are hypotheses based on general phytochemical mechanisms and constituent literature [22] [23] [42] [54] [59] [60]. There is also a lack of mechanistic evidence for *Aloe perryi* [17] [21]. Isolated aloe-emodin, hydroxyanthracene derivative studies or synthetic phosphoramidate analogues do not provide evidence of the mechanism of *A. perryi* extracts [32] [33] [40] [61]. There is species-specific evidence on antibacterial and antiplasmodial properties for *Punica protopunica* [15] [19] [20] and the proposed mechanisms of action of tannins were mainly represented by those of *Punica granatum* or by the tannin literature [30] [50] [62]. Mechanistic claims have not been made for *Commiphora ornifola* and *Boswellia elongata* from other species. Although traditional co-use of resins or bark or leaves gives an ethnopharmacological basis for investigation [43]-[45] it does not show synergy. Future studies should involve integration of bioactivity-guided fractionation and chemical profiling [37] [38] with controlled membrane, enzyme, biofilm, omics, docking and ADMET approach [63]-[66].

6. Lead Compound Optimization and Drug Design

6.1. From Extracts to Bioactive Leads (Isolation, SAR)

Isolation and characterization of active constituents are central to progression from crude extracts to candidate leads [37] [38]. Whole extracts and multicomponent materials can show combined biological effects, but pharmacological synergy must be demonstrated quantitatively [35] [36]. Direct profiles of *Dracaena cinnabari* and *Aloe perryi* identify flavonoid-, proanthocyanidin-, and anthraquinone-related constituents [16] [17] [21]-[23] [32]. Bioactivity-guided fractionation can then associate individual constituents with measured effects [37]. Structure-activity relationship analysis evaluates how functional groups and stereo-

chemistry influence potency, selectivity, and safety [39]; the aloe-emodin derivatives and broader anthraquinone literature illustrate this principle [40] [61]. The prism and pharmacophylogenetic perspectives can further assist in prioritizing taxa and scaffolds [11]-[14].

6.2. Optimization Strategies (Semi-Synthetic, Nanoformulation)

Once bioactive leads have been identified, optimization may be required to address potency, solubility, stability, and pharmacokinetic limitations [4] [67]. Semisynthetic modification is a general strategy for improving natural-product scaffolds [4]. For Boswellia, however, relevant chemistry and pharmacology derive largely from *Boswellia serrata* or general boswellic-acid literature and should not be attributed directly to *Boswellia elongata* [26] [27]. Modification of *Punica protopunica* ellagitannin-related scaffolds remains a prospective strategy; the rapid biotransformation of dietary tannins provides a rationale for investigating stability and metabolism but does not demonstrate an optimized *P. protopunica* derivative [62]. Nanoformulation may improve delivery of poorly soluble plant compounds, as discussed for aloe-emodin and natural products more generally [4] [33].

Plant extracts may also serve as reducing and stabilizing agents in the green synthesis of metal-based nanomaterials. In one study, dragon's blood extract solution derived from *Dracaena cinnabari* was used to synthesize Ag/Ag_2O core/shell nanostructures, as **Figure 6** illustrates [51]. However, the resulting product is a synthetic silver-containing nanomaterial rather than a naturally occurring constituent of *D. cinnabari* resin. Therefore, any antibacterial activity observed for the final Ag/Ag_2O material may arise from the silver component, its nanoscale properties, or interactions between silver and plant-derived molecules. This study should consequently be interpreted as an example of extract-assisted nanomaterial development and not as evidence of the intrinsic antimicrobial activity or mechanism of *D. cinnabari* resin.

Figure 6. Dragon's blood extract solution used in the extract-assisted synthesis of Ag/Ag_2O core/shell nanostructures [51]. The resulting product is a synthetic silver-containing nanomaterial and should not be interpreted as evidence of the intrinsic antimicrobial activity of *Dracaena cinnabari* resin.

For example, nanoparticle formulations of aloe-emodin may improve antimicrobial activity while limiting gastrointestinal irritation. Nevertheless, such formulations are engineered delivery systems and do not establish the activity or mechanism of constituents naturally isolated from *Aloe perryi*. Aloe-emodin may also serve as a chemical scaffold for semisynthetic lead optimization. α-Amino phosphoramidate derivatives of aloe-emodin, shown in Figure 7, have been synthesized and evaluated for DNA interaction and biological activity [61]. These derivatives are designed synthetic analogues and are not constituents isolated from *Aloe perryi*. Consequently, their reported DNA-interaction, antimicrobial, or cytotoxic effects illustrate the optimization potential of an anthraquinone scaffold but do not establish the efficacy, potency, or mechanism of *A. perryi* extracts or of the naturally occurring constituents present in the plant.

