drugs and drug candidates

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Review

The Readiness to Harness the Floristic Uniqueness of Mauritius in Biomedicine

Nawraj Rummun [1,2,*] and Vidushi S. Neergheen [1]

[1] Biopharmaceutical Unit, Centre for Biomedical and Biomaterials Research, MSIRI Building, University of Mauritius, Réduit 80837, Mauritius
[2] Department of Health Sciences, Faculty of Medicine and Health Sciences, University of Mauritius, Réduit 80837, Mauritius
* Correspondence: n.rajeevr10@gmail.com

Abstract: Resistance to the existing arsenal of therapeutic agents significantly impedes successful drug therapy. One approach to combat this burgeoning global crisis is to provide novel and more effective clinical agents. Terrestrial plants have long been exploited as a source of novel drug candidates. In this line, the endemic floral diversity of the Republic of Mauritius cannot be ignored. However, developing drugs from these plants is a multi-stepped, lengthy process that requires multistakeholder involvement from scientists, policymakers, and conservationists as well as the local community. This review aims at summarising the reported bioactivities of the endemic plants. The electronic databases were searched using relevant keywords. A total of 33 original research articles were considered. A repertoire of 17 families comprising 53 Mauritian-endemic plant species has been reported for their anticancer activity (n = 20), antimicrobial activity (n = 36), antidiabetic activity (n = 3), and clinical enzyme inhibitory activity (n = 25). Five plant extracts, namely *Acalypha integrifolia*, *Labourdonaisia glauca*, *Eugenia tinifolia*, *Syzygium coriaceum*, and *Terminalia bentzoë*, have been earmarked as worthy to be further investigated for their anticancer potential. Moreover, two *Psiadia* species, namely *P. arguta* and *P. terebinthina*, have shown promising antimicrobial activity. This review highlights the extracts' potent anticancer and antimicrobial activities, focussing on their proposed mechanism of action. Moreover, the need for metabolite profiling for identifying bioactive ingredient(s) is emphasised.

Keywords: drug resistance; Mauritius; endemic plants; anticancer; antimicrobial; bioactivity

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1. Introduction

Even though the modern age is characterised by personalised medicine and the availability of monoclonal antibodies-based therapeutics in healthcare, failure in drug response is a frequent problem faced by clinicians [1,2]. A staggering 90% failure rate in cancer chemotherapy is reported [3]. Along a similar line, a study assessing the treatment outcome of initial antibiotic treatment in patients across five countries revealed an astounding 60% or higher antibiotic therapy failure rate for each country [4]. Similarly, the death toll due to the failure of drug regimens in treating life-threatening ailments is projected to rise annually [5,6]. Chemoresistance has been reported against almost all the anticancer agents in clinical use. About 90% of the 10 million cancer-related deaths in 2020 can be ascribed to drug resistance [7–9]. Likewise, nearly 5 million deaths in the year 2019 were attributed to antimicrobial drug resistance (AMR) [10]. The death toll due to AMR was projected to increase from an estimated 700,000 annual cases in 2016 to 10 million cases annually by the year 2050 [5].

The exacerbating threat that AMR poses has been acknowledged by international institutions such as the World Health Organisation (WHO), the United Nations (UN), and the (Group of Twenty) G20 leaders. Drug resistance to the available arsenal of pharmaceutical agents, coupled with their associated adverse drug reactions, further impedes the burgeoning burden of disease management. Furthermore, AMR considerably hinders the

achievement of the UN sustainable development goals (SDGs), in particular SDG 3, which is "Good health and well-being" [11]. As such, a national action plan to tackle drug resistance, alleviate patient suffering, and curb the mortality rate has been adopted globally [12]. One approach to combatting drug resistance is to provide a perpetual addition of novel and innovative therapeutic agents to the existing armamentarium of clinical drugs [10,13]. This emphasises the need for ongoing research endeavours targeted toward identifying new drug candidates with the potential to be developed into clinically efficient therapeutic agents, preferably with an alternative mechanism of action.

1.1. Plants as a Source of Therapeutic Agents

The contribution of terrestrial plant-based natural products in the mitigation of human ailments, in particular oncologic and infectious diseases, is well established [14,15]. Aside from therapeutic agents, the health benefits of plants are also exploited as an important source of nutraceuticals and functional foods [16,17]. To adapt to their immediate environment and ensure their survival, plants have evolved to produce thousands to millions of structurally diverse and unique natural products that can also be exploited to human advantage in the development of life-saving drugs or herbal supplements [18]. Approximately 25% of the marketed therapeutic agents have their structural backbone originating from natural products [19]. For instance, digoxin (antidysrhythmic) from *Digitalis latanata* Ehrh (Plantaginaceae), artemisinin (antimalarial) from *Artemisia annua* (Asteraceae), metformin (antidiabetic) from *Galega officinalis* (Fabaceae), morphine (opioid analgesic) from *Papaver somniferum* (Papaveraceae), colchicine (uricosuric agent) from *Colchicum autumnale* (Colchicaceae), and cannabidiol (antiseizure) from *Cannabis sativa* (Cannabaceae) are notable examples of life-saving drugs derived from plants [20]. However, only a minute fraction of the global plant species have so far been evaluated for their therapeutic benefits [21]. Thus, novel compounds from biodiversity-rich tropical forests, particularly the untapped endemic floral species, still await to be explored.

