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Antimicrobial properties of alternative medicines used in the management of infections in diabetic patients: A comprehensive review

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ABSTRACT

Introduction: Diabetes mellitus poses major health risks due to increased vulnerability to infections stemming from weakened immune systems and physiological complications. With antimicrobial resistance worsening prognosis, diabetic infections affecting multiple body systems present critical treatment challenges. This review examines the antimicrobial properties of alternative medicines used in the management of diabetic infections and addresses the apparent research gap in this area.

Method: A comprehensive literature search was conducted on databases (PubMed, Scopus, ScienceDirect, and Google Scholar) using specified keywords. Exclusion criteria removed non-relevant articles, resulting in the selection of articles published between 2012 and 2023, focusing on medicinal plants, polyherbal formulations, and antimicrobial effects against pathogens associated with diabetic infections.

Results: The study revealed a significant research gap regarding the use of alternative medicines for diabetic infection treatment, as only 14 articles published between 2012 and 2023 were relevant to this review. Selected articles primarily addressed wound infections (39 %), diabetic foot ulcers (28 %), foot infections (17 %), urinary tract 11 %), and skin infections (5 %). Commonly used medicinal plants include *Curcuma longa, Azadirachta indica, Zingiber officinale*, and *Glycyrrhiza glabra* among others. The alternative medicines demonstrated significant antimicrobial potential against common microorganisms associated with diabetic infections, especially Gram-positive bacteria.

Discussion: This review shows the potential of alternative medicines in the management of diabetic infections. This efficacy was attributed to diverse secondary metabolites present in medicinal plants, offering promising prospects for novel antimicrobial agents. Given the susceptibility of diabetic patients to microbial infections, further investigation into the efficacy of medicinal plants for the treatment of infections in diabetic patients is essential. Further research is also imperative to validate and standardize these therapies and conduct clinical trials to evaluate their safety and efficacy in diabetic infection management.

Introduction

Diabetes mellitus (DM) is a chronic, non-infectious endocrine condition characterized by high blood sugar levels (hyperglycaemia) due to insufficient insulin synthesis, inadequate insulin utilization, or both. According to the World Health Organization, approximately 422 million people worldwide have diabetes, the majority living in low-middle-income countries, and 1.5 million deaths are directly attributed to diabetes every year [1]. Diabetes is one of the top 10 causes of death globally [2], exerting the second most substantial adverse impact on the enhancement of global health-adjusted life expectancy worldwide [3]. This disease is comorbid with cardiovascular disease, cancer, and respiratory disease which collectively account for more than 80 % of premature deaths caused by noncommunicable diseases (NCDs) [4]. Diabetes is linked to increased mortality rates stemming from infections, cardiovascular disease, stroke, chronic kidney disease, chronic liver

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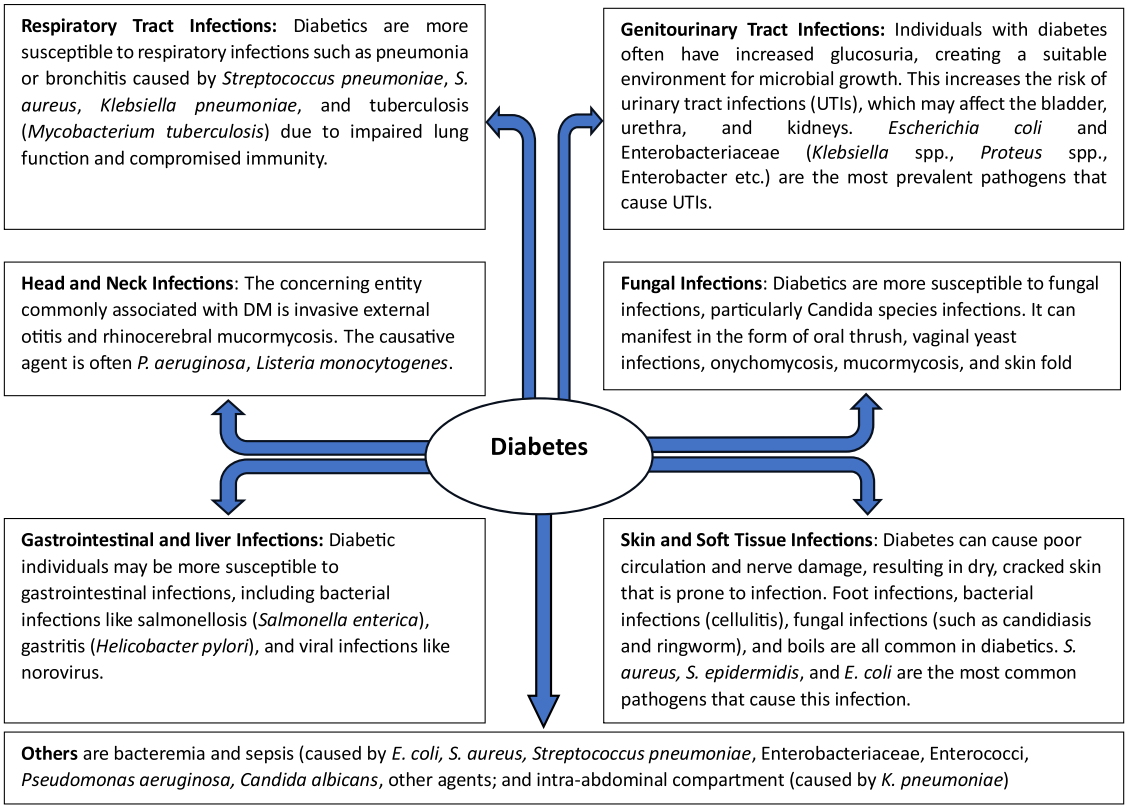
disease, and cancer [2]. In the year 2019, diabetes was accountable for approximately 4.2 million deaths among individuals aged 20 to 79 years old. The condition was estimated to have contributed to about 11.3 % of all deaths worldwide, with rates ranging from 6.8 % in the African region to 16.2 % in the Middle East and North Africa [5].

Diabetes is classified into four primary categories: type 1 diabetes mellitus, which is an autoimmune-mediated disease, characterized by beta cell destruction that typically leads to absolute insulin deficiency; type 2 diabetes mellitus, also known as non-insulin-dependent diabetes or adult-onset diabetes, is characterized by a progressive reduction in beta cell insulin secretion often coupled with insulin resistance; gestational diabetes mellitus, is characterized by the onset or first recognition of abnormal glucose tolerance during pregnancy; and diabetes linked to various other conditions including genetic defects in beta cell function or insulin action, diseases of the exocrine pancreas, endocrinopathies, drug or chemical induced causes, infections, rare immune-mediated diabetic syndromes, and certain genetic syndromes occassionally associated with diabetes [6]. Clinical manifestations of diabetes encompass polydipsia, polyuria, polyphagia, fatigue, nausea, vomiting, erectile dysfunction, delayed wound healing, and visual abnormalities [7].

Diabetic patients are often susceptible to various types of microbial infections due to their hyperglycaemia-induced compromised immune systems and altered physiological conditions [8]. There is a notable attenuation in humoral immunity, compromised T-cell responsiveness, impaired phagocytic activity, and diminished neutrophil functionality in individuals with diabetes. Notably, these collective immunological alterations make diabetic patients significantly more susceptible to a wide range of infectious agents [9,10]. The different types of microbiological infections that are common among diabetic patients are shown in SmartArt graphic 1. Infections of the respiratory tract, skin and soft tissues, gastrointestinal tract, and genitourinary tract are more prevalent in individuals with diabetes. Furthermore, these infections not only have a greater incidence rate, but they also have a lower response rate to treatment and a faster progression to severe forms of illness [8,11–13].

A Canadian study involving over 500,000 individuals living with diabetes, discovered a substantial relationship between diabetes and infectious diseases. Approximately 46 % of diabetics were hospitalized or sought medical care for infectious diseases, compared to 38 % of non-diabetics. Among the various types of infections reported, bacterial infections such as osteomyelitis, pyelonephritis, cystitis, pneumonia, cellulitis, sepsis, or peritonitis were the most common. The risk was consistent across genders and income levels, although it increased with age. Hospitalization rates for infectious diseases were also higher in the diabetic group. Infection-related mortality was higher in diabetic patients, with an 8 % absolute risk increase and a risk ratio of 1.84 [20]. Korbel and Spencer [21] found that since 2006, approximately 10 million diabetics in the United States have sought emergency care each year, with infections accounting for 10 % of these visits. Urinary tract infections were the most prevalent, accounting for more than 30 % of infection-related cases. Diabetic patients were more than twice as likely non-diabetic individuals to require hospitalization for infection management. . In 2011, in-patient care for diabetic patients with infections incurred over $48 billion in hospital charges, highlighting the substantial economic impact on the healthcare system and the need for cost-effective prevention strategies for diabetes-related infections. Another prospective cohort study, which aimed to assess the association between diabetes mellitus (DM) types 1 and 2 and common infections, found that patients with DM1 and DM2 had a higher risk of lower respiratory tract infections, urinary tract infections, bacterial skin and mucous membrane infections, and mycotic skin and mucous membrane infections than patients with hypertension but no diabetes. The findings highlight the increased infection risks in both DM1 and DM2 patients, calling for further research on infection management in diabetes care [22].

The traditional medical practices, involving the utilization of herbs, are regarded as an integral component of the cultural heritage within



SmartArt graphic 1. Microbiological infections that are commonly seen among diabetic patients.
References [8,14–19].

developing countries [23,24]. It is believed that there has been a discernible upward trajectory in the utilization of Traditional Medicine (TM) and complementary medicines. The global utilization of herbal medicines, phytonutrients, and nutraceuticals is experiencing significant growth, as an increasing number of individuals are turning to these products to manage a variety of health conditions, within diverse national healthcare frameworks [25,26]. It is estimated that up to four billion individuals, constituting approximately 80 % of the global population residing in developing regions, depend on herbal medicinal products as a primary healthcare resource. According to the World Ethnobotanical Database, approximately 800 medicinal plants are employed for diabetes mellitus treatment. However, clinical research has substantiated the anti-diabetic properties of only 450 of these medicinal plants, with 109 among them demonstrating a fully elucidated mode of action [7]. The exploration of alternative medicines for the management or treatment of infections in diabetic individuals is crucial due to the unique challenges presented by diabetes and the potential for a more holistic, individualized, and sustainable approach that can improve these patient's overall well-being while reducing antibiotic reliance and minimizing the risk of antibiotic resistance. In addition, traditional plant-based formulations and specific natural medicinal remedies can offer a potentially safer therapeutic approach in addressing infectious diseases than synthetic pharmaceuticals, owing to their inherent antimicrobial attributes, which can exhibit bactericidal or bacteriostatic effects [27]. Some of these compelling rationales are elucidated in SmartArt graphic 2.