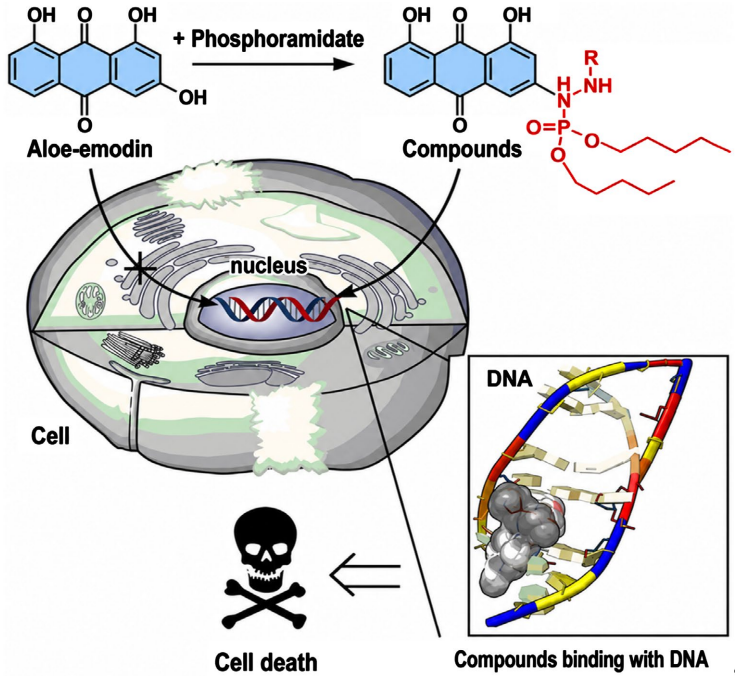


Figure 7. Synthesis and DNA interaction of synthetic aloe-emodin *α*-amino phosphoramidate derivatives [61]. These compounds are designed synthetic analogues and are not constituents isolated from *Aloe perryi*; therefore, the findings do not establish the activity or mechanism of the plant or its naturally occurring constituents.

Advanced delivery systems can enable targeted release, reduce systemic toxicity, and improve therapeutic outcomes. The integration of semisynthetic chemistry and nanotechnology therefore provides a powerful set of tools for converting plant-derived molecules into clinically useful drug candidates.

6.3. Computational Approaches (Docking, ADMET, AI)

Computational methods can help prioritize plant-derived compounds for experimental testing. Published docking studies illustrate approaches for evaluating plant compounds or peptides against microbial targets [63]-[65], while in silico

polypharmacology provides a framework for assessing interactions across multiple targets [68]. These studies are methodological analogues and do not establish species-specific binding of *Dracaena cinnabari* or *Aloe perryi* constituents unless the named compound and target were examined directly. ADME and toxicity properties can be estimated using herbal-medicine pharmacokinetic principles and tools such as SwissADME and pkCSM [66] [67]. Machine-learning methods can support pattern recognition, activity prediction, and structure optimization [69]. Computational predictions should guide, not replace, biochemical and *in vivo* validation.

7. Conservation, Bioprospecting, and ABS

Socotra's medicinal flora is exceptionally endemic and faces documented pressures from habitat degradation, climate, limited regeneration, and unsustainable resource use [5]-[7] [47]. Evidence from threatened medicinal plants in other regions is useful for comparison but is not direct evidence of conditions on Socotra [70]. Conservation strategies should protect both biodiversity and local ethnopharmacological knowledge. Indigenous and local knowledge can make an important contribution to stewardship and conservation [43] [71] [72], while spatial phylogenetics and biocultural analysis can help identify priorities [73]. Ethical bioprospecting should involve local stakeholders and equitable benefit-sharing. In this context, the Nagoya Protocol provides the relevant international framework for access to genetic resources and fair and equitable sharing of benefits.

8. Conclusion and Outlook

The available evidence supports the medicinal importance of Socotra's flora but varies substantially by species and endpoint. Species-specific anti-infective evidence is strongest for selected *Dracaena cinnabari* and *Punica protopunica* extracts [15] [16] [18]-[20] [22] [23], while *Aloe perryi* has stronger phytochemical and preliminary pharmacological evidence than direct antimicrobial validation [17] [21]. Claims concerning *Boswellia elongata* and *Commiphora ornifolia* should remain cautious when they derive from related taxa [24] [26] [27]. Future work should use authenticated materials, standardized bioassays, bioactivity-guided fractionation, mechanistic validation, and safety testing [37] [38] [48] [52]. Phylogenetic and spatial prioritization [11]-[14] [73], followed by docking, ADMET, and machine-learning workflows [63]-[66] [68] [69], may accelerate lead identification but cannot substitute for experimental confirmation. Conservation, community stewardship, and equitable bioprospecting remain essential to sustainable development of this resource [71]-[73].

