Scientific African 28 (2025) e02644

Contents lists available at ScienceDirect

Scientific African

journal homepage: www.elsevier.com/locate/sciaf

Effectiveness of African herbal preparations against multidrug-resistant *Klebsiella pneumoniae*: A systematic review

Rachel A. A. Akorful, Karikari Asafo-Adjei, Fleischer C. N. Kotey, Eric S. Donkor [*]

Department of Medical Microbiology, University of Ghana Medical School, Korle Bu, P.O. Box KB 4236, Accra 00233, Ghana

ARTICLE INFO

Editor: DR B Gyampoh

Keywords:
Multidrug-resistant *Klebsiella pneumoniae*
Herbal preparations
Antimicrobial activity
Minimum inhibitory concentration
Minimum bactericidal concentration
Zone of inhibition
New treatment options
Traditional medicine
Antibiotic resistance

ABSTRACT

Multidrug-resistant *Klebsiella pneumoniae* (MDR-Kp) poses a significant public health challenge due to limited treatment options and growing antimicrobial resistance (AMR). The rise in MDR-Kp infections underscores the critical need for new strategies against antibiotic resistance, especially in Africa, where AMR is a pressing concern. This systematic review evaluated the antimicrobial activity of herbal preparations against MDR-Kp by assessing parameters such as minimum bactericidal concentration (MBC), zone of inhibition, and minimum inhibitory concentration (MIC). A literature search was done following the PRISMA guidelines, and relevant articles from PubMed, Scopus, and ScienceDirect were included. The search identified 2094 articles, of which 848 were selected for a full assessment and 31 were included. Data extraction included information on plant scientific names, botanical families, plant parts, country of origin, extract types, isolated compounds, and antimicrobial parameters. Of the 124 plants studied, *Withania frutescens L.*, *Plumbago zeylanica, Plectranthus glandulosus, Eruca sativa*, and *Donella welwitschii*, emerged as plants that could be further explored for anti-MDR-Kp therapeutics. Further research is needed to explore their mechanisms of action, active compounds, and potential synergies. Integrating traditional knowledge with modern healthcare practices, standardised research methodologies, and clinical validations can advance plant-based therapies. Additionally, conservation efforts are vital to preserve the biodiversity of these medicinal plants, ensuring their availability for future research and therapeutic use, while supporting environmental and public health.

Introduction

Klebsiella pneumoniae is a key clinically significant member of the Enterobacteriaceae family and is responsible for more than 70 % of human infections, such as those of the urinary, respiratory, and circulatory systems [1–5]. It ranks second among Gram-negative bacteria that cause hospital-acquired infections, contributing to about 10 % of such cases [4–6]. Populations that are most prone to *K. pneumoniae* infections include long-term care patients and immunocompromised persons, such as the elderly and neonates, in whom high fatalities occur [7–10]. In neonates, for example, it causes over 1.6 million deaths annually, especially in low-income regions [11]. Of prime concern is the emergence and rapid global dissemination of hypervirulent and multidrug-resistant strains of *K. pneumoniae*, an organism on the priority pathogen list of the World Health Organization (WHO) [6,12]. Prominent among the

---

[*] Corresponding author.
E-mail addresses: akorfulrachel@gmail.com (R.A.A. Akorful), kkasafoadjei@gmail.com (K. Asafo-Adjei), fleischarles@gmail.com (F.C.N. Kotey), esampane-donkor@ug.edu.gh (E.S. Donkor).

https://doi.org/10.1016/j.sciaf.2025.e02644
Received 16 November 2024; Received in revised form 5 January 2025; Accepted 12 March 2025

multidrug-resistant *K. pneumoniae* (MDR-Kp) strains are those that harbour extended-spectrum β-lactamases (ESBLs) and carbapenemases, which potentially confer resistance of the pathogen to even last-resort antimicrobials like carbapenems, increasing treatment failure and mortality [6,13–18]. In 2019, for instance, MDR-Kp caused 624,000 deaths globally due to AMR [19].

Africa, which shoulders a disproportionate share of the infectious diseases and antimicrobial resistance (AMR) burden, has seen an elevated occurrence of MDR-Kp infections in recent times [19]. As an example, up to 80 % prevalence of MDR-Kp cases have been reported in Kenya [20]. Similarly, prevalences of 87 % and 98.5 % of MDR-Kp have been reported in Ghana and Ethiopia, respectively [13,14]. The prevailing MDR-Kp crisis in the region demands that alternative sources of antimicrobials that could be effective against MDR-Kp are explored. To that end, medicinal plants, which are heavily relied on for disease management in Africa and other parts of the world, and products of which have been demonstrated to have varying effectiveness against multidrug-resistant pathogens, are suitable candidates [21–31]. Africa has a wealth of diverse plants and traditional knowledge with great potential for discovering new treatments [32]. The high burden of multidrug-resistant infections in the region [19], combined with limited access to effective antibiotics [33], makes African herbal remedies especially important to study. Unlike medicinal plants from other parts of the world, African herbal preparations are deeply rooted in traditional medicine, but remain under-researched, particularly regarding their effects on humans through clinical trials [32]. Due to the limited availability of clinical trial data and the predominance of *in vitro* studies related to antimicrobial activity of medicinal plants, this review aims to synthesise the available *in vitro* evidence related to MDR-Kp. *In vitro* studies provide valuable early insights into the antimicrobial potential of these herbal remedies against MDR-Kp and serve as a foundation for future clinical investigations. This review addresses the gap in systematic evidence on the subject by evaluating the antimicrobial activity of African herbal preparations against MDR-Kp, thereby contributing to the understanding of their therapeutic applications.

Materials and methods

Search strategy

A thorough systematic review, conducted following the guidelines outlined by the Preferred Reporting Items for Systematic

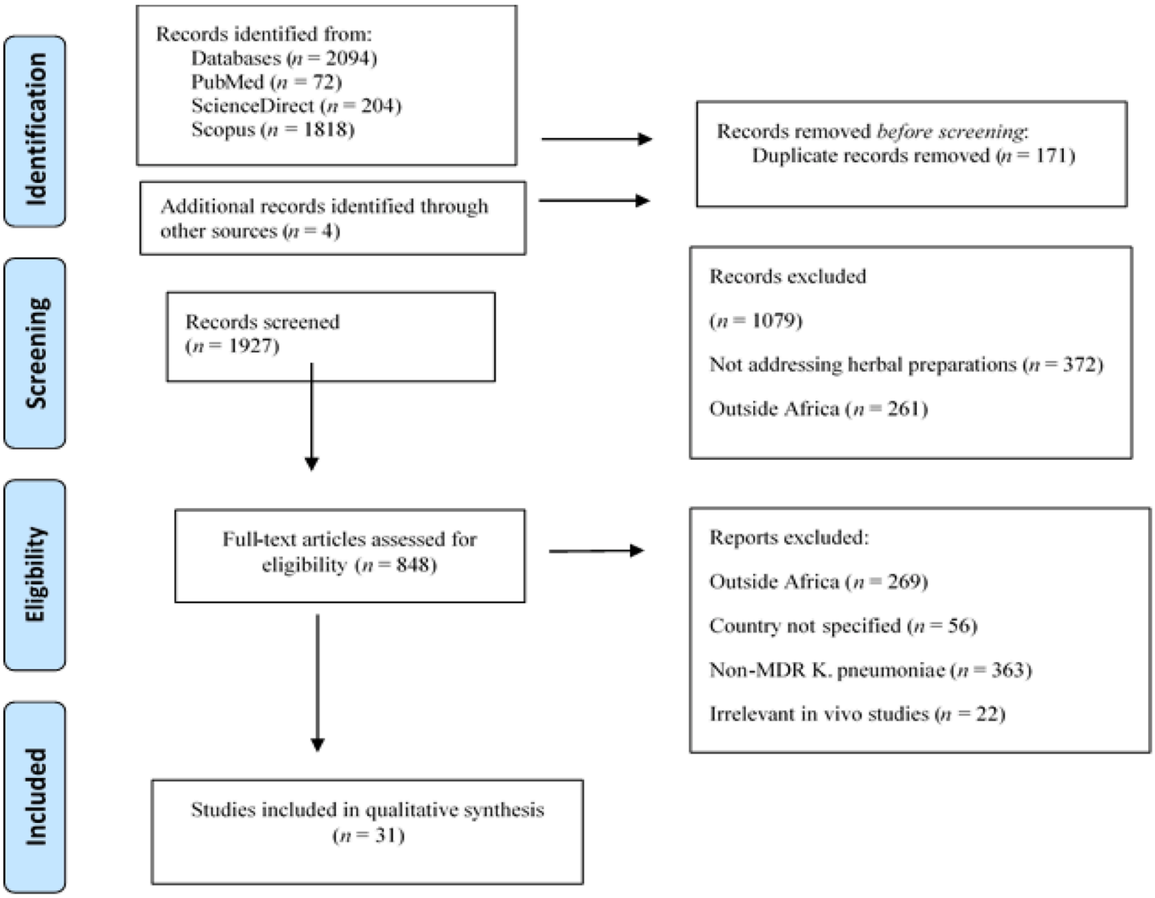

Fig. 1. PRISMA flow diagram of study selection.

Reviews and Meta-Analyses (PRISMA), was carried out via web-based platforms in March 2024. A comprehensive search on PubMed, Scopus, and ScienceDirect for *in vitro* studies evaluating the activity of African medicinal plants against bacteria was done to gather the relevant literature. The search was limited to articles that had been published by January 2024, and involved using MeSH terms in PubMed and a combination of keywords and African country names in Scopus and ScienceDirect.