Antimicrobial agents are important in diabetic infection care because diabetes weakens the immune system, making infections more difficult to combat [28]. Effective antimicrobials aid in the prevention of complications, the improvement of diabetic patients' health, the acceleration of wound healing and reduction of the risk of infection, reduction of healthcare costs, overall improvement of patient outcomes, and prevention of antibiotic resistance. There are numerous drugs (such as cephalosporins, penicillin, fluoroquinolones, clindamycin, imipenem and pexiganan) available to treat infections in diabetics [29,30]; however, there are concerns about their limited efficacy and associated side effects. In addition, the swift escalation of antimicrobial resistance (AMR) poses a worldwide dilemma that hampers the efficacy of treating

SmartArt graphic 2. Rationale for exploring alternative treatments for the treatment of infections in diabetic patients.

infectious diseases [31]. Nevertheless, among the auspicious approaches, herbal medicine stands out, blending antimicrobial properties within its constituents and bolstering resilience. As the surge in AMR narrows antibiotic choices, herbal medicine strategies gain heightened relevance [32]. Hence, researchers are striving to address drug resistance through the exploration of natural sources for complementary and alternative medicines, seeking alternative solutions [33].

The global prevalence of diabetes has been on a relentless rise, with projections indicating further increases in the coming years [34]. Individuals living with diabetes are particularly susceptible to infections due to the disease's multifaceted impact on the immune system and physiological responses [28]. As infections in diabetic individuals can have severe consequences, documenting alternative approaches to infection management using alternative medicine is both timely and essential. Furthermore, the widespread and indiscriminate use of antibiotics has given rise to a burgeoning global health concern-antimicrobial resistance. Given that individuals with diabetes often require antibiotics for managing infections, it is imperative to explore alternative therapies with inherent antimicrobial properties. Thus, collating, evaluating, and consolidating the existing body of knowledge regarding the antimicrobial properties of medicinal plants and herbal formulations in the context of infection management among people living with diabetes is essential. It is important to note that alternative medicines encompass a rich and diverse spectrum of therapies, including traditional herbal remedies, complementary therapies, and integrative approaches. Many of these alternative modalities are known to possess inherent antimicrobial properties. However, the fragmented nature of the available research necessitates a comprehensive review to identify and critically review the existing evidence regarding their effectiveness in managing infections among people with diabetes. In addition, diabetes management is inherently individualized, and patient preferences play a pivotal role in treatment decisions. Conducting this comprehensive review of alternative medicines with antimicrobial properties empowers patients and healthcare providers with a well-informed understanding of these therapies, facilitating patient-centred care choices tailored to the unique needs and preferences of individuals, as well as contributing to the optimization of infection control and prevention strategies, ultimately reducing the burden of diabetes-related complications. Thus, this literature review aims to explore the antimicrobial potential of alternative medicines in treating infections in diabetic patients.

Approach and methods

Data sources such as PubMed, Scopus, ScienceDirect, and Google Scholar were searched for publication across the world. The search terms used were "medicinal plant" OR phytomedic* OR herb* OR Polyherb* OR phyto*OR "alternative medicine" OR "traditional medicine" OR "complementary medicine" OR "traditional Chinese medicine" AND antimicrob* OR antifungi OR antibacter* OR Infectio* OR bacteri* OR fungi AND diabet* OR hyperglyc* OR "high blood glucose" OR "high blood sugar."

The literature search retrieved 844 articles, but only 13 were selected based on specific criteria. The inclusion criteria were original research articles between 2012 and 2023, published articles or book chapters, and studies that focused on using medicinal plants or alternative medicines to treat infections in diabetic patients. Exclusion criteria included review articles, letters, conference papers, erratum, notes, unpublished data, unavailable full-text articles, duplicates, and abstract-only papers. The relevant information from the selected studies was systematically organized in a dedicated spreadsheet, including author names, study titles, publication year, plant names, formulations, plant parts used, infection types, isolate investigated, research models, dosages, solvents, research findings, and identified secondary metabolites. The selection process involved an initial screening of titles and abstracts, followed by a thorough review of the full-text content to ensure relevance and eliminate duplicates.

Results

The screening process yielded a total of 14 articles, published between 2012 and 2022, which were subsequently subjected to a comprehensive review to explore the antimicrobial activities of medicinal plants and polyherbal formulations against infections in the context of diabetes. (Fig. 1).

A comprehensive overview of the alternative medicines, the types of infections addressed, the antimicrobial findings, and the potential metabolites responsible for the antimicrobial properties of medicinal plants and polyherbal formulations is presented in Table 1. The articles retrieved cover a diverse range of diabetic infections, with wound infections comprising the majority at 39 %, followed by diabetic foot ulcers (28 %), urinary tract infections (17 %), wound infections (11 %) and skin infections (5 %) as depicted in Fig. 2.

The commonly used medicinal plants across the alternative medicines are *Curcuma longa, Azadirachta indica, Zingiber officinale, Glycyrrhiza glabra, Centella asiatica, Psidium guajava, Allium sativum, Piper nigrum, Garcinia mangostana, Areca catechu*, and *Acalypa indica* as represented in Fig. 3.

Discussion

One notable implication of the limited number of selected articles is an apparent gap in research on the use of alternative medicines for the treatment of infections in diabetic populations. These findings show the need for further investigation in this area.

Individuals with diabetes are twice as likely, compared to those without diabetes to contract community-acquired bacterial infections such as pneumococcal, streptococcal, and enterobacterial infections [48]. The increased prevalence and severity of bacterial infections in diabetic patients have been associated with impaired innate and adaptive immune responses in the hyperglycaemic environment [48]. Aside from hyperglycaemia, several long-term consequences of diabetes may make patients more susceptible to infections. For instance, the combination of neuropathy and peripheral vascular disease can result in skin ulcers and subsequent infections [48]. There exists a two-way connection between diabetes and bacterial infections. While diabetes increases the risk of bacterial infections and their complications, chronic infections such as periodontitis have been linked to increased levels of pro-inflammatory cytokines, which can worsen insulin resistance and glycaemic control [49].

Exploring alternative medicines as promising antimicrobial agents against skin infections in diabetic individuals

The increasing prevalence of skin infections globally can be attributed to shifts in environmental conditions resulting from factors such as industrialization, pollution, deforestation, and related changes. The skin, as the body's external protective barrier, serves as the primary defence against harmful external factors and pathogens. Changes in its local resilience can result in the growth of opportunistic pathogens that are prone to surface injuries and various secondary complications associated with infections [27]. Diabetics are more likely to get skin infections due to weakened immune systems and changed skin microenvironments. These infections, which are frequently caused by a range of bacterial pathogens such as *Staphylococcus aureus, Staphylococcus epidermidis, E. coli, Klebsiella* sp., *Proteus* sp., and Peptostreptococcus are a major public health concern [15]. To address this, several studies have investigated the antimicrobial potential of alternative medicines used to combat infections in diabetics. In a study by Kota et al. [35], a polyherbal extract consisting of *Acacia ferruginea* (bark and fruit), *Chloroxylon swietenia* (bark, leaf, and root), *Casearia elliptica* (bark), and *Terminalia alata* (root, leaf) demonstrated significant antibacterial

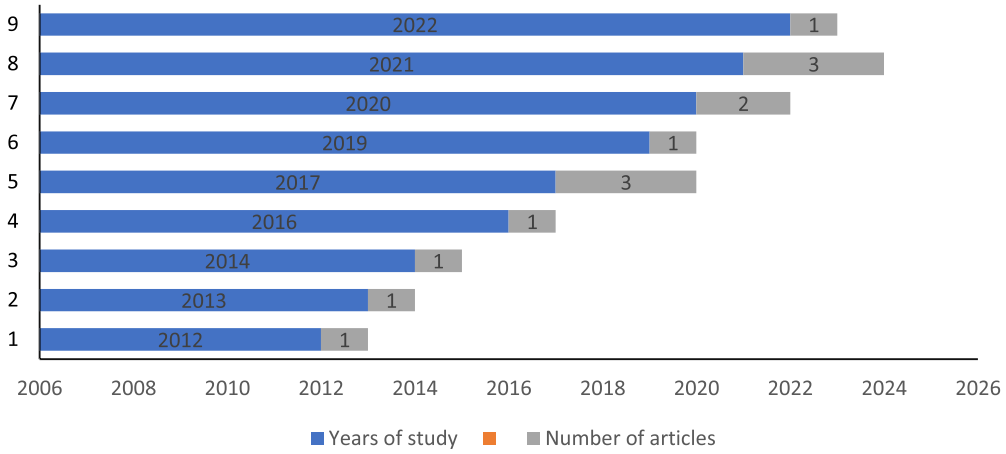


Fig. 1. Publications on alternative medicines and diabetic infections between the year 2012 and 2022.

activities against both Gram-positive bacteria like *S. aureus* and *B. subtilis*, as well as Gram-negative bacteria including *P. aeruginosa, E. coli, K. pneumonia*, and *P. vulgaris*, which were comparable to the antibiotic Gentamicin. The PHF exhibited the highest inhibitory activity against *Bacillus subtilis*, with a mean ZOI of 3.3 cm, followed by *P. vulgaris, K. pneumoniae, E. coli, P. aeruginosa*, and *S. aureus* at 3.22 cm, 2.97 cm, 2.92 cm, 2.57 cm, 2.42 cm and 2.7 cm respectively. The PHF exhibited a broad-spectrum antimicrobial effect, and the observed antimicrobial potential can be attributed to its constituent secondary metabolites, including flavonoids, alkaloids, steroids, triterpenoids, and phenolic compounds like tannins. In addition, the PHF's mixture of several plant components may have a synergistic impact, increasing its overall antibacterial potency.

Exploring herbal solutions for managing multidrug-resistant urinary tract infections in diabetic patients

A urinary tract infection (UTI) is a prevalent clinical issue, accounting for 1–6 % of medical referrals and encompassing infections in the urinary tract, bladder, and kidneys [50]. Among diabetic patients, UTIs are the most frequently occurring infectious ailment [50,51]. Globally, UTIs and their associated complications contribute to approximately 150 million fatalities each year [52]. It manifests as an infection that develops within the urinary tract, potentially affecting the urethra (known as urethritis), prostate, and bladder (referred to as cystitis), or extending into the kidneys (known as pyelonephritis) [53,54]. Various factors, such as a compromised immune system, reduced white blood cell function, inadequate blood supply, bladder dysfunction resulting from nephropathy, and glycosuria, can cause UTIs in diabetic individuals [11,55,56]. Diabetic patients may experience dysuria as a complication of UTIs due to organ damage, and potentially life-threatening conditions may arise from pyelonephritis and related kidney damage. UTIs pose challenges for blood glucose control in diabetics, necessitating continuous blood glucose monitoring, which in turn diminishes the quality of life for patients and imposes a substantial healthcare burden in terms of cost [57]. Diabetic infections, including urinary tract infections (UTIs), pose significant challenges to healthcare due to the increasing prevalence of multidrug-resistant organisms (MDROs) associated with diabetic patients [58]. The emergence of drug-resistant microorganisms necessitates the exploration of alternative medicines, such as herbs, herbal extracts, and polyherbal formulations, for their potential antimicrobial properties.