1.2. Biouniqueness of Mauritius Flora

Endemic plants are species that grow in a restricted geographical region and have evolved apart from the rest of the world. Thus, endemic plants are a highly promising and fertile source of novel therapeutic agents [22]. The Mascarene archipelago, along with Madagascar island, is a biodiversity hotspot with exceptional floristic diversity and a high level of endemism [23]. The Mascarene Islands, consisting of Réunion, Mauritius, and Rodrigues Island, are located in the Indian Ocean, off the southeast coast of the African continent. Mauritius, a small-island developing state, has a documented floral diversity comprising 691 angiosperms. The latter harbours a high level of plant endemicity, with 39.5% of the recorded flowering plant taxa being strictly contained to the island and 61.2% being native to the Mascarenes archipelago only [24].

Along with being home to the highest number of single-island-endemic (SIE) plant species among the Mascarene Islands, Mauritius also has the highest level of threatened SIE (81.7%) [24]. Looking at the global distribution pattern of geographical regions with the highest recorded extinct plant species, Mauritius ranks in third place [25]. In less than four centuries, Mauritius has lost above 95% of its pristine forest canopy [26], therefore jeopardising the survival of most of the island's indigenous plants. Nonetheless, the surviving endemic taxa are of inestimable value in the search for structurally unique chemotypes of pharmaceutical relevance.

The past decades have witnessed increased research endeavours aiming at investigating the bioactivities of Mauritian indigenous flora. Using optimised methodologies, researchers have attempted to evaluate the pharmacological properties of endemic plant extracts. This review aims to consolidate the peer-reviewed scientific literature highlighting the biological activities and phytoconstituents of the Mauritius-endemic plants. Analysis of the so-far published works should allow for the identification of endemic taxa that are of interest in the search for novel hits as drug candidates. It is anticipated that this paper

will provide a platform for the rational selection of plants for future in-depth investigations geared toward elucidation of the bioactive constituent of therapeutically active herbal extracts and establishing their mechanisms of action. In addition, key challenges and future prospective studies to exploit the potential of lead extract for drug development are highlighted.

2. Results and Discussion

Since time immemorial, terrestrial plants have been used to alleviate diseases and enhance human health. Plants have either been used in their crude form as part of the different ethnomedicinal systems or to develop pharmaceutical catalogues having clinical relevance in modern medicine [27,28]. The evolving crisis of drug resistance rendering existing medications ineffective in disease management warrants the need to search for novel therapeutic molecules [1,10,13]. The tropical island of Mauritius has evolved into a fertile microsome endowed with a diverse range of unique floral taxa [23]. However, endemic plants are also highly threatened with extinction due to human-driven developments around the island [24,25]. The health benefits of Mauritian-endemic plants have been exploited by the local inhabitants as part of the ethnomedicinal practice since the initial human settlement on the island around four centuries ago [29].

Drug discovery research endeavours in Mauritius involving the local endemic flora are at their infancy stage. The broad-spectrum uses of the different endemic plants as part of traditional Mauritian medicine have been previously reviewed [29]. However, despite reports on their long-standing utilisation and acceptance, only a limited number of endemic taxa have been scientifically validated for their medicinal claims. It is therefore of utmost importance to assess the existing scientific literature reporting the bioactivities of these plants. This will eventually set the baseline for further detailed pharmacological and pharmaceutical investigation alongside promoting their conservation. Bioprospecting the Mauritian-endemic flora will allow for the identification of lead compounds with the prospect of being developed into therapeutic agents, thereby aligning with the UN SDGs, namely SDG-3 and SDG-15. A repertoire of 17 families comprising 53 Mauritius-endemic plant species appears interesting in this line (Table 1). Anticancer and antimicrobial activities are the two predominant reported bioactivities of endemic plant extracts. Although all the endemic plant species represent an untapped treasure trove for potential drug leads, the ensuing discussion will focus on the strength and limitations of scientific works published by the end of January 2023, with emphasis on the plants' cancer cell cytotoxicity and antimicrobial potential. Furthermore, the molecules contributing to the extracts' bioactivity are also indicated for extracts whose bioactive constituents have been elucidated.