For PubMed, the following MeSH search terms were used: ((“Plants, Medicinal” [Mesh]) OR “Drug Resistance, Multiple, Bacterial” [Mesh]) AND “*Klebsiella pneumoniae*” [Mesh]) AND “Africa” [Mesh]. Additionally, a separate search was performed using the terms ((“Plants, Medicinal” [Mesh]) OR “Drug Resistance, Multiple, Bacterial” [Mesh]) AND “Africa” [Mesh] to capture papers addressing multidrug-resistant bacteria without specifically focusing on *Klebsiella pneumoniae*.

In the case of Scopus, the search terms used were: ALL (“plant extracts” OR “phytotherapy” OR “traditional healing” OR “medicinal plants” OR “ethnobotany” OR “botanical preparations”) AND ALL (“antibacterial properties” OR “antimicrobial activity” OR “drug resistance, microbial” OR “antibiotic resistance” OR “multidrug-resistant”) AND ALL (“*Klebsiella pneumoniae*”) AND ALL (specific African countries).

Regarding ScienceDirect, the search terms used were: (“herbal preparations” OR “herbal remedies” OR “herbal medicine” OR “plant extracts” OR “medicinal plants” OR “botanical preparations”) AND (“multidrug-resistant *Klebsiella pneumonia*” OR “resistant

Created with mapchart.net

Fig. 2. Distribution and number of included studies by country of plant origin.

Klebsiella pneumoniae") AND ("specific African country") as well as ("herbal preparations" OR "herbal remedies" OR "herbal medicine" OR "plant extracts" OR "medicinal plants" OR "botanical preparations") AND ("multidrug-resistant bacteria" OR "antibiotic-resistant bacteria") AND ("specific African country").

Inclusion and exclusion criteria

Filters for open access, English language, and research papers were consistently applied. The detailed search strategy can be found in Fig. 1. Titles and abstracts were screened to identify relevant articles, and full versions of potentially relevant articles were obtained for eligibility assessment. Peer-reviewed journal articles and conference proceedings were included in the review. Publications excluded from the review included commentaries, case-control studies, letters to editors, review articles, and reports. Additionally, papers that did not report on MDR-Kp or were not conducted in Africa were excluded.

Study selection

A total of 2094 articles were found from the initial database search, and four were found through other sources (Fig. 1). After removing the duplicates ($n = 171$), 1079 studies were excluded based on title and abstract. The resultant 848 full-text articles were assessed for eligibility, of which 816 were excluded. A total of 31 studies about the *in vitro* antibacterial activity of medicinal plants from Africa against MDR-Kp were found [12,18,21–49].

Data extraction and analysis

Data from the reviewed studies were organised using Microsoft Excel 365. Three authors (R.A.A.A., K.A.-A., and F.C.N.K.) extracted study data using a data extraction format created in Excel. Data regarding scientific names of plants, botanical families, plant parts, country of plant origin, type of extract, isolated compounds, and inhibition diameter measured in millimeters (mm), minimum inhibitory concentration (MIC), and minimal bactericidal concentration (MBC) were independently gathered from the publications. These data were systematically documented in a standardised Word form. The results are presented in Supplementary Table 1 and visually represented in a map (Fig. 2) created with MapChart (https://www.mapchart.net/).

Results

Database search results

Based on the inclusion and exclusion criteria and the PRISMA checklist, we selected 31 studies that reported on the *in vitro* antibacterial activity of medicinal plants from Africa against MDR-Kp. The studies were conducted in 7 different countries. The majority of the studies were from Cameroon (20 studies); other countries from which the studies emanated include Morocco (three studies), Egypt (three studies), South Africa (two studies), Kenya (one study), Burkina Faso (one study), and Zimbabwe (one study) (Fig. 2). The included articles were published between 2011 and 2024 (Supplementary Table 1).

Results of the in vitro studies

A total of 124 medicinal plants from Africa were studied for *in vitro* activity against MDR-Kp, and these belong to 53 families. Plants from Fabaceae (10 studies) [12,21,22,24,28,31,36,39,42,49], Rutaceae (eight studies) [21,24,25,31,34,39,40,42], Asteraceae (eight studies) [12,22–24,26,29,39,46], Polygonaceae (one study) [12], and Lauraceae (seven studies) [22,24,32,34,39,42,47] families were the most common. Four plants, namely *Allium cepa* (two studies) [32,40], *Allium sativum* (two studies) [40,47], *Carica papaya* (two studies) [22,40], *Phaseolus vulgaris* (two studies) [31,51] and *Persea americana* (two studies) [22,34] were analysed in more than one research. The most analysed plant parts were leaves (14 studies) [21,22,26,28,30,31,34,35,37–39,41,42,47], bark from stem and root (16 studies) [21,22,24,25,27,28,30–32,34–39,42], and fruits (six studies) [24,26,34,39,40,42]. Methanol (19 studies) [21,22,24–26,28,30,31,34–40,42,44,47,49] was the most used solvent for plant extract preparation, while water (one study) [41], dichloromethane (four studies) [18,22,25,28], crude (three studies) [27,45,48], chloroform (one study) [29] and hexane (one study) [28] were seldom used.

The studies included in the review assessed the antibacterial activity of the herbal preparations using three methods: MIC, MBC, and zone of inhibition determination via the disk diffusion method. There were variations in the units used to report MIC values – in milligrams per milliliter (mg/ml), micrograms per milliliter (μg/ml), and expression as percentage. All 31 studies utilised MIC as a measure of antimicrobial effectiveness [12,18,21–49]. Three studies combined MIC determination with zone of inhibition measurement to assess both the concentration-dependent effects and the ability of the herbal preparations to create a clear zone of inhibition against the bacteria [29,33,46]. Fifteen studies combined MIC and MBC determination to evaluate both the inhibitory and bactericidal properties of the herbal preparations [18,22,27,30–32,34–39,42,45,48]. Additionally, three studies combined all three parameters to provide a comprehensive evaluation of the antibacterial activity of the herbal preparations [43,47]. Table 1 presents a comprehensive summary of the tested plants evaluated with their respective family names, type of extract, plant parts, isolated compounds, bacterial strains used, zones of inhibition, MIC values, and MBC values (Supplementary Table 1).

Among the studied plants, *Withania frutescens* [33] exhibited the highest antimicrobial activity, with its essential oil and hydrolat extracts from the aerial part showing MICs of 0.003 μg/ml and 6.125 μg/ml, respectively. Other plants, such as *Eruca sativa* [32], *A. negrei* [46], and *Beilschmiedia obscura* (Staph). Engl [39], also demonstrated significant antimicrobial activity, with MIC values of 31.25 μg/ml, 6.25 μg/ml, and 32.00 μg/ml, respectively. *Phaseolus vulgaris* [49] exhibited MIC values of 64 μg/ml and 16.00 μg/ml, and *Centaurea pumilio* [29] displayed MIC values of 15.62 μg/ml, 62.5 μg/ml, and 31.25 μg/ml. *Donella welwitschii* [18] displayed MIC values of 4.00 μg/ml, 16.00 μg/ml, and 32.00 μg/ml. *Xylopia aethiopica* [24] exhibited an MIC of 64.00 μg/ml against the KP63 strain of *K. pneumoniae*.

Sixty-two pure compounds were isolated from 17 plants and tested against *K. pneumoniae* strains KP55 and KP63 [12,18,48]. Plumbagin, a naphthoquinone from *Plumbago zeylanica* [12], displayed the highest efficacy with MIC values of 2.00 mg/ml and 4.00 μg/ml against the KP55 and KP63 strains, respectively. Among the fractions of crude extract of *Plectranthus glandulosus* [48], Fraction C showed the most effectiveness against KP55, with an MIC of 64 μg/ml.

Discussion

This study aimed to evaluate the *in vitro* antimicrobial activities of African medicinal plants against MDR-Kp. The findings underscore ongoing efforts in the region to identify plant-based solutions for treating infections caused by *K. pneumoniae*.

The studies included in the review assessed the antibacterial activity of the herbal preparations using methods such as MIC, MBC, and zone of inhibition from the disk diffusion method. The disk diffusion method has limitations, especially in its inability to accurately quantify the concentration of an extract needed to inhibit bacterial growth. Its results could also be influenced by variables such as the compound concentration, test solution volume, inoculum density, diffusion time and temperature before incubation, medium composition and thickness, and incubation conditions. These limitations highlight the advantage of the broth microdilution method, which provides more accurate and reliable data for determining MIC values of plant extracts and isolated compounds [52]. Thus, we emphasise the importance of using broth microdilution to study the MIC values for plant extracts and isolated chemicals.

Furthermore, the different MIC values reported by various studies, such as milligrams per milliliter (mg/ml), micrograms per milliliter (μg/ml), and percentages, highlight the need for caution when comparing and evaluating the antimicrobial potential of the tested compounds across different studies.

Additionally, leaves and bark were the most frequently studied plant parts, reflecting their significance in traditional ethnobotanical practices [53]. Also, methanol was the most commonly used solvent, likely due to its effectiveness in extracting a broad spectrum of active compounds and its relatively low toxicity [12,54].

The antibacterial activity of a plant extract can be evaluated based on its MIC values. According to Kuete et al. [55,56], an extract is considered significant when MIC $<$ 100 μg/mL, moderate when 100 $\leq$ MIC $\leq$ 625 μg/mL, and weak when MIC $>$ 625 μg/ml. Similarly, Pessini et al. [57] classified extracts with MIC $<$ 100 μg/mL as having very high activity, 100–500 μg/mL as high activity, 500–1000 μg/mL as moderate activity, 1000–4000 μg/mL as low activity, and MIC $>$ 4000μg/mL as inactive. These classifications help determine the strength and effectiveness of plant extracts in inhibiting bacterial growth. The MBC/MIC ratios observed in this study were mostly above four, suggesting that the studied extracts, including the most active ones, generally showed bacteriostatic effects (MBC/MIC $>$ 4). However, a few extracts, such as *Eruca sativa, Cinnamomum zeylanicum, Petroselinum crispum, Allium cepa* L., *Anethum graveolens* L., *Cassia sieberiana* DC., and *Beilschmiedia obscura* (Staph). Engl. demonstrated bactericidal effects, as their MBC/MIC ratios were equal to or below four [58].