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Declaration of Generative AI and AI-Assisted Technologies in Manuscript Preparation

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) and Claude (Anthropic) solely for limited language editing, grammar correction, and improvement of the clarity and readability of selected sections of the manuscript. Neither AI tool was used to generate or fabricate research data, analyze data, interpret results, develop scientific findings, or prepare references. The research ideas, methodology, data, results, conclusions, and intellectual contributions of the manuscript are entirely those of the authors. All AI-assisted suggestions were carefully reviewed and revised where necessary by the authors, who take full responsibility for the accuracy, integrity, and final content of the manuscript.

Author Contributions

Ahmed Al-shawafi: Conceptualization; methodology; validation; formal analysis; investigation; data curation; writing—original draft preparation; visualization; project administration.

Rehab Al-shawafi: Methodology; validation; investigation; writing—review and editing.

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Conflicts of Interest

The authors declare no conflict of interest.

References

[1] Maděra, P., Forrest, A., Hanáček, P., Vahalík, P., Gebauer, R., Plichta, R., *et al.* (2020) What We Know and What We Do Not Know about Dragon Trees? *Forests*, **11**, Article No. 236. https://doi.org/10.3390/f11020236

[2] Alara, J.A. and Alara, O.R. (2024) An Overview of the Global Alarming Increase of Multiple Drug Resistant: A Major Challenge in Clinical Diagnosis. *Infectious Disorders—Drug Targets*, **24**, 26-42. https://doi.org/10.2174/1871526523666230725103902

[3] Davis, C.C. and Choisy, P. (2024) Medicinal Plants Meet Modern Biodiversity Science. *Current Biology*, **34**, R158-R173. https://doi.org/10.1016/j.cub.2023.12.038

[4] Attorre, F. and Van Damme, K. (2020) Twenty Years of Biodiversity Research and Nature Conservation in the Socotra Archipelago (Yemen). *Rendiconti Lincei. Scienze Fisiche e Naturali*, **31**, 563-569. https://doi.org/10.1007/s12210-020-00941-7

[5] Saraf, S. (2021) Preserving the Perishing Endangered Natural Biodiversity of Socotra Island. *Open Journal of Ecology*, **11**, 148-162. https://doi.org/10.4236/oje.2021.112013

[6] Hao, D.-C. and Xiao, P.G. (2026) Medicinal Plants: Chemistry, Biology and Omics. Elsevier/Woodhead Publishing.

[7] Hao, D., Spjut, R.W., Deng, D., He, C. and Yao, R. (2025) Editorial: Plant Metabolites in Drug Discovery: The Prism Perspective between Plant Phylogeny, Chemical Composition, and Medicinal Efficacy, Volume IV. *Frontiers in Pharmacology*, **16**, Article ID: 1666900. https://doi.org/10.3389/fphar.2025.1666900

[8] Mothana, R., Al-Musayeib, N., Matheeussen, A., Cos, P. and Maes, L. (2012) Assessment of the *in Vitro* Antiprotozoal and Cytotoxic Potential of 20 Selected Medicinal Plants from the Island of Soqotra. *Molecules*, **17**, 14349-14360. https://doi.org/10.3390/molecules171214349

[9] Hao, D.-C., Wang, Y.X., Xiao, P.G. and Gu, X. (2024) Phylogenetic and Spatial Patterns of Herbal Medicine Compounds: Which Medicinal Plants Are Phytochemically Characterized? *Chinese Herbal Medicines*, **16**, 589-598. https://doi.org/10.1016/j.chmed.2024.07.001

[10] Kaur, N. and Ahmed, T. (2021) Bioactive Secondary Metabolites of Medicinal and Aromatic Plants and Their Disease-Fighting Properties. In: Aftab, T. and Hakeem, K.R., Eds., *Medicinal and Aromatic Plants: Healthcare and Industrial Applications*, Springer International Publishing, 113-142. https://doi.org/10.1007/978-3-030-58975-2_4