2.1. Oncotherapeutic Potential of Mauritian-Endemic Plants

Twenty endemic plant leaf extracts' cytotoxic effects have been reported against human cancer cell lines (Table 1). For all the investigated extracts, the cell viability post extract treatment was assessed using either Alamar blue or MTT tetrazolium salt to measure the cellular metabolic activity and the reported IC_{50} value ranged from 5 µg/mL (for *Psiadia terebinthina* against Hs578T breast cancer cells) to 533 µg/mL (for *Phyllantus phillyreifolius* against HeLa cervical cancer cells) (Table 1). According to the United States National Cancer Institute criteria for cytotoxicity guidelines, crude extracts having an IC_{50} value below 20 µg/mL are considered potent candidates for further investigation regarding their anticancer potential, while extracts having an IC_{50} value above 100 µg/mL are considered inactive [30]. As such, only extracts having an IC_{50} value below 100 µg/mL with a reported anticancer mechanism of action are discussed here.

Leaves extracts of *Acalypha integrifolia* Willd (Euphorbiaceae), *Eugenia tinifolia* Lam. (Myrtaceace,) and *Labourdonaisia glauca* Bojer (Sapotaceae) have been reported to increase the intracellular level of 5′-adenosine monophosphate-activated kinase, thereby arresting oesophageal squamous cell carcinoma (KYSE-30) in the G2/M phase of the cell cycle. All three extracts had IC_{50} values below 10 µg/mL against KYSE-30 cells [31]. *Syzygium co-*

riaceum Bosser & J. Guého leaves extract inhibited the growth of human epithelial breast cancer (MDA-MB-231), liposarcoma (SW872), lung carcinoma (A549), and hepatocellular carcinoma (HepG2) cells, with an IC_{50} value ranging from 24 μg/mL to 53 μg/mL [32–34]. Likewise, *Terminalia bentzoë* leaves' extract inhibited the growth of human ovarian carcinoma (OVCAR-4 and OVCAR-8), SW872, A549, and HepG2 cells, with IC_{50} values ranging from 23 μg/mL to 97 μg/mL, with HepG2 cells being the most susceptible cell line [35]. *S. coriaceum* was reported to trigger apoptosis in MDA-MB-231 cells via the downregulation of anti-apoptotic genes, notably BCL-2 and BIRC5 genes. Moreover, a decline in the gene expression of microtubule-associated protein 1 light chain 3 (LC3), beclin, and telomerase reverse transcriptase (TERT) was observed following *S. coriaceum* leaves' extract treatment in MDA-MB-231 cells [32]. In the case of HepG2 cells, both *S. coriaceum* and *T. bentzoë* extracts treatment caused a surge in intracellular reactive oxygen species (ROS) level, inducing oxidative damage to DNA and provoking the collapse of the mitochondrial membrane potential (MMP), thereby arresting the cell in the G0/G1 phase of the replicative cycle [33–35]. Methyl gallate and gallic acid were demonstrated to be among the active constituents responsible for *S. coriaceum* extract-induced HepG2 growth inhibitory activity [33]. Along a similar vein, the cytotoxic activity of *T. bentzoë* against HepG2 was attributed to the presence of punicalagin, isoterchebulin, terflavin A, 3,4,6-trigalloylbeta-beta-*D*-glucopyranose, 2″-*O*-galloyl-orientin, 2″-*O*-galloylisoorientin, 2″-*O*-galloylvitexin, and ellagic acid in the active purified fraction.

The above five Mauritian-endemic plant leaves' extracts have demonstrated potent in vitro cancer cell cytotoxicity and have shown the ability to induce cell cycle arrest in malignant cells. The data generated so far suggest these five extracts as promising candidates that could be exploited in the search for novel anticancer agents. As such, these extracts warrant further in-depth investigation to enhance our understanding of the distinctive mechanism of action of the bioactive constituent thereof derived.

Table 1. Biological activity of endemic plants from Mauritius.