In our study, several plants, such as *Psidium guajava* Linn (Myrtaceae), and *Persea americana* Mill. (Lauraceae), *Citrus sinensis* Linn. (Rutaceae), *Mangifera indica* Linn. (Anacardiaceae), *Camellia sinensis* Linn. (Theaceae), *Allium sativum* (Amaryllidaceae), *Buchholsia coriacea* (Capparaceae), *Picralima nitida* (Apocynaceae), *Entada gigas* (Fabaceae), *Spathodea campanulata* (Bignoniaceae), and *Citrus médica* (Rutaceae), exhibited low antibacterial activities against MDR-Kp strains, with a high MIC greater than 1000 μg/ml [36,42]. These results imply that these plants may not contain sufficient concentrations of active compounds to effectively stop the growth of MDR-Kp.

The antimicrobial activities observed in African medicinal plants strongly align with their ethnomedicinal applications, demonstrating the potential of traditional knowledge in guiding modern antimicrobial research. This section highlights the critical connections between traditional uses, bioactive constituents, and the mechanisms of action underlying the biological effects of key plants reviewed in this study.

Several plants demonstrated significant antimicrobial effects that reflect their traditional medicinal uses. For instance, *E. sativa*, traditionally used for digestive health and inflammation [59], exhibited strong antimicrobial properties against several resistant pathogens [34,60]. The broad-spectrum antimicrobial activity of *E. sativa*'s arugula oil is attributed to its high content of flavonoids and phenolic compounds, which neutralise free radicals and inhibit pro-inflammatory markers such as COX2 and TLR4 [61], along with specific compounds like sulforaphonenitrile [62], 2-pentanonitrile, and 5-methylthiopentanonitrile [34].

Similarly, *W. frutescens* L., widely used for its anti-inflammatory and antimicrobial properties [63], displayed bacteriostatic activities through the action of withanolides, thymol, and carvacrol [35]. These compounds disrupt bacterial membranes [64–66], inhibit inflammatory cytokines, and neutralise oxidative stress [67], aligning with the ethnomedicinal application of *W. frutescens* L. in managing systemic infections and inflammatory diseases [68].

B. obscura, known for treating gastrointestinal infections, demonstrated remarkable antibacterial activities, with MIC values below 100 μg/mL [22]. Its efficacy comes from alkaloids, flavonoids, and saponins, which disrupt bacterial cell walls and inhibit efflux pumps [69]. These mechanisms validate its traditional use in gastrointestinal disorders caused by antibiotic-resistant pathogens [22].

In the case of *P. vulgaris*, its ethnobotanical role in promoting digestive health and managing infections is supported by the presence of catechol and hesperidin [51,70]. These compounds strengthen intestinal mucosal barriers and inhibit bacterial invasion, effectively reducing infections caused by multidrug-resistant *K. pneumoniae* [71].

P. zeylanica, traditionally used in treating chronic colds, coughs, and diabetes [72,73], disrupts bacterial cell walls and enzymatic pathways, yielding strong antimicrobial activities, through its naphthoquinone plumbagin [73–75]. *C. pumilio*, an endangered rare plant [76], known for its antioxidant and antimicrobial properties [77], contains sesquiterpenes like β-caryophyllene and esters such as hexyl isovalerate. These compounds exhibit broad-spectrum antimicrobial activity, with MIC values ranging from 15.62 to 250 μg/mL. This underscores the potential of *C. pumilio* in addressing multidrug-resistant infections [29].

P. glandulosus, traditionally used to treat internal inflammation, lower abdominal and nerve aches, and gastrointestinal disorders, contains a fraction rich in oleanolic acid [50,78,79], which has shown high antimicrobial activity. Oleanolic acid disrupts bacterial cell membranes, inhibits DNA polymerase, and binds to peptidoglycan and teichoic acids, preventing cell wall turnover [80]. It also inhibits glucosyltransferase, suppressing plaque formation, and inhibits both β-lactamases and haemolysin activity [81]. These mechanisms may enhance its therapeutic efficacy in addressing gastrointestinal infections.

The bioactive compounds in *D. welwitschii* and *X. aethiopica* further emphasise the alignment between traditional uses and observed biological effects. *D. welwitschii*, used to cure coughs, contains diospyric acid and oleanolic acid, which inhibit bacterial ATP production and efflux pumps, resulting in low MIC values ($<$10 μg/mL) [18]. Similarly, *X. aethiopica*, employed in managing bronchitis and asthma [82,83], is rich in withanolides and sesquiterpenes [24], which reduce inflammation and effectively combat resistant bacterial strains [84].

Moreover, phytochemical families such as flavonoids, alkaloids, terpenoids, and phenolic compounds frequently emerged as key contributors to the observed antimicrobial effects. The detailed mechanisms of action of these bioactive compounds in plant extracts, as discussed, could be further linked to their phytochemistry and family-specific distribution. Different plant families are characterised by distinct phytochemical profiles that show their antimicrobial activities, providing insights into their mechanisms of action [60]. These mechanisms, often broad-spectrum, are crucial for combating both Gram-positive and Gram-negative bacteria, including multidrug-resistant (MDR) strains of *K. pneumoniae* [85]. Understanding these relationships is important for advancing the development of new therapeutic strategies.

The Lamiaceae family, represented by *P. glandulosus* and *Lavandula coronopifolia*, is rich in terpenoids such as carvacrol [45,50,86]. These compounds are known for their ability to disrupt bacterial membranes, collapse the proton motive force, and inhibit biofilm formation. The hydrophobic nature of these terpenoids allows them to partition into lipid bilayers, enhancing their efficacy across a broad spectrum of pathogens [87–90]. This phytochemical profile explains the strong antimicrobial activity observed for members of this family and their potential for combination therapies.

The Solanaceae and Lauraceae families, including *Solanum melongena, Beilschmiedia cinnamomea, B. obscura,* and *B. acuta*, are characterised by the presence of alkaloids [21,24,91,92]. These compounds, such as berberine and michellamine B, are potent inhibitors of bacterial efflux pumps and enzymes. Alkaloids also demonstrate DNA intercalation and membrane permeability enhancement, making Lauraceae plants particularly effective against MDR strains. The ability of alkaloids to inhibit metabolic pathways and cytokinesis further underscores their broad-spectrum potential [93–95]. However, El Moussaoui et al. [35] reported that *W. frutescens* L. from the Solanaceae family contained predominantly terpenoids, particularly carvacrol, and thymol, rather than the typical alkaloids characteristic of this family.

The Fabaceae family, known for its rich content of polyphenols, includes plants like *P. vulgaris* [31,51,96,97]. These polyphenols exhibit significant antimicrobial properties through various mechanisms, such as disrupting bacterial DNA replication by inhibiting DNA gyrase, altering the function of bacterial cell membranes, and reducing biofilm formation that protects bacterial cells. They also influence protein biosynthesis, modify metabolic processes, and inhibit virulence factors, including enzymes and toxins. Additionally, polyphenols decrease bacterial cell attachment and can deprive bacteria of essential substrates [98–100]. Within this family, a prominent subclass is flavonoids. Examples include hesperidin, catechin, and quercetin, which play key roles in antimicrobial activity by inhibiting bacterial ATP synthesis, damaging membranes, and generating reactive oxygen species. Their capacity to inhibit DNA gyrase and efflux pumps enhances their effectiveness against infections with antibiotic-resistant bacteria, underscoring the therapeutic potential of flavonoids in combating bacterial pathogens [101–103].

The family Brassicaceae, which includes *E. sativa*, is dominated by terpenoids and phenolic compounds [34,104,105]. Terpenoids, such as cinnamaldehyde and carvacrol, disrupt bacterial membranes and inhibit quorum sensing [69], while phenolics like gallic acid target bacterial DNA and enzymes [105]. The synergy between these phytochemicals enhances the antimicrobial efficacy of Brassicaceae plants, making them suitable candidates for targeting biofilms and resistant bacterial populations.

The family Plumbaginaceae, represented by *P. zeylanica*, is known for its naphthoquinones [12,106]. These compounds exert their antimicrobial effects through redox disruption and DNA intercalation [107]. By generating reactive oxygen species and interfering with bacterial transcription, naphthoquinones provide a dual mechanism of action that is highly effective against persistent bacterial infections [108]. The presence of these compounds underscores the potential of Plumbaginaceae plants in developing adjunct therapies for MDR pathogens.

The family Rutaceae, which includes *Fagara macrophylla* and *Fagara xanthoxyloides*, is characterised by alkaloids and flavonoids [24,40,109]. These phytochemicals contribute to efflux pump inhibition, DNA synthesis disruption, and oxidative stress induction [94,103]. Rutaceae plants exhibit broad-spectrum activity, making them effective against both Gram-positive and Gram-negative bacteria [110,111].

By linking the phytochemical profiles to their plant families, better insights into the antimicrobial activity mechanisms could be discerned. Families such as Lauraceae and Fabaceae, with their alkaloid and flavonoid dominance, excel in targeting efflux pumps and metabolic pathways [91,101]. In contrast, families like Brassicaceae and Lamiaceae, which are rich in terpenoids and phenolics, specialise in membrane disruption and biofilm inhibition [59,112]. This family-specific distribution of phytochemicals offers a guide for focused research on plant-based antimicrobial agents, highlighting the importance of utilising these natural resources to combat antibiotic resistance.