Dsouza & Nanjaiah [36], evaluated the antibacterial activity of *Justicia wynaadensis* leaf extracts against a variety of MDROs associated with diabetic wounds and urinary tract infections. At a concentration of 0.5 mg/mL, four fractions of the plant (hexane, chloroform, ethyl acetate, and methanol-water) displayed considerable antibacterial activity. Notably, the chloroform fraction was the most potent when compared to the other fractions. In addition, the researchers extracted and discovered 3,3′,4′-Trihydroxyflavone from *Justicia wynaadensis*, which showed substantial antimicrobial activity against drug-resistant microbes linked with diabetes infections. This compound demonstrated promising minimum inhibitory concentrations (MICs) ranging from 32 μg/mL to 1.2 mg/mL, with significant activity against *E. faecalis* and *S. aureus* at an MIC value of 32 μg/mL, as well as *K. pneumoniae, E. aerogenes*, and *E. coli* at 32, 64, and 128 μg/mL, respectively. These findings imply that 3,3′, 4′-Trihydroxyflavone could be used as an antibacterial agent in future medication development. The antimicrobial potential of *Justicia wynaadensis* extracts could be attributed to a variety of secondary metabolites present in the plant, including alkaloids, tannins, saponins, terpenoids, flavonoids, glycosides, phlobatannins, and steroids.

Furthermore, Subbu lakshmi et al. [42] evaluated the antimicrobial potential of different medicinal plants and spice extracts against MDROs isolated from diabetic foot ulcers and urine samples of diabetic individuals. Among the tested extracts, the methanol extract of *Tragia involucrata* at the concentration of 20 mg/mL inhibited the growth of all bacteria isolated from diabetic foot ulcers. Additionally, extracts from *Acalypa indica, Azadirachta indica, Cyanodon dactylon, Leucas aspera*, and *Thymus vulgaris* inhibited the growth of *S. aureus*. Several extracts also showed inhibition of *E. coli*, except for *Acalypa indica, Leucas aspera*, and *Cyanodon dactylon*. Notably, *Ocimum sanctum* and *Psidium guajava* methanol extracts exhibited inhibitory activity against *E. aerogenes* and *P. aeruginosa*. Moreover, the extracts of some spices, including *Allium sativum, Zingiber officinale*, and *Piper nigrum*, also demonstrated antimicrobial activity against various microorganisms. It is important to mention that standard drugs such as Streptomycin and Oxacillin showed inhibitory activity against the bacteria isolated from diabetic foot ulcers and urine samples [42]. The presence of diverse secondary metabolites such as aliphatic group, and phenolic compounds in these plant extracts could be responsible for their bioactive properties and possible application in future drug development efforts.

Exploring alternative antimicrobial medicines for diabetic foot infections and ulcers

One of the primary areas of concern in diabetic patients is the susceptibility to diabetic foot infections, often caused by a variety of bacterial strains [59,60]. Diabetic foot infections and foot ulcers are prevalent and serious complications of diabetes mellitus [41,43]. These conditions are not only a source of immense suffering for individuals with diabetes but also pose significant healthcare challenges and cost implications [61,62].

Diabetic foot infections are common and often result from minor injuries, such as cuts or wounds, in individuals with diabetes [62].

Table 1
Antimicrobial properties of alternative medicines used in the treatment of diabetic infections.

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
PHF	*Acacia ferruginea* (bark and fruit), *Chloroxylon swietenia* (bark, leaf, and root), Casearia *elliptica* (bark), and *Terminalia alata* (root, leaf)	Skin and diabetic foot infections	Gram-positive bacteria: *Staphylococcus aureus, Bacillus subtilis*; Gram-negative bacteria: *Pseudomonas aeruginosa, E. coli, Klebsiella pneumonia*, and *Proteus vulgaris*	Agar diffusion disc	50 mg/mL	At 50 mg/ ml concentration, the polyherbal extract demonstrated significant antibacterial activity against Gram-positive and Gram-negative bacteria comparable to the Gentamicin. The PHF exert more inhibition on *B. subtilis* with a mean zone of inhibition (ZOI) of 3.3 cm, followed by *P. vulgaris, K. pneumoniae, E. coli, P. aeruginosa,* and *S. aureus* 3.22 cm, 2.97 cm, 2.92 cm, 2.57 cm, 2.42 cm and 2.7 cm respectively.	Flavonoids, alkaloids, steroids, triterpenoids, phenolic compounds like tannins	Methanol	[35]
Justicia wynaadensis (leaf)	N/A	Wound and urinary tract infections (UTIs)	Diabetic wound infection: Gram-negative: *P. aeruginosa* – KY069054; *K. pneumoniae* – KY069048, *E. aerogenes* – KY069049, *E. coli* – KY069050; Gram-positive: *S. aureus* – KX611101, *E. faecalis* – KY069051, *S. epidermidis* – KY069052, *S. haemolyticus* – KY069053. Urinary tract infection: *E. coli* – KX816955, *K. pneumoniae* – KY021157, *P. aeruginosa* – KX816953, *E. aerogenes* – KX878983, *P. mirabilis* – KX878984; Gram-positive: *S. epidermidis* – KX816954, *S. aureus* – KY021156, *E. faecalis* – KY021157	Micro broth dilution	16 - 1024 μg/mL	The study depicted that the four fractions (hexane (HF), chloroform (CF), ethyl acetate (EF) and methanol-water (MF)) of the plant at 0.5 mg/mL concentration had significant antibacterial activity against the multi-drug resistant organisms (MDRO's) associated with diabetic patients, with chloroform fraction having the highest potency when compared with other fractions. Furthermore, the study revealed that 3,3′,4′-Trihydroxyflavone isolated from *Justicia wynaadensis* has significant potential as an antimicrobial agent against drug-resistant microorganisms associated with diabetic wounds and urinary tract infections at concentrations ranging from 32 μg/mL to 1.2 mg/mL while the standard drug, chloramphenicol showed activity at concentration between 4 and 32 μg/mL. The best activity was observed against *E. faecalis* and *S. aureus* at a MIC value of 32 μg/mL, *K. pneumoniae, E. aerogenes* and *E. coli* at MIC values of 32, 64 and 128 μg/mL respectively. The compound exhibited promising minimal inhibitory	Alkaloids, tannins, saponins, terpenoids, flavonoids, glycosides, phlobatannins, and steroids	Methanol	[36]

(*continued on next page*)

Table 1 (*continued*)

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
						concentrations (MICs) against the tested bacteria, suggesting its potential use as an antimicrobial agent in future drug development.			
Ya-Samarn-Phlae	*Garcinia mangostana* (pericarp), *Oryza sativa* (seed), *Curcuma longa* (rhizome), and *Areca catechu* (seed)	Diabetic foot ulcers (DFUs) and wound-related pathogens	Methicillin-resistant *S. aureus* (MRSA), coagulase-positive staphylococci (CPS), coagulase-negative staphylococci (CNS), multidrug-resistant (MDR) *P. aeruginosa*, MDR *Acinetobacter baumannii* NPRC034, and MDR *E. coli*	Broth microdilution	2 - 1000 μg/mL	The study showed that the extracts of YaSP and the individual plant extracts showed varied degrees of antibacterial activity against MDR pathogens, with the MIC value ranging from 2 to >1000 μg/mL. YaSP and *G. mangostana* extracts had significant antibacterial activity against *Staphylococcus* spp., including MRSA isolates, with MICs of 2–8 μg/mL and 2–4 μg/mL, respectively. However, the extracts exhibited low activity against Gram-negative pathogens with the MICs ranging from 500 to>1000 μg/mL for YaSP and from 250 to>1000 μg/mL for *G. mangostana*. When compared with the YaSP extract, alpha-mangostin was found to possess similar inhibitory activity against the majority of bacteria tested. The extracts of *C. longa* and *A. catechu* displayed moderate antibacterial activity against Gram-positive and Gram-negative pathogens, with MICs ranging from 31 to >1000 and from 125 to >1000 μg/mL, but O. sativa and curcumin were ineffective against all pathogens tested.		Ethanol	[37]
Jathyadi Thailam (JTAFI) and Jatyadi Ghritam (JTYG)	"JTAFI: *Azadirachta indica* (leaf), *Chrysopogon zizanioides* (root), *Berberis aristate* (stem), *Curcuma longa* (rhizome), *Glycyrrhiza glabra* (root), *Hemidesmus indicus* (root), *Jasminum officinale* (leaf), *Picrorhiza kurroa* (root/ rhizome), *Pongamia pinnata* (seed), *Rubia cordifolia* (root), *Trichosanthes dioica* (leaf); JTYG: *Aerva lanata* (whole	Diabetic chronic wounds	*S. aureus* ATCC 25,923, *S. aureus* (MRSA) ATCC 33,592, *S. epidermidis* RP62 A, *Enterococcus faecalis* 29,212, *E. coli* ATCC 25,922, *Pseudomonas aeruginosa* ATCC 27,853, multidrug-resistant (MDR) *P. aeruginosa* ATCC BAA-2108, *Proteus mirabilis* ATCC 29,245, and *Klebsiella pneumoniae* ATCC 33,495	Broth microdilution	250 mg/mL (starting concentration)	The study showed that in general, Jatyadi extracts had higher antibacterial activity against Gram-positive bacteria (*S. aureus*, MRSA, *S. epidermidis* and *E. faecalis*), with the MICs varying from 1.95 to 62.5 mg/mL; while the Gram-negative bacteria (*E. coli, P. aeruginosa*, MDR *P. aeruginosa, P. mirabilis*, and *K. pneumoniae*) were only susceptible to ethanol extracts.	Phenols, tannins, sterols, terpenoids, flavonoids, alkaloids, saponins, glycosides, and anthocyanins	Hexane and ethanol	[38]

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Table 1 (*continued*)

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
	plant), *Calycopteris floribunda* (leaf), *Curcuma longa* (rhizome), *Cynodon dactylon* (whole plant), *Erythrina variegate* (leaf), *Glycyrrhiza glabra* (root), *Jasminum flexile* (leaf), *Murraya koenigii* (leaf), *Nigella sativa* (seed), *Oldenlandia corymbose* (whole plant), *Physalis minima* (whole plant), *Pupalia atropurpurea* (whole plant), *Vitex negundo* (leaf)					The study further showed that 100 % of Gram-positive and 40 % of Gram-negative bacterial strains were inhibited by extracts. Both hexane and ethanol extracts of JTYG showed lower MIC for Gram-positive bacterial reference strains (median 11.7) than the MIC for Gram-negative strains (median ≥125.0), while both hexane and ethanol extracts of JTAFI showed more active against Gram-positive (median 31.25) than the MIC for Gram-negative (median 93.75) reference strains.			
Jatyadi thailam: Ayurvedic Formulary of India (AFI) and Yogagrantha (YG)	Not mentioned	Diabetic foot ulcers	Gram-positive bacteria (*S. aureus, B. subtilis*) and Gram-negative bacteria (*P. aeruginosa, E. coli, K. pneumoniae*); fungal isolates (*Aspergillus fumigatus, A. flavus, Candida albicans*, and *Cryptococcus neoformans*)	Broth microdilution	0.156–2.5 mg/mL	The results of the MIC revealed that both Gram-positive and Gram-negative bacteria tested were susceptible to the two formulations with AFI having the stronger antibacterial activity than YG. The MIC values of AFI formulation were 0.625 mg/mL for all the Gram-negative bacteria, 1.250 mg/mL for *B. subtilis*, and 0.312 mg/mL for *S. aureus* with MBC values ranging from 0.312 mg/mL to 2.5 mg/mL. Both formulations exhibited their best antibacterial activity against *S. aureus*. The standard drugs ciprofloxacin and streptomycin showed good antibacterial activity with MIC values ranging from 0.031 mg/mL to 0.125 mg/mL. The formulations also exhibited good antifungal activity against all the tested fungi isolates with more activity against *A. fumigatus* at the concentration of 0.156 mg/mL. Nystatin also showed a high antifungal activity on the tested organisms with MIC ranging from 0.03 mg/mL to 0.5 mg/mL.			[27]
Justicia secunda (Whole plant)		Diabetic Wound Infections	*S. aureus* ATCC 25,923, *P. aeruginosa* ATCC 27,853, and *E. feacalis*	Disk diffusion	200, 100, 10, and 1 mg/mL	The result indicated that methanol and acetone extracts of *J. secunda* do not possess		Methanol and acetone	[39]