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
1	*Acalypha integrifolia* Willd (Euphorbiaceae)	Anticancer activity In vitro modulation of hematopoietic cells.	Organic extract was prepared using maceration method.	The extract inhibited the growth of cervical adenocarcinoma (HeLa, IC_{50} = 7.7 µg/mL), colorectal carcinoma (HCT 116, IC_{50} = 14.5 µg/mL), oesophageal adenocarcinoma (OE 33, IC_{50} = 28.0 µg/mL; FLO-1, IC_{50} = 10.4 µg/mL; OE 19, IC_{50} = 39.3 µg/mL)), oesophageal squamous cell carcinoma, (KYSE-30, IC_{50} = 6.4 µg/mL), and non-malignant retinal pigment (RPE-1, IC_{50} = 44 µg/mL) as well as fibroblast (FIBR, IC_{50} = 37 µg/mL) cells. The extract induced G2/M phase cell cycle arrest in KYSE-30 cells by upregulating intracellular level 5′AMP-activated kinase. The leaves' extract stimulated lymphoid cells in (E110 C57BL/6 mice embryonic cultured cells.	Gallic acid	[31,36]
2	*Aloe purpurea Lam* (Xanthorrhoeaceae)	Antimicrobial activity	Organic extract was prepared by heating the sample under reflux followed by sonication and Soxhlet extraction.	Leaves' extract inhibited the growth of *Staphylococcus aureus* (ATCC 12600), *Klebsiella pneumoniae* (ATCC 13883), *Bacillus cereus* (ATCC 11778), and *Escherichia coli* (ATCC 11775).	3-*O*-caffeoylquinic acid, Aloesin, 4-*O*-p-coumaroylquinic acid, Isoorientin pentoside, Vitexin/isovitexin hexoside, Vitexin/isovitexin pentoside, vitexin/isovitexin, 2″-*O*-trans-*p*-coumaroylaloenin, Aloin B, Aloin A, Aloeresin A, Malonylnataloin, Aloe emodin dianthrone di-*O*-hexoside	[37,38]
3	*Aloe tormentorii* (Marais) L.E. Newton & G.D. Rowley (Xanthorrhoeaceae)	Antimicrobial activity	Organic extract was prepared by heating the sample under reflux followed by sonication and Soxhlet extraction.	Leaves' extract inhibited the growth of *Staphylococcus aureus* (ATCC 12600), *Klebsiella pneumoniae* (ATCC 13883), *Bacillus cereus* (ATCC 11778), and *Escherichia coli* (ATCC 11775).	Aloesin, 4-*O*-*p*-coumaroylquinic acid, Vitexin/isovitexin hexoside, Isoorientin pentoside, Isoorientin, Vitexin/isovitexin hexoside, Vitexin/isovitexin pentoside, Vitexin/isovitexin, 2″-*O*-trans-p-coumaroylaloenin, Aloin B, Aloin A, Aloeresin A, Malonylnataloin, Aloe emodin dianthrone di-*O*-hexoside, Microdontin A or B.	[37,38]
4	*Antirhea borbonica* J.F. Gmelin (Rubiaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract showed antibacterial activity against clinical isolates of *Pseudomonas aeruginosa* and *Staphylococcus aureus*.	Not reported	[39]
5	*Badula multiflora A.D.C* (Primulaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 12 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 116.5 µg/mL). Leaves' extract showed antibacterial activity against *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes.	Kaempferol	[40]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
6	*Chassalia coriacea* Verdc. (Rubiaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract showed antibacterial activity against clinical isolates of *Pseudomonas aeruginosa* and antifungal activity against *Aspergillus niger*.	Not reported	[39]
7	*Croton vaughanii* Croizat (Euphorbiaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 13 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 47 µg/mL). Leaves' extract showed antibacterial activity against *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes	Kaempferol	[40]
8	*Distephanus populifolius* (Lam.) Cass. (Asteraceae)	Antimicrobial activity	Organic extract was prepared using sequential extraction using solvent of varying polarity.	Leaves' extract displayed antibacterial activity against *Escherichia coli* (ATCC 27853), *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Klebsiella pneumoniae* (ATCC27853), *Pseudomonas aeruginosa* (ATCC 27853), and *Bacillus cereus* (ATCC 11778).	Not reported	[41]
9	*Diospyros boutoniana* A.DC (Ebenaceae)	Pro-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract increased concanavalin-A-induced proliferation of T cells in C57BL/6 mice spleen culture.	Not reported	[42]
10	*Diospyros chrysophyllos* Poir (Ebenaceae)	Anti-inflammatory activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture. Leaves' extract inhibited elastase enzyme.	Not reported	[42,43]
11	*Diospyros egrettarum* I. Richardson (Ebenaceae)	Anti-inflammatory In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture. Leaves' extract inhibited the elastase enzyme.	Not reported	[42,43]
12	*Diospyros leucomelas* Poir (Ebenaceae)	Anti-inflammatory In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture. Leaves' extract inhibited elastase enzyme.	Not reported	[42,43]
13	*Diospyros neraudii* A.DC. (Ebenaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 10 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 63 µg/mL). Leaves' extract showed antibacterial activity against *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes.	Kaempferol	[40]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