The antimicrobial activities of the reviewed plants against *K. pneumoniae* demonstrated significant variability across studies, influenced by differences in plant parts used, extraction methods, bacterial strains tested, and phytochemical profiles. This variability underscores the challenges in standardising methodologies and interpreting results across diverse experimental settings.

For example, in *P. vulgaris*, the activity against *K. pneumoniae* varied considerably between studies [31,51]. Ebrahim et al. [51] reported very high activity against a clinical MDR isolate (KP55) resistant to tetracycline, ampicillin, aztreonam, and ceftriaxone. The study tested methanolic extracts of the seeds and isolated protein components, including 7S and 11S globulins. The phytochemicals identified in this study, such as catechol, chlorogenic acid, rutin, naringin, quercetin, and kaempferol, likely contributed to the potent antibacterial effects observed [51]. In contrast, Nayim et al. [31] found low activity when leaves were tested using methanolic extracts. Although the study identified bioactive compounds such as polyphenols, tannins, steroids, and saponins, the broader resistance profile of the bacterial strains tested, which included resistance to ampicillin, ciprofloxacin, tetracycline, and other antibiotics, may have contributed to the limited efficacy [31]. These differences highlight the influence of plant parts on phytochemical concentrations, with seeds concentrating metabolites such as flavonoids and phenolics known for their antimicrobial activity, whereas leaves may contain a different profile or lower concentrations of active compounds.

Similarly, the activity of *Allium cepa* varied between studies [34,42]. Bassyouni et al. [34] demonstrated a high antimicrobial activity in essential oils extracted from onion seeds. The bacterial strains tested in this study were resistant to ceftriaxone, cefpodoxime, cefotaxime, amikacin, and cefepime. The potent activity observed may be attributed to the presence of volatile compounds in the essential oils, which are known to disrupt bacterial membranes and inhibit enzymatic pathways [34]. In contrast, Lacmata et al. [42] reported low activity when fresh and dry onion bulb extracts were tested using methanol as the solvent. This study identified flavonoids, phenols, and tannins as the primary compounds in the methanolic extract, which, despite their known antimicrobial properties, showed limited activity against the tested MDR strains resistant to tetracycline, ampicillin, and aztreonam [42]. The differences between these studies can be attributed to both the plant parts used (seeds vs. bulbs) and the extraction methods employed (essential oil vs. methanolic extraction).

These findings underscore several factors influencing the activity of plant extracts. First, differences in plant metabolite concentrations across plant parts play a critical role [113]. Seeds and essential oils often contain higher levels of potent antimicrobial agents like volatile oils and flavonoids [114], whereas other parts, such as leaves and bulbs, may have lower concentrations or contain bioactives with less efficacy against resistant strains. Secondly, the extraction method significantly impacts the phytochemical profile of the extract [115]. Essential oil extraction isolates highly concentrated volatile compounds that exhibit strong membrane-disruptive effects [116], while methanolic extraction captures a broader spectrum of phytochemicals, some of which may be less effective or require higher concentrations to achieve similar antimicrobial activity [117].

Another crucial factor is the variation in bacterial strains tested. The genetic diversity of *K. pneumoniae* strains, particularly those exhibiting MDR phenotypes, significantly influences the observed efficacy of plant extracts. For example, certain plants, such as *Persea Americana* [118] and *Carica papaya* [119], are known to possess antimicrobial activities against sensitive bacteria and fungi but the specific strains of MDR-Kp (KP55) used in our study showed different responses [22]. MDR-Kp possesses various resistance mechanisms, such as efflux pumps and cell wall alterations, which can limit the effectiveness of certain bioactive compounds [120,121]. Variations in plant parts used, extraction methods, geographical location, solvent choice, and plant chemotype can significantly influence the efficacy of the extracts [23]. Understanding these factors, along with the genetic diversity of MDR *K. pneumoniae* strains, is essential for optimising the use of plant-based antimicrobials. Further research is necessary to isolate and characterise the active compounds and to explore their individual and synergistic effects on bacterial growth and survival.

The observed differences in antimicrobial activity among studies emphasise the need for standardised methodologies in evaluating plant-based antimicrobials. Standardising extraction protocols, ensuring consistency in the plant parts tested, and using a uniform panel of clinically relevant MDR strains are critical steps toward reliable comparisons [122]. Additionally, investigating the specific contributions of individual bioactive compounds through fractionation and bioassay-guided isolation will provide deeper insights into their roles in antimicrobial activity [123]. By addressing these challenges, factors driving variability in antimicrobial activity of plant-based interventions against MDR pathogens could be better understood and optimised.

The antimicrobial efficacy of plant extracts against *K. pneumoniae* was assessed in comparison to chloramphenicol when combined with antibiotics and in the presence of PAβN. The findings highlight significant variability in activity, emphasising the potential of certain extracts as adjunct therapies.

When compared to chloramphenicol, plant extracts displayed mixed efficacy. *D. welwitschii* (diospyric acid) showed superior activity with an MIC of 4 μg/ml, compared to 8 μg/ml for chloramphenicol, demonstrating a 50 % improvement [18]. In contrast, compounds such as oleanolic acid and extracts from plants like *C. schweinfurthii* and *Myrianthus arboreus* showed limited standalone activity, with MICs ranging from 512 to >1024 μg/ml, far higher than chloramphenicol's MIC of 32 μg/ml [40].

Combining plant extracts with antibiotics revealed strong synergistic effects. *D. welwitschii* significantly enhanced the activity of chloramphenicol, ciprofloxacin, and doxycycline, with MIC improvements up to 96.88 % [18]. For instance, the MIC of chloramphenicol decreased from 16 μg/ml to 0.5 μg/ml when combined with ursolic acid. *P. glandulosus* also demonstrated a remarkable reduction in chloramphenicol's MIC from >1024 μg/ml to 32 μg/ml, showcasing its synergistic potential [50].

The addition of PAβN further amplified the activity of plant extracts, indicating the role of efflux pump inhibition in overcoming bacterial resistance. For example, the MIC of *D. welwitschii* compounds, such as ursolic acid and oleanolic acid, decreased to 0.5 μg/ml and 1 μg/ml, respectively, in the presence of PAβN, achieving up to 96.88 % improvement [18].

These results highlight the promise of plant extracts, particularly *D. welwitschii* and *P. glandulosus*, as adjunct therapies for MDR

K. pneumoniae. While some extracts are less effective alone, their ability to enhance antibiotic efficacy and leverage efflux pump inhibition underscores their potential role in combination therapies.

With all that has been discussed regarding the potency of plants and their compounds, it is important to note that the increasing demand for medicinal plants in ethnomedicine has placed significant pressure on wild populations, threatening species like *W. frutescens* L. and *C. pumilio*. To ensure sustainable use, a combination of cultivation, seed banking, habitat protection, and community education is essential [124,125].

Cultivation programmes for frequently used species, such as *W. frutescens* L., can reduce harvesting pressure on wild populations while providing economic benefits to local communities [126]. Successful models, like the cultivation of *Rauvolfia serpentina* in India, demonstrate how controlled farming can balance demand and conservation [127]. For endangered species like *C. pumilio*, seed banking offers a reliable method to preserve genetic diversity [128]. Collaborations with international initiatives, such as the Millennium Seed Bank [129], could strengthen Africa's capacity to conserve its unique flora.

In-situ conservation through habitat protection and *ex-situ* efforts, such as botanical gardens and tissue culture, provide complementary strategies to safeguard threatened species [130]. Tissue culture, in particular, enables the propagation of plants like *C. pumilio*, ensuring survival despite habitat loss [131]. Education and awareness campaigns targeting local stakeholders are critical for promoting sustainable harvesting and preserving traditional knowledge [132].

Learning from successful global examples, such as seed banking and agroforestry systems in India [127], Africa can adapt similar strategies to local contexts. Policy interventions, including incentives for sustainable practices and penalties for overharvesting, will further promote conservation efforts [133]. To enhance the sustainability of these initiatives, incorporating modern biotechnological approaches, such as micropropagation and genetic engineering, can improve production efficiency and decrease reliance on wild populations [134]. By combining these approaches, we can secure the biodiversity of medicinal plants while supporting traditional medicine and community livelihoods.

This review highlights the therapeutic potential of African medicinal plants against MDR-Kp, emphasising their ethnobotanical relevance, diverse phytochemical profiles, and promising bioactivities. However, it also highlights a significant gap in the progression from preclinical studies to clinical trials, as none of the reviewed studies advanced to human testing. The focus of these studies remained primarily on the *in vitro* activity of plant extracts, limiting the understanding of their efficacy, safety, and dosage in clinical settings. Future research should prioritise advancing these studies into clinical trials to validate plant-based therapies as potential adjuncts to conventional antibiotics, addressing challenges such as bioavailability, toxicity, and formulation.

Additionally, while studies on *K. pneumoniae* are prevalent, research specifically investigating plant species with activity against MDR-Kp is scarce. Notably, the majority of MDR-Kp strains are derived from patient samples, yet the plant species studied have not been traditionally used to treat *K. pneumoniae* infections locally. This suggests the need for more targeted research, including a deeper exploration of active compounds, refinement of extraction techniques, and a better understanding of the underlying mechanisms of action. Further, investigating synergistic effects between plant compounds and conventional antibiotics could enhance antimicrobial efficacy.