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Table 1 (*continued*)

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
						antibacterial activity against all the bacterial strains tested; *S. aureus* ATCC 25,923, *P. aeruginosa* ATCC 27,853, and *E. faecalis*			
Brachylaena elliptica (leaf) and *Brachylaena ilicifolia* (leaf)		Wound infections	Gram-positive (*S. aureus* ATCC 2593), *S. pyogenes* (Laboratory strain); Gram-negative (*P. aeruginosa* ATCC 19,582, *P. vulgaris* (KZN) and *P. mirabilis* ATCC 7002)	Agar dilution	0.3 −5.0 mg/mL.	The MIC results showed that the ethanol extract of both plants had a broad spectrum and was able to inhibit the growth of the tested isolates at the MIC value ranging from 0.3- 5 mg/mL. *B. elliptica* and *B. ilicifolia* extracts displayed strong antibacterial activity against *P. aeruginosa* and *S. pyogenes* with the MIC value of 2.5 mg/mL; and 5 mg/mL for *P. mirabilis*. However, *B. elliptica* extract was inactive against *S. aureus*, while *B. ilicifolia* showed no activity against *P. vulgaris*. Furthermore, the standard drugs (amoxicillin and ciprofloxacin) exhibited activity at the MIC values of 0.6 and 0.3 mg/mL respectively.	Tannins, phenols, flavonols, proanthocyanidins, alkaloids and flavonoids	Ethanol	[40]
Polyherbal formulation	*Gymnema sylvestre* (leaf), *Allium sativum* (bulb), *Psidium guava* (leaf), *Centella asiatica, Curcuma longa* (rhizomes), *Trigonella foenum* (seeds), *Acalypha indica* (bulbs), *Momordica charantia* (fruits), *Zingiber officinale* (rhizomes), *Rosmarinus officinalis* (oil).	Diabetic foot infections	*S. aureus, P. aeruginosa, E. coli and B. subtillis.*	Agar well diffusion	Not mentioned	The ethanol extract of the polyherbal formulation exerted good antibacterial activities against the tested bacteria with a zone of inhibition of 12 mm against *S. aureus*, 13 mm against *E. coli* and 14 mm against *P. aeruginosa* and *B. subtilis* while the standard antibiotic had a zone of inhibition of 18 mm against all the isolates	Tannins and phenolic compounds	Ethanol	[41]
Acalypa indica, Azadirachta indica, Calotropis gigantea, Centella asiatica, Cyanodon dactylon, Leucas aspera, Ocimum sanctum, Psidium guajava, Thymus vulgaris, Tragia involucrata and Tridax procumbens; Spices: *Allium cepa* (Onion), *Allium sativum* (Garlic), *Myristica fragrans*		Diabetic foot ulcer and urinary tract infection	Isolate from diabetic foot ulcer: *E. coli, P. aeruginosa, P. vulgaris, S. aureus,* and *E. aerogenes.* Isolates from the urine samples are *Citrobacter fruendi, K. pneumoniae, E. coli, P. aeruginosa, P. vulgaris, S. aureus,* and *E. aerogenes.*	Agar well diffusion	20 mg/mL	The study successfully isolated multi-drug-resistant bacteria from diabetic foot ulcers and urinary tract infections. The methanol extract of *Tragia involucrate* successfully inhibited the growth of all bacteria isolated from diabetic foot ulcers. In addition, the extracts of *Acalypa indica, Azadirachta indica, Cyanodon dactylon, Leucas aspera*, and *Thymus vulgaris* inhibited the growth of *S. aureus*. The	Aliphatic alicyclic compounds, and aromatic cyclic compounds	Methanol	[42]

(*continued on next page*)

Table 1 (*continued*)

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
(Nutmeg), *Zingiber officinale* (Ginger) and *Piper nigrum* (pepper).						extracts also inhibited the growth of *E. coli* except for *Acalypa indica, Leucas aspera* and *Cyanodon dactylon. Ocimum Sanctum* and *Psidium guava* methanol extract showed inhibitory activity against *E. aerogenes* and *P. aeruginosa.* The standard drugs such as Streptomycin and Oxacillin inhibited the growth of bacteria isolated from the diabetic foot ulcer. Methanolic extract of some of the spices also inhibited the growth of bacteria isolated from the urine of diabetic individuals with *S. aureus* inhibited by all the methanolic extracts except *Allium sativum. A. sativum* was effective against *E. aerogenes, P. aeruginosa, E. coli, C. freundii* and *K. pneumonia.* The extract of *Z. officinale* inhibited *E. coil, C. freundii, S. aureus*, and *E. aerogenes.* In addition, *Citrobacter fruendi, K. pneumoniae, E. coli, P. aeruginosa*, and E. aerogenes were resistant to *Myristica fragrans* and *Piper nigrum* while *P. aeruginosa* was resistant to all the methanolic extracts except *Allium sativum.* Also, Streptomycin, Gentamycin, Oxacillin and Ciprofloxacin inhibited the growth of all the bacteria isolated from the urine of the diabetic patients.			
Thai herbal extracts	*Centella asiatica* (leaf), *Curcuma longa* (rhizome), *Zingiber cassumunar* (rhizome), *Garcinia mangostana* (peel), *Zingiber officinale* (rhizome), Eleutherine americana (rhizome), *Piper nigrum* (seed), *Senna alata* (leaf), *Areca catechu* (fruit).	Diabetic foot ulcer	*Staphylococcus aureus* (ATCC strain 25,923)	Broth dilution	10, 5, 2.5, 1.25, 0.625, 0.313, 0.156, 0.078, 0.039, and 0.019 mg/mL	All the Thai herbal extracts (F1, F2, F3) showed antibacterial activity against *S. aureus* with a MIC of 0.156 mg/mL and MBC of 0.313 and 0.625 mg/mL.			[43]
Mentha piperita		Diabetic wound	Gram-positive *Staphylococcus aureus* (ATCC 6538) and Gram-	Colony counting	60 mg/mL	The study showed that Polyurethane/Pluronic F127 nanofibers exhibited no antibacterial activity, while	Phenols and flavonoid	Ethanol/ distilled water (80/ 20)	[44]

(*continued on next page*)

Table 1 (*continued*)

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
			negative *E. coli* (ATCC 8739)			samples containing herbal extract had 99.9 % antibacterial activity against *S. aureus and E. coli* with MIC values of 0.26 and 0.29 mg/mL, respectively.			
Hydrogel formulation	*Blechnum orientale* (leaf), sodium carboxymethylcellulose (NaCMC), propylene glycol (PG) and distilled water	Diabetic ulcer wounds	*B. cereus* (ATCC10876), *E. faecalis* (ATCC14506), *Micrococcus luteus* (ATCC49732), *S. aureus* (ATCC33862), and Methicillin-resistant *S. aureus* (MRSA) (ATCC33862).	Broth microdilution	1 mg/mL	The study showed that the water fractions W5–1 and W5–2 of the formulation exhibited stronger antibacterial activity against the tested bacteria.	Tannins	Water	[45]
Salvia kronenburgii (aerial parts) and *Salvia euphratica* (aerial parts)		wound infections	Gram-positive bacterial strains *S. aureus* (ATCC 25,925) and *B. subtilis* (ATCC 6633); Gram-negative bacterial strains *E. coli* (ATCC 25,923), *A. baumannii* (ATCC 02,026) *Aeromonas hydrophila* (ATCC 95,080), *Mycobacterium tuberculosis* H37Rv, and fungal strains *C. tropicalis* (ATCC 750), *C. glabrata* (ATCC 90,030) and *C. parapsilosis* (ATCC 22,019)	Broth microdilution	1000, 500, 250, 125, 62.5, 31.25, 15.62, 7.8, 3.9 and 1.9 μg/mL	The ethanol extracts of the two plants showed strong antimicrobial activity against the five bacterial and three fungal isolates with MIC values ranging between 250 and 62.5 μg/mL and 125–62.5 μg/mL, respectively. Both extracts had greater antibacterial activity against *A. baumannii* with a MIC of 62.5 μg/mL as compared to the reference drug Ampicillin with a 125 μg/mL MIC value. Furthermore, the *Salvia euphratica* ethanol extract had strong activity against *M. tuberculosis* H37Rv with the MIC valve of 0.24 μg/mL which was stronger than the reference drugs Isoniazid and Ethambutol at 0.97 and 1.95 μg/mL MIC values, respectively.	Phenolic and flavonoid	Ethanol	[46]
Foot bath decoction	Raw Rhubarb (20 g), Coptidis Rhizoma (15 g), Fructus Forsythia (15 g), aluminum potassium sulfate (10 g), and Pseudobulbus Cremastrae Seu Pleiones (10 g).	Diabetic foot infections	Clinical trial on 60 individuals			The research found that the foot bath treatment was effective in reducing bacterial growth in wounds, as evidenced by objective measures such as bacterial culture, IL-6, and TNF-a levels. Furthermore, the overall impact of the foot bath intervention was observed through changes in wound size, walking distance and speed, lower limb blood vessel diameter, blood flow velocity, and traditional Chinese medicine symptom scores. The			[47]

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Table 1 (*continued*)

Plants or Polyherbal formulation and parts used	Composition of PHF and plant parts used	Type of infection	Pathogens	Model Used	Dosage used	Findings on the antimicrobial potential	Secondary Metabolites responsible for the observed activity	Solvent used	Reference
						safety of the treatment was also evaluated through blood, urine, stool, and liver/kidney function tests.			

Additionally, poor blood flow further complicates the healing process, as it limits the body's ability to deliver essential nutrients and immune cells to the affected area. Consequently, even minor wounds can progress to diabetic foot ulcers, which, if left untreated, may lead to life-threatening infections [59]. Recent studies have found that between 19 % and 34 % of people with diabetes will develop a foot ulcer in their lifetime, a statistic that is expected to rise as medical advancements allow people with diabetes to live longer while managing more complex health conditions, underscoring the prevalence of this complication among people with diabetes [63]. As individuals with diabetes age, their susceptibility to diabetic foot infections increases, making early detection and prompt treatment critical to preventing severe consequences like amputations.

Diabetic foot ulcers often result from poorly controlled diabetes complications, neuropathy, peripheral vascular disease, or inadequate foot hygiene [62,64]. Calluses and deformities in the foot can lead to these ulcers, which tend to develop in areas subject to repetitive trauma and pressure. The development of diabetic foot ulcers typically occurs in three stages, starting with the formation of a callus due to neuropathy, followed by physical deformities, sensory loss, and repetitive trauma. These ulcers can progress to involve deeper tissues, including muscles, tendons, bones, and joints, leading to potentially catastrophic outcomes like septic gangrene and amputation [64].