14	*Diospyros tesselleria* Poir. (Ebenaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 27 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 107 µg/mL). Leaves' extract showed antibacterial activity against *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes.	Kaempferol, Quercetin	[40]
15	*Diospyros nodosa* Poir. (Ebenaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen.	Norbergenin, Bergenin, Kaempferol, Kaempferol 7-rhamnoside, Bergenin hydrate, Bergenin	[42]
16	*Diospyros pterocalyx* Bojer ex A.DC. (Ebenaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced proliferation of T cells in C57BL/6 mice spleen.	Not reported	[42]
17	*Dombeya acutangula* Cav. subsp. *rosea* Friedmann (Malvaceae)	Anticancer activity	Organic extract was prepared using maceration method.	The extract inhibited the growth of cervical adenocarcinoma (HeLa, IC_{50} = 14.3 µg/mL), colorectal carcinoma (HCT 116, IC_{50} = 14.1 µg/mL), oesophageal adenocarcinoma (FLO-1, IC_{50} = 45.7 µg/mL), and non-malignant retinal pigment (RPE-1, IC_{50} = 44 µg/mL) as well as fibroblast (FIBR, IC_{50} = 45 µg/mL) cells.	Not reported	[31]
18	*Erythroxylum hypericifolium* Lam. (Erythroxylaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen.	3α-Benzoyloxynortropane	[42,44]
19	*Erythroxylum laurifolium* Lam (Erythroxylaceae)	Pro-inflammatory activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method; Sequential extraction using solvent of varying polarity.	Leaves' extract increased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen. Leaves, extract inhibited the growth of the clinical isolates of *Salmonella enteritidis*, *Enterobacter cloacae*, *Sclerotinia sclerotium*, and *Candida albicans*. Bark extract showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*. Leaves' extract inhibited α-glucosidase activity.	Not reported	[42,45–47]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
20	*Erythroxylum macrocarpum* O.E. Schulz (Erythroxylaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 41 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = not obtained at highest concentration tested). The leaves' extract showed antibacterial activity against, *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Bark extract showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*. Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes	Chlorogenic acid, Kaempferol, 3α-Benzoyloxynortropane, 3α-Benzoyloxynortropan-6β-ol, Tropan-3β-ol, Tropacocaine.	[40,44,47]
21	*Erythroxylum sideroxyloides* Lam. (Erythroxylaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Bark extract showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi* as well as antifungal activity against clinical isolates of *Candida albicans* and *Aspergillus niger.*	3α-Benzoyloxynortropane, 3α-Benzoyloxynortropan-6β-ol, 3α-Benzoyloxytropan-6β-ol, 3α-Benzoyloxytropane, Tropacocaine.	[44,47]
22	*Eugenia elliptica* Lam. (Myrtaceae)	In vitro enzyme inhibitory activity Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes. Leaves extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 7.9 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 20 µg/mL). Leaves' extract showed antibacterial activity against, *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880)' and *Bacillus cereus* (ATCC 11778).	Not reported	[40]
23	*Eugenia orbiculata* Lam. (Myrtaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 47 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 105 µg/mL). Leaves' extract showed antibacterial activity against *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes.	Epigallocatechin, Quercetin	[40]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
24	*Eugenia tinifolia* Lam. (Myrtaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity In vitro modulation of hematopoietic cells.	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 22 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = not obtained at highest concentration tested). The leaves' extract inhibited the growth of cervical adenocarcinoma (HeLa, IC_{50} = 35.3 µg/mL), colorectal carcinoma (HCT 116, IC_{50} = 19.5 µg/mL), oesophageal adenocarcinoma (OE 33, IC_{50} = 45.7 µg/mL; FLO-1, IC_{50} = 48.6 µg/mL; OE 19, IC_{50} = 44.7 µg/mL)), oesophageal squamous cell carcinoma, (KYSE-30, IC_{50} = 7 µg/mL)' and non-malignant retinal pigment (RPE-1, IC_{50} = 39 µg/mL) as well as fibroblast (FIBR, IC_{50} = 27 µg/mL) cells. The extract induced G2/M phase cell cycle arrest in KYSE-30 cells by upregulating the intracellular level of the 5′AMP-activated kinase. Leaves' extract showed antibacterial activity against *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas aeruginosa* (ATCC 27853), *Pseudomonas fluorescens* (ATCC 13525), *Salmonella enterica* (ATCC 14028), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes. The leaves' extract stimulated erythroid and myeloid cells in (E110 C57BL/6 mice embryonic cultured cells.	Kaempferol, Quercetin, (+)-Catechin, Gallocatechin	[31,36,40]