Integrating traditional medicinal knowledge with scientific research represents a promising strategy for addressing the global challenge posed by multidrug-resistant *K. pneumoniae*. Although current studies have provided valuable insights into the antimicrobial potential of African medicinal plants, their clinical applicability remains underexplored. By prioritising research on the most promising plant species, refining extraction methods, and investigating synergistic interactions with antibiotics, we can unlock new therapeutic possibilities. Collaborative efforts that bridge ethnobotanical wisdom with modern biomedical approaches will be pivotal in advancing plant-based therapies from *in vitro* studies to clinical applications. Such efforts can also contribute to preserving Africa's rich biodiversity while addressing pressing global health concerns.

Conclusions

Of the 124 plants studied, *Withania frutescens L.*, *Plumbago zeylanica, Plectranthus glandulosus, Eruca sativa*, and *Donella welwitschii*, emerged as plants that could be further explored for anti-MDR-Kp therapeutics. Further research is required to fully understand the mechanisms of action and potential synergies of these herbal preparations and explore their active compounds. Integrating traditional knowledge with modern healthcare practices is crucial in making use of the healing properties of African medicinal plants.

Institutional review board statement

Not applicable.

Informed consent statement

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This systematic review was supported by the Fogarty International Center of the National Institutes of Health, USA, through the Research and Capacity Building in Antimicrobial Resistance in West Africa (RECABAW) Training Programme hosted at the Department of Medical Microbiology, University of Ghana Medical School (Award Number: D43TW012487). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.sciaf.2025.e02644.

Data Availability

Not applicable.

References

[1] S.T. Bagley, Habitat Association of *Klebsiella* Species, Infect. Control Hospital Epidemiol. 6 (2) (1985) 52–58.
[2] R. Podschun, U. Ullmann, *Klebsiella* spp. As nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors, Clin. Microbiol. Rev. 11 (4) (1998) 589–603.
[3] E.T. Piperaki, G.A. Syrogiannopoulos, L.S. Tzouvelekis, G.L. Daikos, *Klebsiella pneumoniae*: virulence, biofilm and antimicrobial resistance, Pediatr. Infect. Dis. J. 36 (10) (2017) 1002.
[4] P. Nordmann, G. Cuzon, T. Naas, The real threat of *Klebsiella pneumoniae* carbapenemase-producing bacteria, Lancet Infect. Dis. 9 (4) (2009) 228–236.
[5] T.A. Russo, C.M. Marr, Hypervirulent Klebsiella pneumoniae, Clin. Microbiol. Rev. 32 (3) (2019) e00001.
[6] N.A. Mohd Asri, S. Ahmad, R. Mohamud, N. Mohd Hanafi, N.F. Mohd Zaidi, A.A. Irekeola, et al., Global prevalence of nosocomial multidrug-resistant *Klebsiella pneumoniae*: a systematic review and meta-analysis, Antibiotics 10 (12) (2021) 1508.
[7] M.K. Paczosa, J. Mecsas, *Klebsiella pneumoniae*: going on the offense with a strong defense, Microbiol. Mol. Biol. Rev. 80 (3) (2016) 629–661.
[8] C. Rock, K.A. Thom, M. Masnick, J.K. Johnson, A.D. Harris, D.J. Morgan, Frequency of *Klebsiella pneumoniae* carbapenemase (KPC)–Producing and Non-KPC-producing *Klebsiella* species contamination of healthcare workers and the environment, Infect. Control Hospital Epidemiol. 35 (4) (2014) 426–429.
[9] K. Stojowska-Swędrzyńska, A. Łupkowska, D. Kuczyńska-Wiśnik, E. Laskowska, Antibiotic heteroresistance in *Klebsiella pneumonia*e, Int. J. Mol. Sci. 23 (1) (2021) 449.
[10] V.L. Yu, D.S. Hansen, W.C. Ko, A. Sagnimeni, K.P. Klugman, A. von Gottberg, et al., Virulence characteristics of *Klebsiella* and clinical manifestations of *K. pneumoniae* bloodstream infections, Emerg. Infect. Dis. 13 (7) (2007) 986–993.
[11] Y. Jin, C. Dong, C. Shao, Y. Wang, Y. Liu, Molecular epidemiology of clonally related metallo-β-lactamase-producing *Klebsiella pneumoniae* isolated from newborns in a hospital in Shandong, China, Jundishapur. J. Microbiol. 10 (9) (2017) [Internet] [cited 2024 Mar 10] Available from, https://brieflands.com/articles/jjm-14046.html#abstract.
[12] L.K. Omosa, J.O. Midiwo, A.T. Mbaveng, S.B. Tankeo, J.A. Seukep, I.K. Voukeng, et al., Antibacterial activities and structure-activity relationships of a panel of 48 compounds from Kenyan plants against multidrug-resistant phenotypes, Springerplus. 5 (1) (2016) 901.
[13] A.K. Labi, S. Bjerrum, C.C. Enweronu-Laryea, P.K. Ayibor, K.L. Nielsen, R.L. Marvig, et al., High carriage rates of multidrug-resistant gram-negative bacteria in neonatal intensive care units from Ghana, Open. Forum. Infect. Dis. 7 (4) (2020) ofaa109.
[14] T. Awoke, B. Teka, A. Seman, S. Sebre, B. Yeshitela, A. Aseffa, et al., High prevalence of multidrug-resistant *Klebsiella pneumoniae* in a Tertiary Care Hospital in Ethiopia, Antibiotics 10 (8) (2021) 1007.
[15] V. Shriram, T. Khare, R. Bhagwat, R. Shukla, V. Kumar, Inhibiting bacterial drug efflux pumps via Phyto-therapeutics to combat threatening antimicrobial resistance, Front. Microbiol. 9 (2018) [Internet] [cited 2024 Feb 4] Available from, https://www.frontiersin.org/articles/10.3389/fmicb.2018.02990.
[16] A. Kessler, A. Kalske, Plant secondary metabolite diversity and species interactions, Annu Rev. Ecol. Evol. Syst. 49 (1) (2018) 115–138.
[17] D.L. Lentz, A.M. Clark, C.D. Hufford, B. Meurer-Grimes, C.M. Passreiter, J. Cordero, et al., Antimicrobial properties of Honduran medicinal plants, J. Ethnopharmacol. 63 (3) (1998) 253–263.
[18] M.G.F. Guefack, M.O. Ngangoue, A.T. Mbaveng, P. Nayim, J.R.N. Kuete, C.M.N. Ngaffo, et al., Antibacterial and antibiotic-potentiation activity of the constituents from aerial part of *Donella welwitshii* (Sapotaceae) against multidrug resistant phenotypes, BMC. Complement. Med. Ther. 22 (2022) 194.
[19] C.J.L. Murray, K.S. Ikuta, F. Sharara, L. Swetschinski, G.R. Aguilar, A. Gray, et al., Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, The Lancet 399 (10325) (2022) 629–655.
[20] B. Gulumbe, A. Adamu Faggo, Epidemiology of multidrug-resistant organisms in Africa, Mediterr. J. Infect. Microbes Antimicrobials (2019) 8.
[21] S.B. Tankeo, P. Tane, V. Kuete, In vitro antibacterial and antibiotic-potentiation activities of the methanol extracts from *Beilschmiedia acuta, Clausena anisata, Newbouldia laevis* and *Polyscias fulva* against multidrug-resistant gram-negative bacteria, BMC. Complement. Altern. Med. 15 (1) (2015) 1–10.
[22] M.E.S. Tchana, A.G. Fankam, A.T. Mbaveng, E.T. Nkwengoua, J.A. Seukep, F.K. Tchouani, et al., Activities of selected medicinal plants against multi-drug resistant gram-negative bacteria in Cameroon, Afr. Health Sci. 14 (1) (2014) 167–172.
[23] S. van Vuuren, T. Muhlarhi, Do South African medicinal plants used traditionally to treat infections respond differently to resistant microbial strains? South Afr. J. Botan. 112 (2017) 186–192.
[24] A.G. Fankam, V. Kuete, I.K. Voukeng, J.R. Kuiate, J.M. Pages, Antibacterial activities of selected Cameroonian spices and their synergistic effects with antibiotics against multidrug-resistant phenotypes, BMC. Complement. Altern. Med. 11 (1) (2011) 104.
[25] H. Fouotsa, A.T. Mbaveng, C.D. Mbazoa, A.E. Nkengfack, S. Farzana, C.M. Iqbal, et al., Antibacterial constituents of three Cameroonian medicinal plants: *Garcinia nobilis, Oricia suaveolens* and *Balsamocitrus camerunensis*, BMC. Complement. Altern. Med. 13 (2013) 81.
[26] J.A. Noumedem, M. Mihasan, J.R. Kuiate, M. Stefan, D. Cojocaru, J.P. Dzoyem, et al., In Vitro antibacterial and antibiotic-potentiation activities of four edible plants against multidrug-resistant gram-negative species, BMC. Complement. Altern. Med. 13 (1) (2013) 190.
[27] M.M.M. Ambadiang, B.C.K. Atontsa, S.B. Tankeo, P. Nayim, B.E.N. Wamba, G.T.M. Bitchagno, et al., Bark extract of *Cassia sieberiana* DC. (Caesalpiniaceae) displayed good antibacterial activity against MDR gram-negative phenotypes in the presence of phenylalanine-arginine β-naphthylamide, BMC. Complement. Med. Ther. 20 (1) (2020) 1–11.
[28] R.D. Magnini, A. Hilou, H. Millogo-Koné, J.M. Pagès, Davin-Regli A. *Acacia senegal* extract rejuvenates the activity of phenicols on selected enterobacteriaceae multi drug resistant strains, Antibiotics 9 (6) (2020) 1–17.