The microbiology of diabetic foot infections is complex, with various pathogens being isolated from these wounds [42]. Both mono- and polymicrobial infections are common, with Gram-positive cocci, particularly *Staphylococcus* species, and Gram-negative bacilli frequently detected [64–66]. Also, *Pseudomonas* spp., *E. coli, Enterococcus faecalis, Enterobacter cloacae, Citrobacter* spp. *Acinetobacter, Serratia* spp. and *Proteus mirabilis* have also been observed at notable frequencies [65,43]. Methicillin-resistant *Staphylococcus aureus* (MRSA) is present in a significant proportion of diabetic foot infections and is associated with higher treatment failure rates [67]. In addition, clinically significant fungi isolates such as *Candida tropicalis, C. albicans, C. guilliermondii* and *C. pseudotropicalis* have been isolated from diabetic foot ulcers. Moreover, anaerobic pathogens are more likely to be present in necrotic wounds and infections of ischemic feet [41].

The management of diabetic foot infectionsmostly involves the use of antibiotics, but for optimal results, a multidisciplinary team of podiatrists, endocrinologists, primary care physicians, vascular surgeons, and infectious disease experts is often needed. The healthcare system faces the challenge of addressing these complications effectively, as repeated antibiotic courses can lead to antimicrobial resistance, and a significant percentage of patients do not achieve clinical resolution of infection within a year of diagnosis. Timely intervention is crucial to preventing the progression of these infections, as untreated cases can lead to pain, necrosis, and ultimately, amputation [64]. Hence, diabetic patients tend to seek the use of alternative medicines to speed up their recovery.

Zhang et al. [47] conducted a clinical trial on 60 patients suffering from multiple infectious wounds of the diabetic foot using Traditional Chinese Medicine called foot bathe decoction. The formulation which comprises Raw Rhubarb (20 g), Coptidis Rhizoma (15 g), Fructus Forsythia (15 g), aluminum potassium sulfate (10 g), and Pseudobulbus Cremastrae Seu Pleiones (10 g), showed significant effectiveness in reducing bacterial growth in wounds, as evidenced by objective measures such as bacterial culture, IL-6, and TNF-a levels. Furthermore, the overall impact of the foot bath intervention was observed through changes in wound size, walking distance and speed, lower limb blood vessel diameter, blood flow velocity, and traditional Chinese medicine symptom scores. The safety of the treatment was also evaluated and confirmed through blood, urine, stool, and liver/kidney function tests. The activity observed in the formulation could be attributed to the bioactive constituents present in the plants [68–71].

A study by Kota et al. [35] investigated the antimicrobial potential of a PHF composed of *Acacia ferruginea* (bark and fruit), *Chloroxylon swietenia* (bark, leaf, and root), *Casearia elliptica* (bark), and *Terminalia alata* (root, leaf) against diabetic foot infections caused by Gram-positive

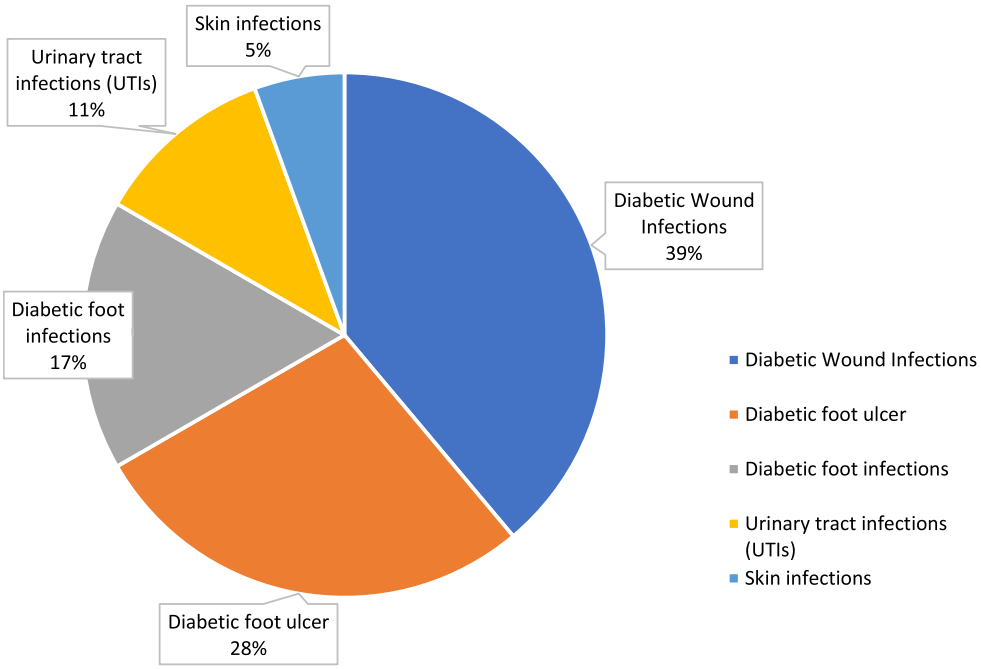


Fig. 2. Infections treated in the reviewed articles.

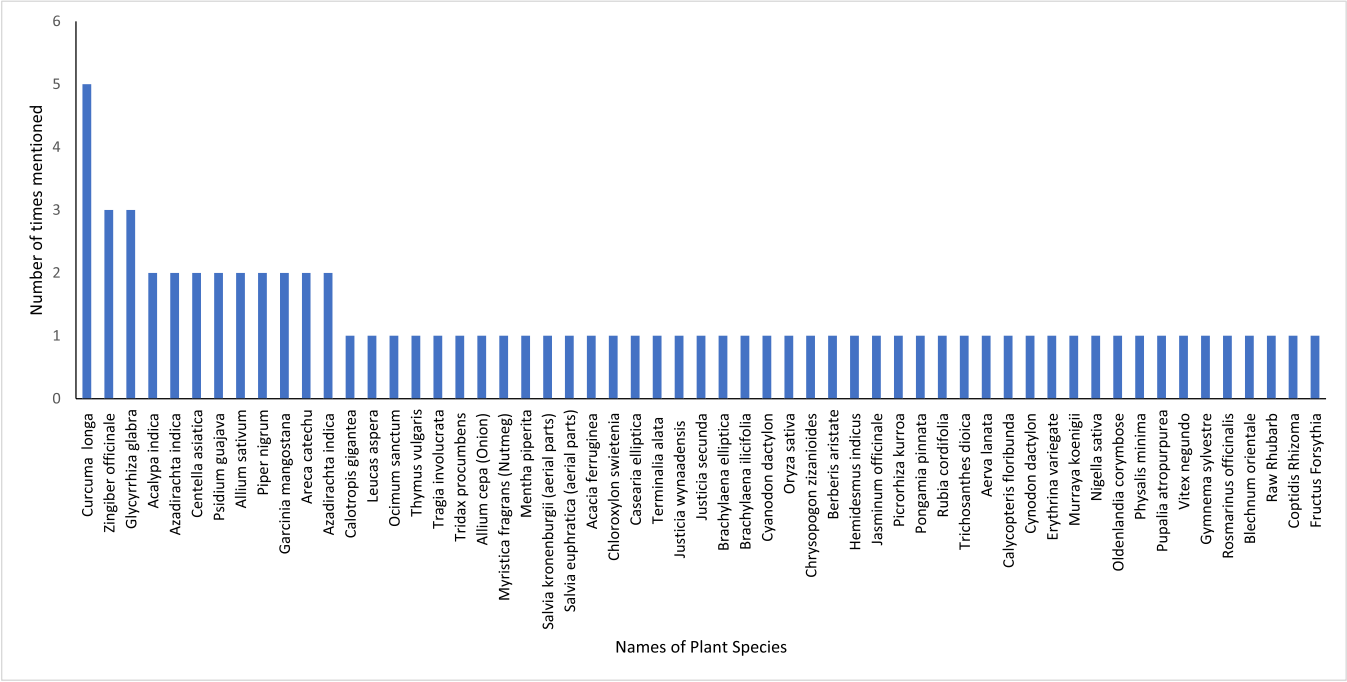


Fig. 3. Medicinal plants used in the reviewed articles.

(*Staphylococcus aureus, Bacillus subtilis*) and Gram-negative bacteria (*Pseudomonas aeruginosa, E. coli, Klebsiella pneumoniae,* and *Proteus vulgaris*). At the concentration of 50 mg/mL, the PHF exhibited significant antibacterial activity against both Gram-positive and Gram-negative bacteria, which was comparable to Gentamicin. Notably, the PHF demonstrated the highest inhibitory effect on *B. subtilis* with a mean zone of inhibition (ZOI) of 3.3 cm, followed by *P. vulgaris, K. pneumoniae, E. coli, P. aeruginosa,* and *S. aureus*, with ZOIs of 3.22 cm, 2.97 cm, 2.92 cm, 2.57 cm, 2.42 cm and 2.7 cm respectively. The secondary metabolites responsible for this antimicrobial activity were identified as flavonoids, alkaloids, steroids, triterpenoids, and phenolic compounds such as tannins. This study highlights the potential of the PHF as a promising alternative treatment for diabetic foot infections, supported by the presence of bioactive compounds known for their antimicrobial properties.

Additionally, Sanpinit et al. [37] examined the antimicrobial activity of Ya-Samarn-Phlae (YaSP), a polyherbal formulation consisting of *Garcinia mangostana* (pericarp), *Oryza sativa* (seed), *Curcuma longa* (rhizome), and *Areca catechu* (seed) against infective bacteria (Methicillin-resistant *S. aureus* (MRSA), coagulase-positive staphylococci (CPS), coagulase-negative staphylococci (CNS), multidrug-resistant (MDR) *P. aeruginosa*, MDR *Acinetobacter baumannii* NPRC034, and

MDR *E. coli* in diabetic foot ulcers and wound-related pathogens. The findings showed that YaSP and *G. mangostana* extracts had significant antibacterial activity against *Staphylococcus* spp., including MRSA isolates, with MICs of 2–8 μg/mL and 2–4 μg/mL, respectively. However, these extracts exhibited lower activity against Gram-negative pathogens with MICs ranging from 500 to >1000 μg/mL for YaSP and from 250 to >1000 μg/mL for *G. mangostana*. Alpha-mangostin, a compound found in *G. mangostana*, exhibited similar inhibitory activity against most bacteria tested. Other components of YaSP, such as *C. longa* and *A. catechu*, exhibited moderate antibacterial activity against both Gram-positive and Gram-negative pathogens. Notably, *O. sativa* and curcumin were ineffective against all tested pathogens. The solvent used for extraction was ethanol. These results suggest that YaSP, particularly *G. mangostana* and alpha-mangostin, have potential as alternative treatments for diabetic foot ulcers and wound-related pathogens, particularly against MRSA infections.