[11] Sychrová, A., Kolářiková, I., Žemlička, M. and Šmejkal, K. (2020) Natural Compounds with Dual Antimicrobial and Anti-Inflammatory Effects. *Phytochemistry Reviews*, **19**, 1471-1502. https://doi.org/10.1007/s11101-020-09694-5

[12] Peres, I.S.A., Conceição, K.A.O., Silva, L.A.F., Khouri, N.G., Yoshida, C.M.P., Concha, V.O.C., *et al.* (2023) Dragon's Blood: Antioxidant Properties for Nutraceuticals and Pharmaceuticals. *Rendiconti Lincei. Scienze Fisiche e Naturali*, **34**, 131-142. https://doi.org/10.1007/s12210-022-01122-4

[13] Shaygannia, E., Bahmani, M., Zamanzad, B. and Rafieian-Kopaei, M. (2016) A Review Study on *Punica granatum* L. *Journal of Evidence-Based Complementary & Alternative Medicine*, **21**, 221-227. https://doi.org/10.1177/2156587215598039

[14] Al-Fatimi, M. (2018) Ethnobotanical Survey of *Dracaena cinnabari* and Investigation of the Pharmacognostical Properties, Antifungal and Antioxidant Activity of Its Resin. *Plants*, **7**, Article No. 91. https://doi.org/10.3390/plants7040091

[15] Bittner Fialová, S., Rendeková, K., Mučaji, P., Nagy, M. and Slobodníková, L. (2021) Antibacterial Activity of Medicinal Plants and Their Constituents in the Context of Skin and Wound Infections, Considering European Legislation and Folk Medicine—A Review. *International Journal of Molecular Sciences*, **22**, Article No. 10746. https://doi.org/10.3390/ijms221910746

[16] Salehi, B., Albayrak, S., Antolak, H., Kręgiel, D., Pawlikowska, E., Sharifi-Rad, M., *et al.* (2018) Aloe Genus Plants: From Farm to Food Applications and Phytopharmacotherapy. *International Journal of Molecular Sciences*, **19**, Article No. 2843. https://doi.org/10.3390/ijms19092843

[17] Almansory, A.H., Al-Shaibani, E.A., Shediwah, F.M., *et al.* (2026) Analysis of Bioactive Phytochemicals in *Aloe perryi* Aqueous Leaf Gel Extract Using FT-IR, GC-MS and HPLC Techniques. *Sana'a University Journal of Applied Sciences and Technology*, **4**, 1844-1856. https://doi.org/10.59628/jast.v4i3.2389

[18] Guerrero-Solano, J.A., Jaramillo-Morales, O.A., Jiménez-Cabrera, T., Urrutia-Hernández, T.A., Chehue-Romero, A., Olvera-Hernández, E.G., *et al.* (2020) *Punica protopunica* Balf., the Forgotten Sister of the Common Pomegranate (*Punica granatum* L.): Features and Medicinal Properties—A Review. *Plants*, **9**, Article No. 1214. https://doi.org/10.3390/plants9091214

[19] Gupta, D., Bleakley, B. and Gupta, R.K. (2008) Dragon's Blood: Botany, Chemistry

and Therapeutic Uses. *Journal of Ethnopharmacology*, **115**, 361-380. https://doi.org/10.1016/j.jep.2007.10.018

[20] Merino, J.J., Durán, A.G., Chinchilla, N. and Macías, F.A. (2025) Biological Activities of Hydroxyanthracene Derivatives (HADs) from Aloe Species and Their Potential Uses. *Phytochemistry Reviews*, **24**, 2387-2415. https://doi.org/10.1007/s11101-025-10089-7

[21] Al-Huqail, A.A., Elgaaly, G.A. and Ibrahim, M.M. (2018) Identification of Bioactive Phytochemical from Two Punica Species Using GC-MS and Estimation of Antioxidant Activity of Seed Extracts. *Saudi Journal of Biological Sciences*, **25**, 1420-1428. https://doi.org/10.1016/j.sjbs.2015.11.009

[22] Al-Arnoot, S., *et al.* (2025) Multitarget Antimicrobial Mechanisms of Plant Extracts: A Review of Harnessing Phytochemicals against Drug-Resistant Pathogens. *Sana'a University Journal of Medicine and Health Sciences*, **19**, 292-309. https://doi.org/10.59628/jchm.v19i4.1936

[23] Sloan, L.M. and Alawi, A.A.O.B. (2023) Sustainable Environmental Practices of Socotra People. In: Slak Valek, N. and Zedan, A.A., Eds., *A Social View of Socotra Island*: *People*, *Culture*, *Heritage*, Springer, 23-52. https://doi.org/10.1007/978-981-99-4358-6_2

[24] Hehmeyer, I., Schönig, H. and Regourd, A. (2012) Herbal Medicine in Yemen: Traditional Knowledge and Practice, and Their Value for Today's World. Brill. https://doi.org/10.1163/9789004232075

[25] Miller, A.G. and Morris, M. (2004) Ethnoflora of the Soqotra Archipelago. Royal Botanic Garden Edinburgh.