[29] H. Naeim, A. El-Hawiet, R.A. Abdel Rahman, A. Hussein, M.A. El Demellawy, A.M. Embaby, Antibacterial activity of *Centaurea pumilio* L. root and aerial part extracts against some multidrug resistant bacteria, BMC. Complement. Med. Ther. 20 (1) (2020) 79.

[30] B.E.N. Wamba, A.T. Mbaveng, P. Nayim, J.K. Dzotam, O.J.T. Ngalani, V. Kuete, Antistaphylococcal and antibiotic resistance modulatory activities of thirteen Cameroonian edible plants against resistant phenotypes, Int. J. Microbiol. 2018 (2018) e1920198.

[31] P. Nayim, A.T. Mbaveng, B.E.N. Wamba, A.G. Fankam, J.K. Dzotam, V. Kuete, Antibacterial and antibiotic-potentiating activities of thirteen Cameroonian edible plants against gram-negative resistant phenotypes, ScientificWorldJournal. 2018 (2018) 4020294.

[32] K. Okaiyeto, OO. Oguntibeju, African herbal medicines: adverse effects and cytotoxic potentials with different therapeutic applications, Int. J. Environ. Res. Public Health 18 (11) (2021) 5988.

[33] E. Owusu, M.M. Ahorlu, E. Afutu, A. Akumwena, G.A. Asare, Antimicrobial activity of selected medicinal plants from a Sub-Saharan African country against bacterial pathogens from post-operative wound infections, Medical Sciences 9 (2) (2021) 23.

[34] R.H. Bassyouni, Z. Kamel, A.A. Algameel, G. Ismail, S.N. Gaber, In-vitro determination of antimicrobial activities of *Eruca sativa* seed oil against antibiotic-resistant gram-negative clinical isolates from neonates: a future prospect, BMC. Complement. Med. Ther. 22 (1) (2022) 1–11.

[35] A.E. Moussaoui, M. Bourhia, F.Z. Jawhari, A.M. Salamatullah, R. Ullah, A. Bari, et al., Chemical profiling, antioxidant, and antimicrobial activity against drug-resistant microbes of essential oil from *Withania frutescens* l, Applied Sciences (Switzerland) [Internet] 11 (11) (2021). Available from, https://www.scopus.com/inward/record.uri?eid=2-s2.0-85107770334&doi=10.3390%2fapp11115168&partnerID=40&md5=56765db9b910f703952f957052c037c2.

[36] J.K. Dzotam, V. Kuete, Antibacterial and antibiotic-modifying activity of methanol extracts from six Cameroonian food plants against multidrug-resistant enteric bacteria, Biomed. Res. Int. 2017 (2017) 1583510.

[37] F.T. Mambe, I.K. Voukeng, V.P. Beng, V. Kuete, Antibacterial activities of methanol extracts from *alchornea cordifolia* and four other Cameroonian plants against MDR phenotypes, J. Taibah. Univ. Med. Sci. 11 (2) (2016) 121–127.

[38] F.T. Mambe, J. Na-Iya, G.W. Fotso, F. Ashu, B. Ngameni, B.T. Ngadjui, et al., Antibacterial and antibiotic modifying potential of crude extracts, fractions, and compounds from *Acacia polyacantha* willd. Against MDR gram-negative bacteria, Evid. Based. Complement. Alternat. Med. 2019 (2019) 7507549.

[39] A.G. Fankam, J.R. Kuiate, V. Kuete, Antibacterial and antibiotic resistance modulatory activities of leaves and bark extracts of *Recinodindron heudelotii* (Euphorbiaceae) against multidrug-resistant gram-negative bacteria, BMC. Complement. Altern. Med. 17 (2017) 168.

[40] J.A. Seukep, B. Ngadjui, V. Kuete, Antibacterial activities of *Fagara macrophylla, Canarium schweinfurthii, Myrianthus arboreus, dischistocalyx grandifolius* and *Tragia benthamii* against multi-drug resistant gram-negative bacteria, Springerplus. 4 (2015) 567.

[41] A.G. Fankam, J.R. Kuiate, V. Kuete, Antibacterial activities of *Beilschmiedia obscura* and six other Cameroonian medicinal plants against multi-drug resistant gram-negative phenotypes, BMC. Complement. Altern. Med. 14 (1) (2014) 241.

[42] S.T. Lacmata, V. Kuete, J.P. Dzoyem, S.B. Tankeo, G.N. Teke, J.R. Kuiate, et al., Antibacterial activities of selected Cameroonian plants and their synergistic effects with antibiotics against bacteria expressing MDR phenotypes, Evid. Based. Complement. Alternat. Med. 2012 (2012) 623723.

[43] A.G. Omokhua-Uyi, J. Van Staden, Extracts of *Gomphrena celosioides* mart as potential treatment for urinary tract infections against antibiotic resistant β-lactamase producing uropathogens, South Afr. J. Botan. 132 (2020) 502–510.

[44] J.A. Seukep, A.G. Fankam, D.E. Djeussi, I.K. Voukeng, S.B. Tankeo, J.A. Noumdem, et al., Antibacterial activities of the methanol extracts of seven Cameroonian dietary plants against bacteria expressing MDR phenotypes, Springerplus. 31 (2) (2013) 363.

[45] L. Ait Said, K. Zahlane, I. Ghalbane, S. El Messoussi, A. Romane, C. Cavaleiro, et al., Chemical composition and antibacterial activity of Lavandula coronopifolia essential oil against antibiotic-resistant bacteria, Nat. Prod. Res. 29 (6) (2015) 582–585.

[46] V. Kuete, R. BetrandTeponno, A.T. Mbaveng, L.A. Tapondjou, J.J.M. Meyer, L. Barboni, et al., Antibacterial activities of the extracts, fractions and compounds from *Dioscorea bulbifera*, BMC. Complement. Altern. Med. 12 (2012) 228.

[47] L. Youmbi, B. Atontsa, S. Tankeo, B. Wamba, N. Paul, N.K. Blaise, et al. Antibacterial potential and mechanism of action of botanicals and phytochemicals from *Stachytarpheta cayennensis* (Verbenaceae) against gram-negative multidrug-resistant phenotypes expressing efflux pumps. 2020 Jan 1.

[48] J. Gou, Y. Lu, M. Xie, X. Tang, L. Chen, J. Zhao, et al., Antimicrobial activity in Asterceae: the selected genera characterization and against multidrug resistance bacteria, Heliyon. 9 (4) (2023) e14985.

[49] C. Gufe, T.N. Mugabe, Z. Makuvara, J. Marumure, M. Benard, In-vitro assessment of the efficacy of herb-herb combinations against multidrug-resistant mastitis-causing bacteria: *Staphylococcus aureus* and *Klebsiella pneumoniae*, Cogent. Food Agric. 9 (1) (2023) 2187250.

[50] G. Nanmeni, A.T. Tedonkeu, A.G. Fankam, A.T. Mbaveng, B.E.N. Wamba, P. Nayim, et al., An efflux pumps inhibitor significantly improved the antibacterial activity of botanicals from *plectranthus glandulosus* towards MDR phenotypes, The Scientific World Journal 2021 (2021) e5597524.

[51] A.E. Ebrahim, N.K. Abd El-Aziz, E.Y.T. Elariny, A. Shindia, A. Osman, W.N. Hozzein, et al., Antibacterial activity of bioactive compounds extracted from red kidney bean (*Phaseolus vulgaris* L.) seeds against multidrug-resistant enterobacterales, Front. Microbiol. 13 (2022) 1035586.

[52] JN. Eloff, Avoiding pitfalls in determining antimicrobial activity of plant extracts and publishing the results, BMC. Complement. Altern. Med. 19 (1) (2019) 106.

[53] J. Zemede, T. Mekuria, C.O. Ochieng, G.E. Onjalalaina, G.W. Hu, Ethnobotanical study of traditional medicinal plants used by the local Gamo people in Boreda Abaya District, Gamo Zone, southern Ethiopia, J. Ethnobiol. Ethnomed. 20 (1) (2024) 28.

[54] V. Kuete, L.K. Omosa, V.R.S. Tala, J.O. Midiwo, A.T. Mbaveng, S. Swaleh, et al., Cytotoxicity of Plumbagin, Rapanone and 12 other naturally occurring quinones from Kenyan Flora towards human carcinoma cells, BMC Pharmacology and Toxicology 17 (1) (2016) 60.

[55] V. Kuete, T. Efferth, Cameroonian medicinal plants: pharmacology and derived natural products, Front. Pharmacol. 1 (2010) 123.

[56] V. Kuete, Potential of Cameroonian plants and derived products against microbial infections: a review, Planta Med. 76 (14) (2010) 1479–1491.

[57] G.L. Pessini, B.P. Dias Filho, C.V. Nakamura, D.A.G. Cortez, Antibacterial activity of extracts and neolignans from *Piper regnellii* (Miq.) C. DC. var. Pallescens (C. DC.) Yunck, Mem. Inst. Oswaldo Cruz. 98 (2003) 1115–1120.

[58] R. Mogana, A. Adhikari, M.N. Tzar, R. Ramliza, C. Wiart, Antibacterial activities of the extracts, fractions and isolated compounds from *Canarium patentinervium* Miq. Against bacterial clinical isolates, BMC. Complement. Med. Ther. 20 (1) (2020) 55.

[59] A. Cicio, R. Serio, M.G. Zizzo, Anti-inflammatory potential of brassicaceae-derived phytochemicals: In vitro and In vivo evidence for a putative role in the prevention and treatment of IBD, Nutrients. 15 (1) (2022) 31.

[60] N. Zouine, N.E. Ghachtouli, S.E. Abed, S.I. Koraichi, A comprehensive review on medicinal plant extracts as antibacterial agents: factors, mechanism insights and future prospects, Sci. Afr. 26 (2024) e02395.