Furthermore, in a study by Swathi et al.[27] the antimicrobial potential of Jatyadi thailam (AFI and YG) Ayurvedic formulations was evaluated against diabetic foot ulcers caused by Gram-positive bacteria (*S. aureus,* and *B. subtilis*), Gram-negative bacteria (*P. aeruginosa, E. coli,* and *K. pneumoniae*), and fungal isolates (*Aspergillus fumigatus, A. flavus, Candida albicans, Cryptococcus neoformans*). The results revealed that both Gram-positive and Gram-negative bacteria tested were susceptible to the two formulations, with AFI displaying stronger antibacterial activity than YG. AFI formulation exhibited MIC values of 0.625 mg/mL for all Gram-negative bacteria, 1.250 mg/mL for *B. subtilis*, and 0.312 mg/mL for *S. aureus*, with MBC values ranging from 0.312 mg/mL to 2.5 mg/mL. Both formulations showed very good antibacterial activity against *S. aureus*. The standard drugs ciprofloxacin and streptomycin also exhibited good antibacterial activity. Additionally, both formulations displayed good antifungal activity against the tested fungal isolates with more activity against *A. fumigatus* at the concentration of 0.156 mg/mL. Nystatin also showed a high antifungal activity on the tested organisms with MIC ranging from 0.03 mg/mL to 0.5 mg/mL. The findings suggest that Jatyadi thailam formulations have strong antimicrobial activity, with secondary metabolites such as tannins contributing to its antimicrobial potential and could be considered for the management of diabetic foot ulcers and associated infections.

Also, Viswasanthi et al. [41] conducted a study on a polyherbal formulation composed of *Gymnema sylvestre* (leaf), *Allium sativum* (bulb), *Psidium guava* (leaf), *Centella asiatica, Curcuma longa* (rhizomes), *Trigonella foenum* (seeds), *Acalypha indica* (bulbs), *Momordica charantia* (fruits), *Zingiber officinale* (rhizomes), and *Rosmarinus officinalis* (oil) against diabetic foot infections. The ethanol extract of this polyherbal formulation exhibited good antibacterial activities against the tested bacteria. It resulted in a zone of inhibition of 12 mm against *S. aureus*, 13 mm against *E. coli*, and 14 mm against *P. aeruginosa* and *B. subtilis*, while the standard antibiotic had a zone of inhibition of 18 mm against all isolates. These results suggest the excellent activity of the polyherbal formulation could be due to the presence of tannins and phenolic compounds in the remedy and suggest that the PHF could be used in the management of diabetic foot infections. The activity was observed to be stronger against Gram-positive bacteria than against Gram-negative bacteria. This is consistent with a previous study that found Gram-negative bacteria to be more resistant to antimicrobial agents than Gram-positive bacteria due to their multilayered structure [72].

Subbu lakshmi et al. [42] conducted a study on various medicinal plants and spices against multi-drug-resistant bacteria isolated from diabetic foot ulcers and urinary tract infections. At the concentration of 20 mg/mL, extracts of *Acalypa indica, Azadirachta indica, Cyanodon dactylon, Leucas aspera, Thymus vulgaris,* and *Tragia involucrata*, inhibited the growth of *S. aureus* and some inhibited *E. coli* as well. In addition, *Ocimum Sanctum* and *Psidium guava* extracts showed inhibitory activity against *E. aerogenes* and *P. aeruginosa*. Several spices, such as *Allium sativum* (garlic), *Zingiber officinale* (ginger), and *Piper nigrum* (pepper), exhibited antibacterial activity against the tested isolates. This study showed the potential of a diverse range of plants and spices for the management of diabetic foot infections, particularly in the context of multi-drug-resistant bacteria. These extracts contained various secondary metabolites, including aliphatic alicyclic compounds, hydroxyl protons, methyl protons, methoxy protons, CH protons, and aromatic cyclic compounds, which contributed to their antimicrobial potential.

Chumpolphant et al. [43] investigated the antimicrobial potential of Thai herbal extracts against *Staphylococcus aureus*. The formulation consisted of *Centella asiatica* (leaf), *Curcuma longa* (rhizome), *Zingiber cassumunar* (rhizome), *Garcinia mangostana* (peel), *Zingiber officinale* (rhizome), *Eleutherine americana* (rhizome), *Piper nigrum* (seed), *Senna alata* (leaf), and *Areca catechu* (fruit). All the Thai herbal extracts (F1, F2, F3) displayed antibacterial activity against *S. aureus*, with an MIC of 0.156 mg/mL and MBCs of 0.313 and 0.625 mg/mL. The study showed that Thai herbal extracts have potential antibacterial activity against *S. aureus*.

Lai et al. [45] examined a hydrogel formulation containing *Blechnum orientale* (leaf) against various bacteria, including *B. cereus, E. faecalis, Micrococcus luteus, S. aureus*, and Methicillin-resistant *S. aureus* (MRSA). The findings indicated that water fractions W5–1 and W5–2 of the hydrogel formulation exhibited stronger antibacterial activity against the tested bacteria and that the secondary metabolites responsible for this activity were tannins.

These studies collectively demonstrate the promising antimicrobial potential of various polyherbal formulations and herbal extracts in combating diabetic foot infections and ulcers. These alternative treatments offer new avenues for combating antimicrobial resistance in diabetic patients and may provide safer and more effective options in the future.

Exploring herbal medicines with antimicrobial potential for diabetic wound infections

Diabetic patients often face the distressing challenge of chronic wounds that do not heal which are exacerbated by poor perfusion, inflammation, and the presence of necrotic tissue [46]. Furthermore, the warm, moist, and nutrient-rich environment within wounds creates an ideal breeding ground for microorganisms, exacerbating the problem [44]. In diabetics, wound infections occur when physical injuries create openings in the skin, allowing the invasion of pathogens in the underlying tissues. Several bacterial species, including *Staphylococcus* spp. and *Clostridium* spp., can exploit these openings to establish infections [40]. Additionally, *Pseudomonas aeruginosa*, characterized by the formation of a green pigment and black lesions, has been implicated as a significant contributor to wound infections in diabetic patients [73–75]. These bacteria often possess genetic resistance mechanisms against antibiotics, diminishing the efficacy of some standard treatments and potentially leading to adverse effects like allergies and immunosuppression [46]. While synthetic drugs have traditionally been used to treat wounds, their high cost, antibiotic resistance of the infecting microorganism, and potential side effects have limited their efficacy in managing diabetic wound infections. This has prompted the exploration of medicinal plants as an alternative approach to wound infections in diabetic patients without the drawbacks of conventional antibiotics [76].

Mandrika et al. [38] investigated the antimicrobial potential of Jathyadi Thailam (JTAFI) and (JTYG) against a range of bacterial strains in diabetic chronic wound infections. The study found that Jatyadi extracts exhibited higher antibacterial activity against Gram-positive bacteria including *S. aureus,* MRSA*, S. epidermidis,* and *E. faecalis*, with MICs ranging from 1.95 to 62.5 mg/mL. In contrast, Gram-negative bacteria such as *E. coli, P. aeruginosa*, MDR *P. aeruginosa, P. mirabilis,* and *K. pneumoniae* were only susceptible to ethanol extracts. The study reported that these extracts inhibited 100 % of Gram-positive and 40 % of Gram-negative bacterial strains. Hexane and ethanol extracts of JTYG showed lower MICs for Gram-positive strains (median 11.7) compared to Gram-negative strains (median ≥125.0). Similarly, JTAFI extracts

displayed higher activity against Gram-positive strains (median 31.25) compared to Gram-negative strains (median 93.75). The bioactive compounds that could be responsible for these antimicrobial activities include phenols, proteins, tannins, sterols, terpenoids, flavonoids, alkaloids, saponins, glycosides, and anthocyanins.

Similarly, Almasian et al. [44] investigated the antimicrobial potential of Polyurethane/Pluronic F127 nanofibers containing *Mentha piperita* against *S. aureus* and *E. coli* in diabetic wounds. The findings showed that the Polyurethane/Pluronic F127 nanofibers containing herbal extract exhibited significant antibacterial activity (99.9 %), with MIC values of 0.26 mg/mL against *S. aureus* and 0.29 mg/mL against *E. coli*. The active compounds responsible for this activity included phenols and flavonoids.

In addition, Sagbo et al. [40] examined the antimicrobial potential of *Brachylaena elliptica* and *Brachylaena ilicifolia* against wound infections. Ethanol extracts of both plants demonstrated broad-spectrum antibacterial activity, inhibiting the growth of tested isolates at MIC values ranging from 0.3 to 5 mg/mL. *B. elliptica* and *B. ilicifolia* extracts displayed strong antibacterial activity against *P. aeruginos*a and *S. pyogenes* with a MIC value of 2.5 mg/mL but showed varying activity against other strains. The extracts contained bioactive compounds such as tannins, phenols, flavonols, proanthocyanidins, alkaloids, and flavonoids, which could be responsible for the antibacterial activity observed.

Güzel et al. [46] examined the antimicrobial potential of ethanol extracts from *Salvia kronenburgii* and *Salvia euphratica* (aerial parts) against a range of bacterial and fungal isolates on wound models in diabetic rats. The ethanol extracts of both plants showed strong activity against various bacterial and fungal isolates, with MIC values ranging from 62.5 to 250 μg/mL for bacteria (*S. aureus, B. subtilis, E. coli, Acinetobacter baumannii,* and *Aeromonas hydrophila)* and 62.5–125 μg/mL for fungi isolates (*Candida glabrata, C. parapsilosis,* and *C. tropicalis*). *Salvia euphratica* extract showed excellent activity against *Mycobacterium tuberculosis*, with a MIC value of 0.24 μg/mL, which was stronger than reference drugs Isoniazid and Ethambutol at 0.97 and 1.95 μg/mL MIC values, respectively. The presence of phenolic and flavonoid compounds in the plants could be responsible for these antimicrobial properties.

Furthermore, Carrington et al. [39]evaluated the antimicrobial potential of methanol and acetone extracts of *Justicia secunda* in diabetic wound infections. The study revealed that methanol and acetone extracts of *J. secunda* at the concentrations of 200, 100, 10, and 1 mg/mL did not exhibit antibacterial activity *against S. aureus* ATCC 25923, *P. aeruginosa* ATCC 27853, and *E. faecalis*. Hence the plant is not likely to treat diabetic wound infections.

Antimicrobial properties of phytochemicals commonly found in the herbal medicines investigated in the reviewed articles

The antimicrobial properties of alternative medicines have been attributed to a range of phytoconstituents, including flavonoids, alkaloids, steroids, triterpenoids, phenols, tannins, saponins, terpenoids, glycosides, phlobatannins, sterols, anthocyanins, flavonols, proanthocyanidins, aliphatic alicyclic compounds, and aromatic cyclic compounds [35,36,38,40–42,44–46]. Extensive research has underscored the association between antibacterial properties and secondary metabolites such as flavonoids, tannins, triterpenoids, phenolic acids, alkaloids, saponins, and terpenoids among others [77–79].