[26] Mothana, R.A.A. and Lindequist, U. (2005) Antimicrobial Activity of Some Medicinal Plants of the Island Soqotra. *Journal of Ethnopharmacology*, **96**, 177-181. https://doi.org/10.1016/j.jep.2004.09.006

[27] Saraf, S. (2023) Dragon's Blood Tree (*Dracaena cinnabari*): A Cenozoic Relict. In: Shah, M.M., Ed., *Endangered Species—Present Status*, IntechOpen, 83-104. https://doi.org/10.5772/intechopen.112282

[28] Armani, M.A., Abu-Taleb, A., Remalli, N., Abdullah, M., Srikanth, V.V.S.S. and Labhasetwar, N.K. (2016) Dragon's Blood-Aided Synthesis of Ag/Ag_2O Core/Shell Nanostructures and Ag/Ag_2O Decked Multi-Layered Graphene for Efficient As(III) Uptake from Water and Antibacterial Activity. *RSC Advances*, **6**, 44145-44153. https://doi.org/10.1039/c6ra05061a

[29] Alam, T., Khan, S.A. and Najam, L. (2021) Chemistry, Biological Activities, and Uses of Resin of *Boswellia serrata* Roxb. In: Murthy, H.N., Ed., *Gums*, *Resins and Latexes of Plant Origin*: *Chemistry*, *Biological Activities and Uses*, Springer International Publishing, 1-43. https://doi.org/10.1007/978-3-030-76523-1_25-1

[30] He, S.-M., Chan, E. and Zhou, S.-F. (2011) ADME Properties of Herbal Medicines in Humans: Evidence, Challenges and Strategies. *Current Pharmaceutical Design*, **17**, 357-407. https://doi.org/10.2174/138161211795164194

[31] Ansari, P., Reberio, A.D., Ansari, N.J., Kumar, S., Khan, J.T., Chowdhury, S., *et al.* (2025) Therapeutic Potential of Medicinal Plants and Their Phytoconstituents in Diabetes, Cancer, Infections, Cardiovascular Diseases, Inflammation and Gastrointestinal Disorders. *Biomedicines*, **13**, Article No. 454. https://doi.org/10.3390/biomedicines13020454

[32] Lavecchia, A. and Cerchia, C. (2016) *In Silico* Methods to Address Polypharmacology: Current Status, Applications and Future Perspectives. *Drug Discovery Today*,

21, 288-298. https://doi.org/10.1016/j.drudis.2015.12.007

[33] Kaiaty, A.M., Salib, F.A., El-Gameel, S.M., Hussien, A.M. and Kamel, M.S. (2021) Anthelmintic Activity of Pomegranate Peel Extract (*Punica granatum*) and Synthetic Anthelmintics against Gastrointestinal Nematodes in Cattle, Sheep, Goats, and Buffalos: *In Vivo* Study. *Parasitology Research*, **120**, 3883-3893. https://doi.org/10.1007/s00436-021-07311-8

[34] Álvarez-Martínez, F.J., Barrajón-Catalán, E., Herranz-López, M. and Micol, V. (2021) Antibacterial Plant Compounds, Extracts and Essential Oils: An Updated Review on Their Effects and Putative Mechanisms of Action. *Phytomedicine*, **90**, Article ID: 153626. https://doi.org/10.1016/j.phymed.2021.153626

[35] Chopra, A., Saluja, M. and Tillu, G. (2010) Ayurveda-Modern Medicine Interface: A Critical Appraisal of Studies of Ayurvedic Medicines to Treat Osteoarthritis and Rheumatoid Arthritis. *Journal of Ayurveda and Integrative Medicine*, **1**, 190-198. https://doi.org/10.4103/0975-9476.72620

[36] Almakhzoum, K.A.A.H., Qasem, K.M.A. and Saleh, H.A.M. (2025) Phytochemical, Antioxidant, and Antimicrobial Screening of *Vernonia amygdalina* Leaf Extract from Socotra, Yemen. *University of Aden Journal of Natural and Applied Sciences*, **29**, 19-28. https://doi.org/10.47372/uajnas.2025.n1.a03

[37] Ncama, K., Malele, J., Govender, D.M., Anumanthoo, T. and Moyo, M. (2025) Effectiveness of Common Extraction Solvents in Obtaining Antioxidant Compounds from African Medicinal Plants. *Antioxidants*, **14**, Article No. 1498. https://doi.org/10.3390/antiox14121498

[38] Almaghrebi, E., Akat, F. and Vatansev, H. (2024) Traditional Use of *Dracaena cinnabari*, Importance of Its Resin, Bioactivity Study of Isolated Chemical Structures. In: Attaur-Rahman, Ed., *Studies in Natural Products Chemistry*, Vol. 83, Elsevier, 431-463.