25	*Faujasiopsis flexuosa* (Lam.) C. Jeffrey (Asteraceae)	Antidiabetic activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method and Soxhlet extraction followed by liquid-liquid fractionation using organic solvent of varying polarity. Aqueous extract prepared using decoction method as well as by crushing the plant material in food blender and distilling the solvent.	Leaves' extract showed anti-glycation activity. Leaves' extract showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Bacillus cereus*, *Bacillus subtilis*, *Enterococcus faecalis*, and *Salmonella typhimurium*. Leaves' extract inhibited lipoxygenase and α-amylase activity.	Not reported	[45,47–50]
26	*Gaertnera psychotrioides* (DC) Baker (Rubiaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract showed antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*.	Not reported	[39]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
27	*Labourdonnaisia glauca* Bojer (Sapotaceae)	Anticancer activity In vitro modulation of hematopoietic cells.	Organic extract was prepared using maceration method.	The leaves' extract inhibited the growth of cervical adenocarcinoma (HeLa, IC_{50} = 41.5 µg/mL), colorectal carcinoma (HCT 116, IC_{50} = 31.6 µg/mL), oesophageal adenocarcinoma (FLO-1, IC_{50} = 11.2 µg/mL), oesophageal squamous cell carcinoma, (KYSE-30, IC_{50} = 9.2 µg/mL), and non-malignant retinal pigment (RPE-1, IC_{50} = 49 µg/mL) as well as fibroblast (FIBR, IC_{50} = 27 µg/mL) cells. The extract induced G2/M phase cell cycle arrest in KYSE-30 cells by upregulating the intracellular level of the 5′AMP-activated kinase. The leaves' extract stimulated myeloid cells in (E110 C57BL/6 mice embryonic cultured cells.	(+)-Catechin, Gallocatechin	[31,36]
28	*Mimusops balata* (Aubl.) C.F. Gaertn (Sapotaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen.	Myricetin, Quercetin	[42]
29	*Mussaenda landia* Poiret var. *landia* (Rubiaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract showed antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*.	Not reported	[39]
30	*Ochna mauritiana* Lam. (Ochnaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 33 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = not obtained at highest concentration tested). The leaves' extract showed antibacterial activity, *Escherichia coli I* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Pseudomonas fluorescens* (ATCC 13525), *Serratia marcescens* (ATCC 13880), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes.	Gallic acid, Quercetin	[40]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
31	*Phyllanthus phillyreifolius* var. commersonii Müll. Arg (Phyllanthaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method; aqueous extract prepared using Soxhlet extraction and decoction.	Leaves' extract inhibited the growth of human cervical cancer (HeLa) cells with IC_{50} value 533.1 µg/mL 48 h post extract treatment. The extract decreased the expression of the apoptosis promoter gene, Bax, and increased the level of BcL-2, an apoptosis inhibitor gene, in HeLa cells. A similar Bax to BcL-2 ratio was observed in human epithelial breast cancer (MDA-MB-231) cells 48 h post extract treatment with an IC_{50} value of 337.4 µg/mL. Apoptosis as a mode of induced cell death was ruled out for the extract. Leaves' extract showed antibacterial activity against *Bacillus cereus* (ATCC 10876), *Escherichia coli* (ATCC 25922), and *Staphylococcus epidermidis* (ATCC 23925). Leaves' extract inhibited tyrosinase and α-glucosidase enzymes.	Gallic acid, Quercetin derivatives, Hexahydroxydiphenoyl-galloyl-glucose, Phyllanthusiin B, Granatin B, Castalagin derivatives, Ellagic acid, Digalloylquinic acid, Citric acid, 5-*O*-caffeoylquinic acid	[51]
32	*Pittosporum senacia* Putterl. subsp. *Senacia* (Pittosporaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Aqueous extract was prepared by crushing the plant material in food blender and distilling the solvent; organic extract prepared using maceration method; essential oils were extracted using hydro distillation method.	Leaves' extract inhibited the growth as well as migration of human epithelial breast cancer (MDA-MB-231) cells. The IC_{50} value 48 h post extract treatment was 118.8 µg/mL. The extract upregulated gene expression of apoptosis promoters, notably Bax and Bak, while decreasing the expression of apoptosis inhibitor genes, i.e., Bcl-2 and Birc5. Moreover, the essential oil from the leaves inhibited the growth of the human malignant melanoma cell line (UCT-MEL1, IC_{50} = 95.52 µg/mL) as well as that of the human keratinocyte non-tumorigenic cell line (HaCat, IC_{50} = 50.33 µg/mL). Leaves' extract inhibited the growth of *Enterococcus faecium* and *Listeria monocytogenes* (ATCC 7644). Leaves' extract showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Bacillus cereus*, and *Bacillus subtilis*. Essential oil from the leaves inhibited the growth of *Mycobacterium smegmatis* (ATCC MC (2) 155) and *Candida tropicalis* (ATCC 750). Essential oil from the leaves inhibited elastase and collagenase enzymes.	Myrcene, Germacrene D, Limonene, 9-octadecanoic acid, *β*-Phellandrene, *δ*-Cadinene, Citric acid, Caffeoylquinic acid derivatives, Coumaroylquinic acid derivatives, 5-Feruloyl quinic acid, Isorhamnetin glycosides, Quercetin glycosides, Oleuropein	[50,52–54]