[61] Q.A. Foods S. and of C&. Quality assurance and safety of crops & foods [Internet]. [cited 2024 Dec 29]. Available from: https://qascf.com.

[62] D. Nowicki, O. Rodzik, A. Herman-Antosiewicz, A. Szalewska-Pałasz, Isothiocyanates as effective agents against enterohemorrhagic Escherichia coli: insight to the mode of action, Sci. Rep. 6 (2016) 22263.

[63] B. Jamal, The Traditional Moroccan Pharmacopee, Ancient Arab Medicine and Popular Knowledge, IBIS Press, Paris, France, 1998.

[64] A. Gafter-Gvili, L. Vidal, E. Goldberg, L. Leibovici, M. Paul, Treatment of invasive candidal infections: systematic review and meta-analysis, Mayo Clin. Proc. 83 (9) (2008) 1011–1021.

[65] Y. El Atki, I. Aouam, F. El Kamari, A. Taroq, B. Lyoussi, B. Oumokhtar, et al., Phytochemistry, antioxidant and antibacterial activities of two Moroccan *Teucrium polium* L. subspecies: preventive approach against nosocomial infections, Arab. J. Chem. 13 (2) (2020) 3866–3874.

[66] P.J. Delaquis, K. Stanich, B. Girard, G. Mazza, Antimicrobial activity of individual and mixed fractions of dill, cilantro, coriander and eucalyptus essential oils, Int. J. Food Microbiol. 74 (1) (2002) 101–109.

[67] E. Logie, W. Vanden Berghe, Tackling chronic inflammation with withanolide phytochemicals—A withaferin A perspective, Antioxidants. (Basel) 9 (11) (2020) 1107.

[68] L. Bouissane, C. Bailly, *Withania frutescens* (L.) Pauquy, a valuable Mediterranean shrub containing bioactive withanolides, Steroids. 207 (2024) 109439.

[69] W. Huang, Y. Wang, W. Tian, X. Cui, P. Tu, J. Li, et al., Biosynthesis investigations of terpenoid, alkaloid, and flavonoid antimicrobial agents derived from medicinal plants, Antibiotics 11 (10) (2022) 1380.

[70] L. Kan, S. Nie, J. Hu, S. Wang, S.W. Cui, Y. Li, et al., Nutrients, phytochemicals and antioxidant activities of 26 kidney bean cultivars, Food and Chemical Toxicology 108 (2017) 467–477.
[71] H.H. Xiong, S.Y. Lin, L.L. Chen, K.H. Ouyang, W.J. Wang, The interaction between flavonoids and intestinal microbes: A review, Foods. 12 (2) (2023) 320.
[72] C. Sunil, V. Duraipandiyan, P. Agastian, S. Ignacimuthu, Antidiabetic effect of plumbagin isolated from *Plumbago zeylanica* L. root and its effect on GLUT4 translocation in streptozotocin-induced diabetic rats, Food and Chemical Toxicology 50 (12) (2012) 4356–4363.
[73] B. Shukla, S. Saxena, S. Usmani, P. Kushwaha, Phytochemistry and pharmacological studies of *Plumbago zeylanica* L.: a medicinal plant review, Clinical Phytoscience 7 (1) (2021) 34.
[74] A. Roy, T. Attre, N. Bharadvaja. Anticancer agent from medicinal plants: a review. In 2017. p. 54–73.
[75] P. Kumari, V. Singh, V. Kant, M. Ahuja, Current status of 1,4-naphthoquinones and their derivatives for wound healing, Eur. J. Med. Chem. Rep. 12 (2024) 100194.
[76] S. Muminovic, I. Kavgic, N. Sajna, Persistence of *Centaurea pumilio* L., a rare sand dune species, Ecologia Mediterranea 40 (2014) 19–25.
[77] E. Mostafa, M.A.A. Fayed, R.A. Radwan, R.O. Bakr, *Centaurea pumilio* L. extract and nanoparticles: A candidate for healthy skin, Colloids and Surfaces B: Biointerfaces 182 (2019) 110350.
[78] A.T. Tedonkeu, J.D.D. Tamokou, J.D.S. Mpetga, R.T. Nzogong, I.C. Kengne, X.J. Hao, et al., A new antimicrobial nor-friedelane-type triterpenoid and other constituents from *Plectranthus glandulosus* Hook. F. (Lamiaceae), Nat. Prod. Res. 36 (18) (2021) 4581–4590.
[79] J.P. Tsopmejio, J. Momeni, F. Nkouam Tsopjio, V. Sielinou Tedjon, P. Mkounga, N. Shehla, et al., Bioactive secondary metabolites from *plectranthus glandulosus* Hook. (Lamiaceae), Phytochem. Lett. 30 (2019) 133–137.
[80] S. Kim, H. Lee, S. Lee, Y. Yoon, K.H. Choi, Antimicrobial action of Oleanolic Acid on *Listeria monocytogenes, Enterococcus faecium*, and *Enterococcus faecalis*, PLoS. One 10 (3) (2015) e0118800.
[81] Y. Zhou, Y. Guo, X. Sun, R. Ding, Y. Wang, X. Niu, et al., Application of oleanolic acid and its analogues in combating pathogenic bacteria In vitro/vivo by a two-pronged strategy of β-lactamases and hemolysins, ACS. Omega 5 (20) (2020) 11424–11438.
[82] T. Fleischer, M.L.K. Mensah, A.Y. Mensah, G. Komlaga, S.Y. Gbedema, H. Skaltsa, Antimicrobial activity of essential oils of *xylopia aethiopica*, Afr. J. Tradit. Complement. Altern. Med. 5 (4) (2008) 391–393.
[83] A.N. Tamfu, O. Ceylan, S. Kucukaydin, M. Ozturk, M.E. Duru, RM. Dinica, Antibiofilm and enzyme inhibitory potentials of two annonaceous food spices, African pepper (*Xylopia aethiopica*) and African nutmeg (*Monodora myristica*), Foods. 9 (12) (2020) 1768.
[84] M. Bourhia, A.A. Alyousef, G. Doumane, H. Saghrouchni, J.P. Giesy, L. Ouahmane, et al., Volatile constituents in essential oil from leaves of *Withania adpressa* Coss. Ex exhibit potent antioxidant and antimicrobial properties against clinically-relevant pathogens, Molecules. 28 (6) (2023) 2839.
[85] A. Gauba, K.M. Rahman, Evaluation of antibiotic resistance mechanisms in gram-negative bacteria, Antibiotics. (Basel) 12 (11) (2023) 1590.
[86] L.R. Ramos da Silva, O.O. Ferreira, J.N. Cruz, C. de Jesus Pereira Franco, T. Oliveira dos Anjos, M.M. Cascaes, et al., Lamiaceae essential oils, phytochemical profile, antioxidant, and biological activities, Evid. Based. Complement. Alternat. Med. 2021 (2021) 6748052.
[87] A. Ultee, M.H.J. Bennik, R. Moezelaar, The phenolic hydroxyl group of carvacrol is essential for action against the food-borne pathogen Bacillus cereus, Appl. Environ. Microbiol. 68 (4) (2002) 1561–1568.
[88] A. Masyita, R. Mustika Sari, A. Dwi Astuti, B. Yasir, N. Rahma Rumata, T.B. Emran, et al., Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives, Food Chem. X. 13 (2022) 100217.
[89] R. Fink, Terpenoids as natural agents against food-borne bacteria—Evaluation of biofilm biomass versus viability reduction, Processes 11 (1) (2023) 148.
[90] K. Kachur, Z. Suntres, The antibacterial properties of phenolic isomers, carvacrol and thymol, Crit. Rev. Food Sci. Nutr. 60 (18) (2020) 3042–3053.
[91] (PDF) A review on chemical constituents and biological activities of the Genus Beilschmiedia (Lauraceae). ResearchGate [Internet]. 2024 Nov 21 [cited 2024 Dec 30]; Available from: https://www.researchgate.net/publication/311572555_A_Review_on_Chemical_Constituents_and_Biological_Activities_of_the_Genus_Beilschmiedia_Lauraceae.
[92] S. Chowański, Z. Adamski, P. Marciniak, G. Rosiński, E. Büyükgüzel, K. Büyükgüzel, et al., A review of bioinsecticidal activity of Solanaceae alkaloids, Toxins. (Basel) 8 (3) (2016) 60.
[93] Y. Yan, X. Li, C. Zhang, L. Lv, B. Gao, M. Li, Research progress on antibacterial activities and mechanisms of natural alkaloids: A review, Antibiotics. (Basel) 10 (3) (2021) 318.
[94] S. Letchuman, H.D.T. Madhuranga, MBLN Kaushalya, A.D. Premarathna, M. Saravanan, Alkaloids unveiled: A comprehensive analysis of novel therapeutic properties, mechanisms, and plant-based innovations, Intelligent Pharmacy [Internet] (2024). Sep 27 [cited 2024 Dec 30] Available from, https://www.sciencedirect.com/science/article/pii/S2949866X24001047.
[95] M. Barati, A.M. Chahardehi, M. Barati, A.M. Chahardehi, Alkaloids: the potential of their antimicrobial activities of medicinal plants. Medicinal Plants - Chemical, Biochemical, and Pharmacological Approaches [Internet], IntechOpen, 2023 [cited 2024 Dec 30] Available from, https://www.intechopen.com/chapters/87809.
[96] D. Tungmunnithum, S. Drouet, J.M. Lorenzo, C. Hano, Characterization of bioactive phenolics and antioxidant capacity of edible bean extracts of 50 Fabaceae populations grown in Thailand, Foods. 10 (12) (2021) 3118.
[97] K. Ganesan, B. Xu, Polyphenol-rich dry common beans (*Phaseolus vulgaris* L.) and their health benefits, Int. J. Mol. Sci. 18 (11) (2017) 2331.
[98] M. Makarewicz, I. Drożdż, T. Tarko, A. Duda-Chodak, The interactions between polyphenols and microorganisms, especially gut microbiota, Antioxidants 10 (2) (2021) 188.
[99] M. Miklasińska-Majdanik, M. Kępa, R.D. Wojtyczka, D. Idzik, T.J. Wąsik, Phenolic compounds diminish antibiotic resistance of *Staphylococcus Aureus* clinical strains, Int. J. Environ. Res. Public Health 15 (10) (2018) 2321.
[100] C. Liu, S. Dong, X. Wang, H. Xu, C. Liu, X. Yang, et al., Research progress of polyphenols in nanoformulations for antibacterial application, Mater. Today Bio 21 (2023) 100729.
[101] J. Morante-Carriel, H. Nájera, A. Samper-Herrero, S. Živković, M.J. Martínez-Esteso, A. Martínez-Márquez, et al., Therapeutic potential of prenylated flavonoids of the Fabaceae Family in Medicinal chemistry: an updated review, Int. J. Mol. Sci. 25 (23) (2024) 13036.
[102] A. Ullah, S. Munir, S.L. Badshah, N. Khan, L. Ghani, B.G. Poulson, et al., Important flavonoids and their role as a therapeutic agent, Molecules. 25 (22) (2020) 5243.
[103] S. Kumar, A.K. Pandey, Chemistry and biological activities of flavonoids: an overview, ScientificWorldJournal. 2013 (2013) 162750.
[104] D. Ramirez, A. Abellán-Victorio, V. Beretta, A. Camargo, D.A. Moreno, Functional ingredients from Brassicaceae species: overview and perspectives, Int. J. Mol. Sci. 21 (6) (2020) 1998.
[105] A. Lobiuc, N.E. Pavăl, I.I. Mangalagiu, R. Gheorghiță, G.C. Teliban, D. Amăriucăi-Mantu, et al., Future antimicrobials: natural and functionalized phenolics, Molecules. 28 (3) (2023) 1114.
[106] G. Petrocelli, P. Marrazzo, L. Bonsi, F. Facchin, F. Alviano, S. Canaider, Plumbagin, a natural compound with several biological effects and anti-inflammatory properties, Life (Basel) 13 (6) (2023) 1303.
[107] G. Navarro-Tovar, S. Vega-Rodríguez, E. Leyva, S. Loredo-Carrillo, D. de Loera, L.I. López-López, The relevance and insights on 1,4-naphthoquinones as antimicrobial and antitumoral molecules: A systematic review, Pharmaceuticals 16 (4) (2023) 496.
[108] N.S. Mone, S.A. Bhagwat, D. Sharma, M. Chaskar, R.H. Patil, P. Zamboni, et al., Naphthoquinones and their derivatives: emerging trends in combating microbial pathogens, Coatings 11 (4) (2021) 434.
[109] I.U. Okagu, J.C. Ndefo, E.C. Aham, C.C. Udenigwe, Zanthoxylum species: A review of traditional uses, phytochemistry and pharmacology in relation to cancer, infectious diseases and sickle cell anemia, Front Pharmacol [Internet] (2021) 12. Sep 15 [cited 2024 Dec 30] Available from, https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2021.713090/full.
[110] J.F. França Orlanda, A.R. Nascimento, Chemical composition and antibacterial activity of *ruta graveolens* L. (Rutaceae) volatile oils, from São Luís, Maranhão, Brazil, South Afr. J. Botan.. 99 (2015) 103–106.