[39] Noites, A., Borges, I., Araújo, B., da Silva, J.C.G.E., de Oliveira, N.M., Machado, J., *et al.* (2023) Antimicrobial Activity of Some Medicinal Herbs to the Treatment of Cutaneous and Mucocutaneous Infections: Preliminary Research. *Microorganisms*, **11**, Article No. 272. https://doi.org/10.3390/microorganisms11020272

[40] Kopel, J., McDonald, J. and Hamood, A. (2022) An Assessment of the *in Vitro* Models and Clinical Trials Related to the Antimicrobial Activities of Phytochemicals. *Antibiotics*, **11**, Article No. 1838. https://doi.org/10.3390/antibiotics11121838

[41] El-Saadony, M.T., Saad, A.M., Mohammed, D.M., Korma, S.A., Alshahrani, M.Y., Ahmed, A.E., *et al.* (2025) Medicinal Plants: Bioactive Compounds, Biological Activities, Combating Multidrug-Resistant Microorganisms, and Human Health Benefits—A Comprehensive Review. *Frontiers in Immunology*, **16**, Article ID: 1491777. https://doi.org/10.3389/fimmu.2025.1491777

[42] Luo, H., Ji, X., Zhang, M., Ren, Y., Tan, R., Jiang, H., *et al.* (2024) Aloe-Emodin: Progress in Pharmacological Activity, Safety, and Pharmaceutical Formulation Applications. *Mini-Reviews in Medicinal Chemistry*, **24**, 1784-1798. https://doi.org/10.2174/0113895575298364240409064833

[43] Al-Afifi, N.A., Alabsi, A.M., Bakri, M.M. and Ramanathan, A. (2018) Acute and Sub-Acute Oral Toxicity of *Dracaena cinnabari* Resin Methanol Extract in Rats. *BMC Complementary and Alternative Medicine*, **18**, Article No. 50. https://doi.org/10.1186/s12906-018-2110-3

[44] Suliman, R.S., Alghamdi, S.S., Ali, R., Aljatli, D.A., Huwaizi, S., Suliman, R., *et al.* (2021) Metabolites Profiling, *in Vitro*, *in Vivo*, Computational Pharmacokinetics and Biological Predictions of *Aloe perryi* Resins Methanolic Extract. *Plants*, **10**, Article

No. 1106. https://doi.org/10.3390/plants10061106

[45] El-Sayed, S.H., Mahmoud, S.S., El-Shenawy, A.M. and Yousof, H.S.A. (2023) Anti-helminthic Effect of *Punica granatum* Peel Extract on *Trichinella spiralis* Worms and Muscle Larvae: *in Vitro* and *in Vivo* Studies. *Journal of Parasitic Diseases*, **47**, 416-424. https://doi.org/10.1007/s12639-023-01586-7

[46] Kunnumakkara, A.B., Banik, K., Bordoloi, D., Harsha, C., Sailo, B.L., Padmavathi, G., *et al.* (2018) Googling the Guggul (Commiphora and Boswellia) for Prevention of Chronic Diseases. *Frontiers in Pharmacology*, **9**, Article No. 686. https://doi.org/10.3389/fphar.2018.00686

[47] Hao, D.-C. and Xiao, P.G. (2020) Pharmaceutical Resource Discovery from Traditional Medicinal Plants: Pharmacophylogeny and Pharmacophylogenomics. *Chinese Herbal Medicines*, **12**, 104-117. https://doi.org/10.1016/j.chmed.2020.03.002

[48] Al-Fatimi, M. (2023) Ethnopharmacological Survey of Endemic Plants Used in Ethnomedicinal Knowledge of Soqotra Island. *Journal of Ethnopharmacology*, **304**, Article ID: 116033. https://doi.org/10.1016/j.jep.2022.116033