33	*Polygonum poiretii* Meisn. (Synonymous: *Persicaria poiretii* (Meisn.) K.L. Wilson) (Polygonaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Both the bark and leaf extracts showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*.	Not reported	[47]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
34	*Psiadia arguta* Voigt (Asteraceae)	Anti-inflammatory activity Antidiabetic activity Antimicrobial activity In vitro toxicity study	Organic solvent was prepared using sequential extraction of varying polarity and exhaustive extraction using accelerated solvent extractor followed by fractionation using column chromatography and maceration method; essential oils were extracted using hydro distillation method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture. Essential oil from leaves showed anti-glycation properties. Leaves' extract displayed antibacterial activity against *Escherichia coli* (ATCC 27853), *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Klebsiella pneumoniae* (ATCC27853), *Pseudomonas aeruginosa* (ATCC 27853), and *Bacillus cereus* (ATCC 11778). Essential oil from the leaves inhibited the growth of *Acinetobacter baumanii* (clinical isolate), *Escherichia coli* (ATCC 25922), *E. coli* (clinical isolate), *Pseudomonas aeruginosa* (ATCC 27853), *P. aeruginosa* (clinical isolate), *Enterococcus faecalis* (clinical isolate), *Propionibacterium acnes* (ATCC 6919), *Staphylococcus aureus* (ATCC 25923). *Staphylococcus epidermidis* (ATCC 12228), *Streptococcus peroris* (clinical isolate), *Bacillus cereus* (NCD 0577), *Pseudomonas aureofaciens* (NCD 02178), *Staphylococcus aureus* (NCIMB 3251), *Aspergillus ochraceus* (NRRL 3174), *Fusarium moniliforme* (C25), *Candida pseudotropicalis* (NCYC 143) and *Kluyveromyces lactis* (NCYC 416), *Aspergillus niger* (ATCC 16404), *Candida albicans* (ATCC 10231), and *Candida tropicalis* (ATCC 750). Moreover, essential oil from the leaves inhibited the biofilms formation of *Staphylococcus epidermidis* (ATCC 35984), *Escherichia coli* (ATCC 35218), and *Candida albicans* (ATCC 10231). The antibiofilm activity mechanism of the essential oil was hypothesised to be via the quenching of the efflux pump in the organisms. The leaves, extract inhibited the growth of 3D7 and W2 strains of *Plasmodium falciparum*. The essential oil was considered to be moderately toxic in *Artemia salina* (brine shrimp) eggs as per Clarkson's toxicity criterion.	Sakuranin, Incensole, Hydroxycinnamic acid, Labdonolic acid, Oleic acid, *β*-Pinene, *β*-Myrcene, Limonene, 1,8-Cineol, Isoeugenol, Vanillin, Methyl eugenol, *β*-Carophyllene, Carophyllene oxide, *α*-cubebene, Methyl eugenol, Methyl salicylate, Ethyl benzoate, Benzyl acetate, Benzyl alcohol, Isoeugenyl acetate, Vanillin acetate, Acetovanillone, *α*-Curcumene, *δ*-Selinene, *β*-Eudesmol, Elemol, Linalool, Linalool oxide, Terpinen-4-ol, *α*-Terpineol, *ρ*-Cymen-8-ol, Ocimene, Geraniol, *β*-Cyclocitral, Nerol, *β*-amyrin, *α*-amyrin, Labdan-13(*E*)-en-8*α*-ol-15-yl acetate, Labdan-8*α*-ol-15-yl acetate, Anticopalic acid, Physanicandiol, 14-*epi*-physanicandiol, 13-*epi*-sclareol, Labdan-13(*E*)-ene-8*α*,15-diol, (8*R*,13*S*)-labdane-8*α*,15-diol, Labdanolic acid, Labdan-8(20)-en-15-ol, Labdan-8*α*-ol-15-yl-(formate), Labdan-8*α*-ol-15-yl-(2-methylbutanoate), Labdan-8*α*-ol-15-yl-(3-methylpentanoate) and Labdan-8*α*-ol-15-yl-(labdanolate).	[41,42,55–59]
35	*Psiadia lithospermifolia* Cordem (Asteraceae)	Anticancer activity Antimicrobial activity Anti-inflammatory activity	Organic solvent was prepared using sequential extraction of varying polarity and maceration method.	Leaves' extract inhibited the growth of murine cancer cells—EL-4 lymphoma (EL4) and B16F10 melanoma (B16) cells. The cell death was induced via the loss of mitochondrial membrane potential and caspase-8-mediated apoptosis in both EL4 and B16 cells. Leaves' extract displayed antibacterial activity against *Escherichia coli* (ATCC 27853), *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Klebsiella pneumoniae* (ATCC27853), *Pseudomonas aeruginosa* (ATCC 27853), and *Bacillus cereus* (ATCC 11778). Essential oils from the leaves inhibited the growth of *Bacillus cereus* (NCD 0577), *Pseudomonas aureofaciens* (NCD 02178), *Staphylococcus aureus* (NCIMB 3251), *Aspergillus ochraceus* (NRRL 3174), *Aspergillus niger* (Udl. 3.37), *Fusarium moniliforme* (C25), *Candida pseudotropicalis* (NCYC 143), and *Kluyveromyces lactis* (NCYC 416). Leaves extract decreased concanavalin A-induced T cells and lipopolysaccharide-induced B cells proliferation in C57BL/6 mice spleen culture.	Cafestol, Stearidonic acid, Isocupressic acid, Taxadienone, Incensole, Geranylgeraniol, Levopimaric acid, (*E*)-Isoasarone, *α*-Curcumene, *δ*-Selinene, *α*-Humulene, *δ*-Elemene, *γ*-Elemene, Selina-4,7(11)-diene, *β*-Bisabolene, *α*-Cedrene, *γ*-Cadinene, (*E*)-Farnesene, (*E*, *Z*)-*α*-Farnesene.	[41,42]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