Antimicrobial potential of flavonoids

The flavonoid is a type of polyphenolic compound that has received a lot of attention due to its potential antimicrobial properties. Several studies [80–82] have highlighted flavonoids' broad antimicrobial spectrum against Gram-positive and Gram-negative bacteria, as well as fungi. The flavonoid 7-hydroxy-3,4-(methylenedioxy) flavan (Table 2) isolated from *Terminalia bellerica* fruit rind has been shown to have activity against *Candida albicans* [80]; additionally, flavonoids isolated from two *Chromolaena* species were active against several bacteria species, particularly *S. aureus* (ATCC 6538 and ATCC 29213) [81]. The proposed mechanisms of action of flavonoids frequently involve disrupting microbial cell membranes, forming biofilm, and inhibiting key enzymes required for microbial growth [82]. Flavonoids also have synergistic effects when combined with conventional antibiotics [83,84]. However, it is important to note that the effectiveness of flavonoids varies depending on the specific compound and microbial strain.

Antimicrobial potential of tannins

Tannins are another class of polyphenolic compounds that have been shown to have potent antibacterial properties in a variety of conventional treatments. Previously, Mailoa et al., [85] described the antimicrobial effects of a tannin-rich extract from *Psidium guajava* L against *Candida albicans, Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *E. coli* [85]. The tannin flavan-3-ol (Table 2) from *Erythrophleum guineensis* bark (Caesalpiniaceae) was found in a previous study to have antifungal and antibacterial activity [86]. In some other studies, tannins exert antimicrobial effects by binding to microbial proteins and enzymes, impairing their activity [87,88]. Despite their promising antibacterial potential, tannins face practical challenges in modern medicine due to absorption issues and potential toxicity.

Antimicrobial potential of triterpenoids

Triterpenoids, a diverse class of plant phytochemicals, have demonstrated significant antimicrobial activity. Several previous studies have shown triterpenoids as effective against a variety of pathogens, including bacteria, fungi, and protozoa. In a previous study, several Triterpenoids especially α- and β-amyrin (Table 2), extracted from *Vernonia auriculifera* Hiern were found to have moderate to significant antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Enterococcus faecium, Stenotrophomonas maltophilia, Klebsiella pneumonia,* and *Pseudomonas aeruginosa* [89]. Singh et al. also discovered significant activity in the triterpenoid taraxerol against *K. pneumoniae*, as well as sitosterol and β-amyrin against *E. coli, K. pneumoniae*, and *P. chrysogenum* [90]. Triterpenoids disrupt microbial cell membranes, inhibit important enzymes, and disrupt cellular processes [91,92]. The combination of these previous discoveries, as well as triterpenoids' low toxicity, positions them as potential drug candidates.

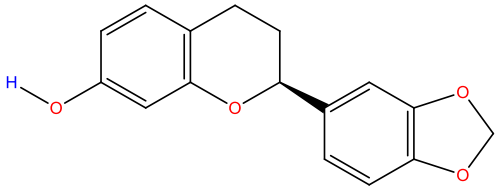
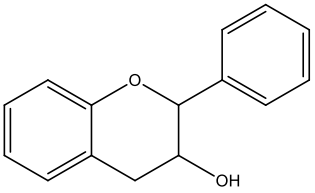
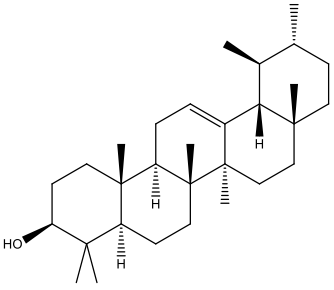
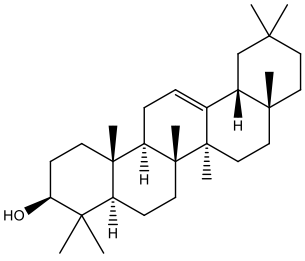
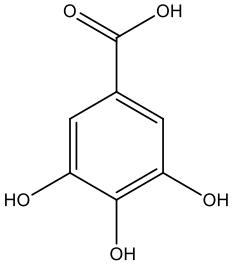
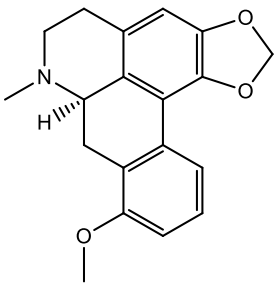
Antimicrobial potential of phenolic acids

Phenolic acids are also important components of traditional remedies. They are effective against a wide range of pathogens, including bacteria, fungi, and viruses [80]. Cueva et al. [93] investigated the antibacterial properties of benzoic, phenylacetic, and phenylpropionic acids, finding that the phenolic acids inhibited the growth of *E. coli* strains O157:H7 and lpxC/tolC by up to 100 % at 1000 mg/mL concentration. Another study also found that gallic acid (Table 2), caffeic acid, gentisate acid, and sinapic acid conjugated to chitosan had significant antimicrobial activities [94]. Several studies have suggested that phenolic acids cause bacterial death by disrupting redox homeostasis [95,96].

Antimicrobial potential of alkaloids

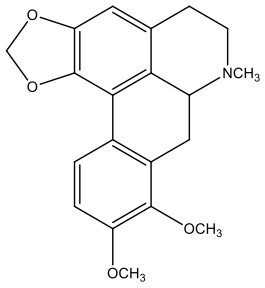
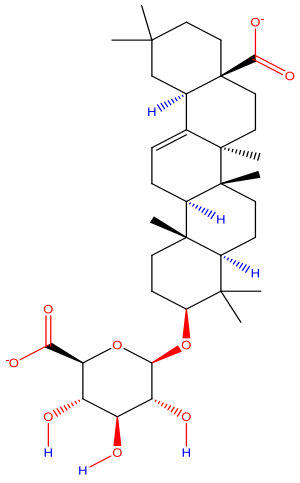
Alkaloids are a diverse group of nitrogen-containing natural compounds found in many plants. They have a long history of use in traditional medicine for a variety of ailments, including infections. In recent years, there has been growing interest in the antimicrobial properties of alkaloids, and research has shown that they can be effective against a wide range of bacteria, fungi, and viruses. A previous study by Garba & Okeniyi [97] reported high activity from the total alkaloids extracted

Table 2
Chemical structures of phytochemicals commonly found in herbal medicines.

S/N	Structure	Name
1.		7-hydroxy-3,4-(methylenedioxy)flavan
2.		Flavan-3-ol
3.		α-Amyrin
4.		β-Amyrin
5.		Gallic acid
6.		Stephanine

(*continued on next page*)

Table 2 (*continued*)

S/N	Structure	Name
7.		Crebanine
8.		3-O-β-d-glucuronopyranosyl-oleanolic acid

from *C. papaya, C. procera, M. indica* and *P. guajava* against *S. aureus, Streptococci, Lactobacillus* spp. and *C. albicans* with zones of inhibition ranging from 23 to 26 mm at a concentration of 6×10^2 μg/cm^3. Another study also reported antimicrobial activities in alkaloids, especially in stephanine and crebanine (Table 2) which were found to have broad-spectrum antimicrobial activity against tested plant pathogenic fungi and gram-positive animal pathogenic bacteria. The antimicrobial activity of stephanine against most of the plant-pathogenic fungi and gram-positive animal pathogenic bacteria was higher than crebanine [98].

Traditional medicine alkaloids have the potential to be a valuable new source of antimicrobial drugs. More research, however, is required to understand their mechanisms of action fully and to develop safe and effective clinical formulations.

Antimicrobial potential of saponins

Saponins are glycosidic compounds found in medicinal plants. They have exhibited promising antimicrobial properties. In a study by Ravi et al. [99], a crude saponin extract demonstrated a significant minimal inhibitory concentration (MIC) of 1.11 mg/ml against *S. aureus* and *E. coli*. Also, another study reported significant microbial inhibition against *C. parapsilosis, C. albicans* and *C. neoformans* by four saponin extracts, with the highest MIC value recorded for 3-O-β-d-glucuronopyranosyl-oleanolic acid, 3-O-β-d-glucuronopyranosyloleanolic acid 28-O-β-d-glucopyranosyl ester (Table 2). The antimicrobial properties of saponins have made them attractive candidates for the development of new drugs to treat infectious diseases. However, more research is needed to fully understand the mechanisms of action of saponins and to develop safe and effective formulations for clinical use.

Antimicrobial potential of terpenoids

Terpenoids are a large and diverse group of natural compounds found in plants' leaves, stems, roots, flowers, and fruits. They are responsible for many plants' distinctive aromas, including lavender, mint, and eucalyptus. Terpenoids also have antimicrobial, anti-inflammatory, and antioxidant properties [100]. For centuries, traditional medicine systems around the world have used terpenoid-containing plants to treat a variety of infections [101]. Previous research has also confirmed terpenoids' antimicrobial properties. Studies have shown the sesquiterpene artemisinin (Table 2) as an effective antimalarial [102,103]. Singh & Singh [104] also discovered significant inhibition activity in the terpenoid hexa-cosane (IZ = 13.39) against *E. coli* and hexacosanoic acid against *A. flavus* (IZ = 11.56). In recent years, the scientific community has become increasingly interested in the potential of plant terpenoids as new antimicrobial agents. This is due to the growing problem of antimicrobial resistance, which is a major global health threat that is estimated to kill over 700,000 people each year [105]. Terpenoids have antimicrobial activity via several mechanisms. Some terpenoids cause bacterial cell death by disrupting the cell membrane [106]. Others prevent the production of vital bacterial proteins or enzymes [107]. Others, on the other hand, interfere with bacteria's ability to communicate with one another [108].

Traditional medicines' antimicrobial properties provide a rich source of potential therapeutic agents. However, it is vital to recognise that factors such as compound structure, microbial strain, and delivery methods can all have an impact on the effectiveness of these compounds. More research and clinical trials are required to fully realise the antimicrobial potential of these phytochemicals.

Pharmacological importance of the commonly mentioned medicinal plants

As indicated in Fig. 3 above, the commonly used medicinal plants

across the alternative medicines are *Curcuma longa, Azadirachta indica, Zingiber officinale*, and *Glycyrrhiza glabra*.

Curcuma longa L. commonly known as Turmeric, is a member of the *Zingiberaceae* family and the Curcuma genus (Fig. 4). It is celebrated as the "golden spice" due to its numerous health benefits and versatile applications across various fields, including traditional medicine, dietary spice, food, textiles, and medicine [113]. The vibrant yellow colour of turmeric primarily results from the presence of fat-soluble polyphenolic pigments called curcuminoids. Among these, curcumin stands out as the principal and most active constituent. Additional curcuminoids found in turmeric include demethoxycurcumin and bis-demethoxycurcumin [114]. Turmeric transcends being merely a spice; it is considered a therapeutic agent for the management of numerous diseases such as cancer, inflammation, microbial infections, diabetes, arthritis, muscular disorders, biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, and sinusitis. Moreover, curcumin has been linked to various pharmacological activities, including antioxidant, antineoplastic, antiviral, anti-inflammatory, antibacterial, antifungal, antidiabetic, anticoagulant, antifertility, cardiovascular protective, hepatoprotective, and immunostimulant properties in animal studies [115]. Studies have shown that both turmeric extract and essential oil from *Curcuma longa* exhibit inhibitory properties against a range of bacteria, parasites, and pathogenic fungi [114]. Additionally, several studies have documented the antimicrobial potential of this plant [116–120]. Furthermore, a comprehensive review has summarized the various therapeutic roles of *Curcuma longa* [117].