[49] Hao, D., Wang, Y., Spjut, R.W. and He, C. (2024) Editorial: Plant Metabolites in Drug Discovery: The Prism Perspective between Plant Phylogeny, Chemical Composition, and Medicinal Efficacy, Volume III. *Frontiers in Pharmacology*, **15**, Article ID: 1530039. https://doi.org/10.3389/fphar.2024.1530039

[50] Zhang, Q., Wang, J., Lan, F., Zhai, H., Li, F., Ma, T., *et al.* (2023) Synthesis and DNA Interaction of Aloe-Emodin *α*-Amino Phosphate Derivatives. *Journal of Molecular Structure*, **1279**, Article ID: 134950. https://doi.org/10.1016/j.molstruc.2023.134950

[51] Tiwari, R., Latheef, S.K., Ahmed, I., Iqbal, H.M.N., Bule, M.H., Dhama, K., *et al.* (2018) Herbal Immunomodulators—A Remedial Panacea for Designing and Developing Effective Drugs and Medicines: Current Scenario and Future Prospects. *Current Drug Metabolism*, **19**, 264-301. https://doi.org/10.2174/1389200219666180129125436

[52] Yang, Y., Sun, X., Peng, C., Wei, J. and Yang, X. (2024) The Genus Commiphora: An Overview of Its Traditional Uses, Phytochemistry, Pharmacology, and Quality Control. *Pharmaceuticals*, **17**, Article No. 1524. https://doi.org/10.3390/ph17111524

[53] Shao, M., Bigham, A., Yousefiasl, S., Yiu, C.K.Y., Girish, Y.R., Ghomi, M., *et al.* (2023) Recapitulating Antioxidant and Antibacterial Compounds into a Package for Tissue Regeneration: Dual Function Materials with Synergistic Effect. *Small*, **19**, e2207057. https://doi.org/10.1002/smll.202207057

[54] Ahmad, I., Husain, F.M., Maheshwari, M. and Zahin, M. (2014) Medicinal Plants and Phytocompounds: A Potential Source of Novel Antibiofilm Agents. In: Rumbaugh, K.P. and Ahmad, I., Eds., *Antibiofilm Agents: From Diagnosis to Treatment and Prevention*, Springer, 205-232. https://doi.org/10.1007/978-3-642-53833-9_10

[55] AL-Azzawi, M.K., Hasan, N.A. and Barrak, M.M. (2024) A Review of the Development of an Understanding of Antibiotic Interactions, from Mechanisms of Action to Novel Resistance and the Search for Natural Alternatives. *Journal of Medical Genetics and Clinical Biology*, **1**, 78-102. https://doi.org/10.61796/jmgcb.v1i6.585

[56] Fernandes, E.S., da Silva Figueiredo, I.F., Monteiro, C.R.A.V. and Monteiro-Neto, V. (2023) Antimicrobial and Anti-Infective Activity of Natural Products—Gaining Knowledge from Novel Studies. *Antibiotics*, **12**, Article No. 1051. https://doi.org/10.3390/antibiotics12061051

[57] Garcia Porta, J. (2014) Evolution and Diversification of the Geckos of the Arabian Peninsula and Socotra Archipelago, Compared to Other Mainland-Island Systems.

Doctoral Thesis, Universitat de Barcelona. https://hdl.handle.net/2445/60455

[58] Das, D. and Shafi, S. (2023) Bioactivity-Guided Fractionation and Identification of Bioactive Molecules: A Basic Method in Drug Discovery. In: Rajput, V.S. and Runthala, A., Eds., *Drugs and a Methodological Compendium*: *From Bench to Bedside*, Springer, 41-78. https://doi.org/10.1007/978-981-19-7952-1_3

[59] Ogbuagu, O.O., Mbata, A.O., Balogun, O.D., Oladapo, O. and Ojo, O.O. (2022) Novel Phytochemicals in Traditional Medicine: Isolation and Pharmacological Profiling of Bioactive Compounds. *International Journal of Medical and All Body Health Research*, **3**, 63-71. https://doi.org/10.54660/ijmbhr.2022.3.1.63-71

[60] Atef, A.A.A., Ismail, S.M.A. and Saeed, A.A.M. (2025) Synergistic Anticancer Effects of *Dracaena cinnabari* and *Aloe perryi* Extracts on Colorectal Cancer Cells: A Flow Cytometry Analysis of Toxicity, Cell Cycle, Apoptosis, and Autophagy. *Letters in Drug Design & Discovery*, **22**, Article ID: 100196. https://doi.org/10.1016/j.lddd.2025.100196