[111] S. Al-Majmaie, L. Nahar, M.M. Rahman, S. Nath, P. Saha, A.D. Talukdar, et al., Anti-MRSA constituents from *ruta chalepensis* (Rutaceae) grown in Iraq, and In Silico studies on two of most active compounds, chalepensin and 6-hydroxy-rutin 3′,7-dimethyl ether, Molecules. 26 (4) (2021) 1114.
[112] M. Oalđe Pavlović, S. Kolarević, J. Đorđević Aleksić, B. Vuković-Gačić, Exploring the antibacterial potential of Lamiaceae plant extracts: inhibition of bacterial growth, adhesion, invasion, and biofilm formation and degradation in Pseudomonas aeruginosa PAO1, Plants 13 (12) (2024) 1616.
[113] U. Salam, S. Ullah, Z.H. Tang, A.A. Elateeq, Y. Khan, J. Khan, et al., Plant metabolomics: an overview of the role of primary and secondary metabolites against different environmental stress factors, Life 13 (3) (2023) 706.
[114] A. Roy, A. Khan, I. Ahmad, S. Alghamdi, B.S. Rajab, A.O. Babalghith, et al., Flavonoids a bioactive compound from medicinal plants and its therapeutic applications, Biomed. Res. Int. 2022 (2022) 5445291.
[115] Q.W. Zhang, L.G. Lin, W.C. Ye, Techniques for extraction and isolation of natural products: a comprehensive review, Chin. Med. 13 (1) (2018) 20.
[116] M. Abers, S. Schroeder, L. Goelz, A. Sulser, T. St. Rose, K. Puchalski, et al., Antimicrobial activity of the volatile substances from essential oils, BMC Complementary Medicine and Therapies [Internet] 21 (1) (2021). Available from, https://www.scopus.com/inward/record.uri?eid=2-s2.0-85104494749&doi=10.1186%2fs12906-021-03285-3&partnerID=40&md5=ea776ed127004dbcc7bf395434be7f1d.
[117] J.E. Lee, J.T.M. Jayakody, J.I. Kim, J.W. Jeong, K.M. Choi, T.S. Kim, et al., The influence of solvent choice on the extraction of bioactive compounds from asteraceae: A comparative review, Foods. 13 (19) (2024) 3151.
[118] S. Idris, G. Ndukwe, C. Gimba, Preliminary phytochemical screening and antimicrobial activity of seed extracts of *Persea americana* (avocado pear), Bayero Journal of Pure and Applied Sciences 2 (1) (2009) 173–176.
[119] A.A. Ogunjobi, T. Ogunjobi, Comparative study of antibacterial activities of ethanol extracts of the bark and seeds of garcinia kola and caricapapaya, Afr. J. Biomed. Res. 14 (2) (2011) 147–152.
[120] J.A. Bohnert, W.V. Kern, Selected arylpiperazines are capable of reversing multidrug resistance in *Escherichia coli* overexpressing RND efflux pumps, Antimicrob. Agents Chemother 49 (2) (2005) 849–852.
[121] M.M. Cowan, Plant products as antimicrobial agents, Clin. Microbiol. Rev. 12 (4) (1999) 564–582.
[122] M. Bubonja-Šonje, S. Knežević, M. Abram, Challenges to antimicrobial susceptibility testing of plant-derived polyphenolic compounds, Arh. Hig. Rada Toksikol. 71 (4) (2020) 300–311.
[123] L. Ory, E.H. Nazih, S. Daoud, J. Mocquard, M. Bourjot, L. Margueritte, et al., Targeting bioactive compounds in natural extracts - development of a comprehensive workflow combining chemical and biological data, Anal. Chim. Acta 1070 (2019) 29–42.
[124] R. Vernooy, J. Adokorach, A. Gupta, G. Otieno, J. Rana, P. Shrestha, et al., Promising strategies to enhance the sustainability of community seed banks, Sustainability. 16 (19) (2024) 8665.
[125] M. Asigbaase, D. Adusu, L. Anaba, S. Abugre, S. Kang-Milung, S.A. Acheamfour, et al., Conservation and economic benefits of medicinal plants: insights from forest-fringe communities of Southwestern Ghana, Trees. For. People 14 (2023) 100462.
[126] S.L. Chen, H. Yu, H.M. Luo, Q. Wu, C.F. Li, A. Steinmetz, Conservation and sustainable use of medicinal plants: problems, progress, and prospects, Chin. Med. 11 (1) (2016) 37.
[127] P.A. Singh, N. Bajwa, S. Chinnam, A. Chandan, A. Baldi, An overview of some important deliberations to promote medicinal plants cultivation, J. Appl. Res. Med. Aromat. Plants. 31 (2022) 100400.
[128] P.W. Wambugu, D.O. Nyamongo, E.C. Kirwa, Role of seed banks in supporting ecosystem and biodiversity conservation and restoration, Diversity. (Basel) 15 (8) (2023) 896.
[129] W. van Slageren, The Millennium Seed Bank: building partnerships in arid regions for the conservation of wild species, J. Arid. Environ. 54 (1) (2003) 195–201.
[130] A. Mamo*, Biodiversity organization, threats and conservation methods, Journal of Biodiversity and Conservation Research (2023) 1–12.
[131] C. Sudhersan, M. AboEl-Nil, J. Hussain, Tissue culture technology for the conservation and propagation of certain native plants, J. Arid. Environ. 54 (1) (2003) 133–147.
[132] Z. Mbelebele, L. Mdoda, S.S. Ntlanga, Y. Nontu, L.S. Gidi, Harmonizing traditional knowledge with environmental preservation: sustainable strategies for the conservation of indigenous medicinal plants (IMPs) and their implications for economic well-being, Sustainability. 16 (14) (2024) 5841.
[133] T. Volenzo, J. Odiyo, Integrating endemic medicinal plants into the global value chains: the ecological degradation challenges and opportunities, Heliyon. 6 (9) (2020) e04970.
[134] G. Dida, Biotechnology towards energy crops, CABI. Agric. Biosci. 5 (1) (2024) 45.