Azadirachta indica (A. Juss), commonly known as Neem, is a member of the *Meliaceae* family and is rich in antioxidants, which contributes to its health-promoting effects (Fig. 4) [121]. It is known for its diverse therapeutic implications in disease management, owing to its complex composition of bioactive compounds such as azadirachtin, nimbin, nimbidin, nimbolide, nimbidol, sodium nimbinate, gedunin, salannin and limonoids. These constituents play a pivotal role in modulating various genetic pathways and physiological activities. Additionally, quercetin and ß-sitosterol, polyphenolic flavonoids found in neem leaves, exhibit antibacterial and antifungal properties [121]. The pharmacological importance of *Azadirachta indica* covers a wide range of activities, including antibacterial, antifungal, anti-inflammatory, antiviral, antipyretic, hypoglycaemic, antigastric ulcer, antitumour, immunostimulant effects as reported in several review studies [121–124]. It also possesses neuroprotective activity, hepatoprotective, and wound-healing effects [121]. In addition to the ability of the leaves of *A. indica* as a sedative and relaxant agent, they are known for their antibacterial, anticarcinogenic, antifungal, antihyperglycemic, anti-inflammatory, antimalarial, antimutagenic, antioxidant, antiulcer, antiviral, and immunomodulatory activities [125]. This versatile tree has been traditionally used in various parts of the world for pest control in agriculture and as a remedy for numerous human ailments. Nearly every part of the neem tree, including the stem, bark, roots, leaves, gum, seeds, fruits, and flowers, has been employed in traditional medicine and household remedies [124].

Several studies have reported that the essential oil, methanol, ethanol, and aqueous extracts from various parts of *A. Indica* possesses antimicrobial activity against microorganisms such as *Staphylococcus sciuri, S. aureus, E. coli, Proteus vulgaris, Klebsiella pneumonia, Bacillus subtilis, Micrococcus luteus, Streptococcus faecalis Enterococcus feacalis, Proteus mirabilis, P. aeuroginosa, B. cerus, P. vulgaris, Salmonella enterica, S. typhi, K. pneumoniae, S dysenteriae* and fungi isolates such as *Aspergillus fumigatus, A. flavus, A. fumigates, A. niger, Candida albicans, F. oxysporum, Cladosporium* sp., *M. canis, M. gypseum, T. rubrum, T. mentagrophytes, P. notatum,* and *P. citrinum* etc. at different concentrations [126–131].

Zingiber officinale Rosc., commonly referred to as ginger, is a widely recognized and valued spice with both culinary and medicinal applications (Fig. 4). This herbaceous plant, belonging to the *Zingiberaceae*

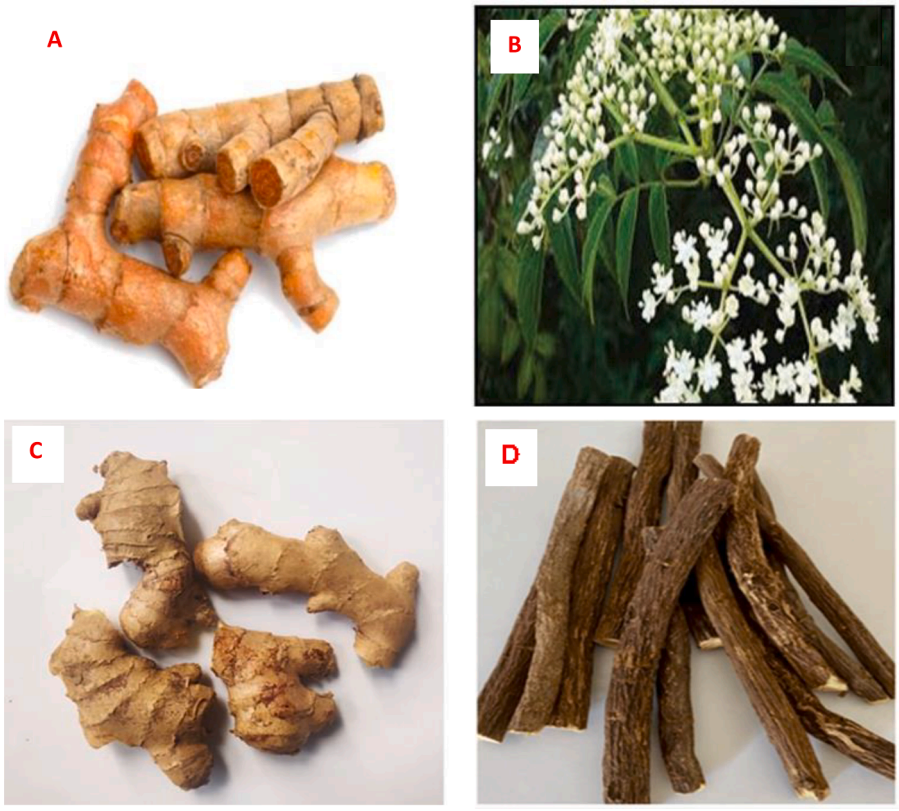


Fig. 4. Photographs of the commonly mentioned medicinal plants. (A) *Curcuma longa* L., (B) *Azadirachta indica* (A. Juss), (C) *Zingiber officinale* Rosc., (D) *Glycyrrhiza glabra* L. Photograph A was extracted from Vo et al. [109]; B was extracted from Patil et al. [110], C was extracted from Zhang et al. [111] and D was extracted from Abraham et al. [112].

family, thrives in the tropical and subtropical regions, and has been utilized for centuries for its various health benefits [132]. The bioactive compounds found in ginger contribute significantly to its pharmacological importance. Phenolic and terpene molecules are among the primary active ingredients. Notably, ginger contains phenolic constituents such as paradols, shogaols, and gingerols, with gingerols being the most abundant in fresh ginger [133]. These bioactive compounds are associated with numerous health-promoting properties, including antioxidant, anti-inflammatory, analgesic, hypoglycaemic, antithrombotic, and antimicrobial effects [134–136]. Ginger has been employed to alleviate conditions such as arthritis, cramps, rheumatism, sprains, sore throats, muscular aches, pains, constipation, vomiting, hypertension, indigestion, dementia, fever, and infectious diseases. The broad range of benefits associated with ginger includes its anti-inflammatory, anti-arthritis, antidiabetic, antibacterial, antifungal, anticancer, analgesic, antipyretic, antiviral, anti-helminthic, antioxidant properties and various other therapeutic benefits [137]. Moreover, ginger is recommended for gastrointestinal and respiratory disorders [138].

Several reviews and research studies [136,138,139] have reported that the essential oil, methanol, ethyl acetate, n-butanol, n-hexane, chloroform, ethanol, hydroalcoholic, and aqueous extracts of *Z. officinale* possess antimicrobial activity against several microorganisms, including *Salmonella* sp., *P. aeruginosa, K. pneumoniae, S. aureus, E. coli,* L. *monocytogenesis, Bacillus* sp., Streptococcus mutans, Enterococcus faecalis, and Lactobacillus spp. Enterobacter sp., Proteus sp., *Ralstonia solanacearum, Fusarium oxysporum, Pyricularia oryzae, Colletotrichum falcatum, Ganoderma boninense,* and *Rigidoporus microporus.* This antimicrobial activity has been linked to the bioactive compounds found in ginger [132,135,137,140–143].

Glycyrrhiza glabra L., commonly known as Licorice and belonging to the Family *Fabaceae*, is a widely utilized plant in traditional medicine, nutraceuticals, food and beverage worldwide (Fig. 4) [144]. With roots deeply embedded in the traditions of China and Europe, Licorice has been employed for medicinal purposes for over 4000 years [145]. The plant is rich in bioactive compounds, including glycyrrhizin, glabridin, glycyrrhizin, sugars, flavonoids, saponins, starches, amino acids, triterpene glycosides, phenolic constituents, amines, sterols, gums, and essential oils [144,146]. These constituents contribute to its pharmacological importance such as anti-inflammatory, antiviral, antimicrobial, anticancer, immunomodulatory, hepatoprotective, and cardioprotective effects [147]. Additionally, it is recognized for its soothing properties, beneficial in alimentary tract disorders and mouth ulcers [148]. Licorice is renowned for its holistic digestive health advantages, particularly in treating oral, gastrointestinal, and liver disorders. Its positive impact on digestive health is linked to the regulation of host metabolism and immune functions [144].

Studies have highlighted the antimicrobial activities of *Glycyrrhiza glabra* extracts against a range of bacteria and fungi. Ethanol and aqueous extracts demonstrated activity against *Bacillus subtilis, Enterococcus faecalis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, E. coli*, and *Candida albicans*. The root and leaf extracts displayed dose-dependent activity against *Candida albicans* and tested gram-positive bacteria [149]. The study of Sedighinia et al. [145] has shown that *G. glabra* ethanolic extract showed good antibacterial activity *against Streptococcus mutans, Streptococcus sanguis, Actinomyces viscosus, Enterococcus faecalis, Staphylococcus aureus* and *E. coli. G. glabra* ethyl acetate extracts showed antibacterial activity against the Gram-positive bacteria *S. aureus, S. mutans*, and L. *buchneri*, however, the plant showed no antifungal activity against *Z. parabailli* and *Y. lipolytica* [150]. Moreover, the chloroform, acetone and ether extracts of Licorice roots exhibited remarkable antibacterial effects against various bacteria [151]. Several studies have reported the plant's antiviral [152], and antimicrobial properties [153–155], further emphasizing its potential in the field of natural medicine.

Conclusion

The findings from the reviewed studies highlighted and showed that alternative medicines, particularly medicinal plant extracts and polyherbal formulations have demonstrated significant antimicrobial potential against microorganisms commonly associated with diabetic infections. The antimicrobial activity observed in the study showed that Gram-positive bacteria were more susceptible to alternative medicines than Gram-negative bacteria. Gram-positive bacteria are more susceptible to antimicrobial agents because of their cell wall structure. They possess a simpler cell wall with a strong peptidoglycan layer, which allows antimicrobial agents to penetrate more easily unlike Gram-negative bacteria, which have an extra outer membrane that acts as a barrier to the entry of many medications. The absence of this outer membrane in Gram-positive bacteria makes them more vulnerable to the therapeutic actions of antibiotics and plant bioactive compounds, providing a foundation for targeted treatment efforts. The antimicrobial activity of these natural products is attributed to diverse secondary metabolites present in medicinal plants. These findings suggest that the bioactive compounds found in these herbal medicines can effectively combat bacterial and fungal pathogens, making them promising options for managing diabetic infections. As a result, offers promising prospects for developing novel antimicrobial agents. While the mechanisms of action may vary, these studies collectively emphasize the potential of alternative medicines in improving the treatment outcomes of diabetic patients with infections. Further research is needed, as there are limited published articles focusing on the antimicrobial potential of alternative medicines used to treat or manage diabetic infections. In addition, future research should focus on standardizing these herbal formulations and conducting clinical trials to evaluate their efficacy and safety in diabetic infection management.

CRediT authorship contribution statement

Elizabeth Bosede Aladejana: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Olusesan Adeyemi Adelabu:** Writing – review & editing, Writing – original draft. **Adebowale Emmanuel Aladejana:** Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation, Conceptualization. **Sizwe Innocent Ndlovu:** Writing – review & editing.

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.

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