[61] Vaishnav, Y., Verma, S. and Mishra, A. (2025) The Role of Structure-Activity Relationship (SAR) in Drug Discovery. *Indian Journal of Pharmaceutical Chemistry and Analytical Techniques*, **1**, 67-83. https://ijpcat.com/index.php/1/article/view/6

[62] Robin, Choudhary, S., Gupta, V., Kaur, P. and Thind, T.S. (2025) Anthraquinones: Integrated Perspectives on Analytical Methodologies and Functional Applications. In: Kaur, P., Kumar, A., Robin, *et al.*, Eds., *Anthraquinones*: *Bioactive Multifaceted Therapeutic Agents*, Bentham Science Publishers, 1-59. https://doi.org/10.2174/9789815313987125030004

[63] Sah, A.K., Patel, S., Kumar, R., Mishra, P.S., Mishra, R., Umarovich, A.I., *et al.* (2026) Therapeutic Applications of Natural Products in Biomedicine and Pharmacotherapy. *Life*, **16**, Article No. 873. https://doi.org/10.3390/life16060873

[64] Sallam, I.E., Abdelwareth, A., Attia, H., Aziz, R.K., Homsi, M.N., von Bergen, M., *et al.* (2021) Effect of Gut Microbiota Biotransformation on Dietary Tannins and Human Health Implications. *Microorganisms*, **9**, Article No. 965. https://doi.org/10.3390/microorganisms9050965

[65] Boreak, N., Al Mahde, R.Z., Otayn, W.A., Alamer, A.Y., Alrajhi, T., Jafri, S., *et al.* (2024) Exploring Plant-Based Compounds as Alternatives for Targeting Enterococcus Faecalis in Endodontic Therapy: A Molecular Docking Approach. *International Journal of Molecular Sciences*, **25**, Article No. 7727. https://doi.org/10.3390/ijms25147727

[66] Bhat, B.A., Mir, W.R., Sheikh, B.A., Alkanani, M. and Mir, M.A. (2022) Metabolite Fingerprinting of Phytoconstituents from *Fritillaria cirrhosa* D. Don and Molecular Docking Analysis of Bioactive Peonidin with Microbial Drug Target Proteins. *Scientific Reports*, **12**, Article No. 7296. https://doi.org/10.1038/s41598-022-10796-7

[67] Mustafa, G., Mehmood, R., Mahrosh, H.S., Mehmood, K. and Ahmed, S. (2022) Investigation of Plant Antimicrobial Peptides against Selected Pathogenic Bacterial Species Using a Peptide-Protein Docking Approach. *BioMed Research International*, **2022**, Article ID: 1077814. https://doi.org/10.1155/2022/1077814

[68] Azzam, K.A. (2023) SwissADME and pkCSM Webservers Predictors: An Integrated Online Platform for Accurate and Comprehensive Predictions for *in Silico* ADME/T Properties of Artemisinin and Its Derivatives. *Kompleksnoe Ispolzovanie Mineralnogo Syra*, **325**, 14-21. https://doi.org/10.31643/2023/6445.13

[69] Lavecchia, A. (2015) Machine-Learning Approaches in Drug Discovery: Methods and Applications. *Drug Discovery Today*, **20**, 318-331. https://doi.org/10.1016/j.drudis.2014.10.012

[70] Groner, V.P., Nicholas, O., Mabhaudhi, T., Slotow, R., Akçakaya, H.R., Mace, G.M., *et al.* (2022) Climate Change, Land Cover Change, and Overharvesting Threaten a Widely Used Medicinal Plant in South Africa. *Ecological Applications*, **32**, e2545. https://doi.org/10.1002/eap.2545

[71] Abas, A., Aziz, A. and Awang, A. (2022) A Systematic Review on the Local Wisdom of Indigenous People in Nature Conservation. *Sustainability*, **14**, Article No. 3415. https://doi.org/10.3390/su14063415

[72] Hao, D., Wang, Y., Deng, D., Chen, Z., Spjut, R.W. and Xiao, P. (2026) Local Ecological Knowledge with Stewardship Sustains Medicinal Plants Used by Ethnic Minorities in China. *Trends in Ecology & Evolution*, **41**, 275-278. https://doi.org/10.1016/j.tree.2026.01.006

[73] Hao, D.-C., Wang, Y.X., Chen, Z.D., *et al.* (2026) Spatial Phylogenetics and Biocultural Conservation of Medicinal Plants in Ethnic Minority Communities of China: Implications for Environmental Sustainability. *Biodiversity and Conservation*, **35**, Article No. 18. https://doi.org/10.1007/s10531-025-03239-y