36	*Psiadia terebinthina* A.J. Scott (Asteraceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity In vitro toxicity study	Organic extract was prepared using maceration method and fractionated using column chromatography; essential oils were extracted using hydro distillation method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 5 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 33 µg/mL). Essential oil from the leaves inhibited the growth of *Acinetobacter baumanii* (clinical isolate), *Escherichia coli* (ATCC 25922), *E. coli* (clinical isolate), *Pseudomonas aeruginosa* (ATCC 27853), *P. aeruginosa* (clinical isolate), *Proteus vulgaris* (clinical isolate), *Enterococcus faecalis* (clinical isolate), *Propionibacterium acnes* (ATCC 6919), *Staphylococcus aureus* (ATCC 25923), *Staphylococcus epidermidis* (ATCC 12228), *Streptococcus peroris* (clinical isolate), methicillin-resistant *Staphylococcus aureus* (clinical isolate) and *Klebsiella pneumonia* (clinical isolate), *Bacillus cereus* (NCD 0577), *Pseudomonas aureofaciens* (NCD 02178), *Staphylococcus aureus* (NCIMB 3251), *Aspergillus ochraceus* (NRRL 3174), *Fusarium moniliforme* (C25), *Candida pseudotropicalis* (NCYC 143), and *Kluyveromyces lactis* (NCYC 416). Leaves' essential oil displayed antifungal activity against *Aspergillus niger* (ATCC 16404), *Candida albicans* (ATCC 10231), and *Candida tropicalis* (ATCC 750). Leaves' extract showed antibacterial activity, *Klebsiella oxytoca* (ATCC 43086), *Salmonella enterica* (ATCC 14028), and *Bacillus cereus* (ATCC 11778). Essential oil from the leaves inhibited the biofilms formation of *Staphylococcus epidermidis* (ATCC 35984), *Escherichia coli* (ATCC 35218), and *Candida albicans* (ATCC 10231). The antibiofilm activity mechanism of the essential oils was hypothesised to be via the quenching of the efflux pump in the organisms. Leaves, extract inhibited acetylcholinesterase and xanthine oxidase enzymes. Essential oils from leaves inhibited α-glucosidase activity. The essential oil was considered to be moderately toxic in *Artemia salina* (brine shrimp) eggs as per Clarkson's toxicity criterion.	α-Pinene, β-Pinene, β-Myrcene, Andrographolide, α-Cucumene, Acetyl eugenol, Naphthalene, β-Carotene, Ambreinolide, Eugenol, Methyl eugenol, Eugenyl acetate, β-Asarone, Methyl salicylate, Vanillin, α+ β-Curcumene, Germacrene-D, β-Maaliene, Isoledene, β-Caryophyllene, δ-Cadinene, β-Elemene, α-Genjumene, γ-Eudesmol, Caryophyllene-oxide, Linalool, Terpinen-4-ol, α-Terpineol, ρ-Cymen-8-ol, β-Phellandrene and 1,8-cineole.	[40,55–58,60]
37	*Psiadia viscosa* (Lam.) A.J. Scott (Asteraceae)	Antimicrobial activity Anti-inflammatory activity	Organic solvent was prepared using sequential extraction of varying polarity and maceration method; essential oils were extracted using hydro distillation method.	Leaves' extract displayed antibacterial activity against *Escherichia coli* (ATCC 27853), *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Klebsiella pneumoniae* (ATCC27853), *Pseudomonas aeruginosa* (ATCC 27853)' and *Bacillus cereus* (ATCC 11778). Essential oil from the leaves inhibited the growth of *Bacillus cereus* (NCD 0577), *Pseudomonas aureofaciens* (NCD 02178), *Staphylococcus aureus* (NCIMB 3251), *Aspergillus ochraceus* (NRRL 3174), *Candida pseudotropicalis* (NCYC 143), and *Kluyveromyces lactis* (NCYC 416). Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen.	Methyl eugenol, Pentyl 4-(1-methyl ethyl benzoate), (*Z*)-Isoasarone, Selina-4,7(11)-diene, β-Patchoulene, β-Cedrene, α-Himachalene, γ-Cadinene, α-Patchoulene, Cadina-1,4-diene, Calarene, Agarospirol, Guiaol, Aristolone, Linalool, Terpinen-4-ol, α-Terpineol, β-Phellandrene, 1,8-Cineole, α-Thujene, α-Terpinene.	[41,42,58]
38	*Psiloxylon mauritianum* (Bouton ex Hook.f.) Baill. (Myrtaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract inhibited growth of *Staphylococcal aureus* (ATCC 29213) with MIC < 51 µg/mL. Bioassay-guided fraction revealed corosolic acid and Asiatic acid as active anti-staphylococcal compounds.	Corosolic acid, Asiatic acid.	[61]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
39	*Sideroxylon boutonianum* A.DC (Sapotaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin A-induced proliferation of T cells in C57BL/6 mice spleen culture.	Not reported	[42]
40	*Sideroxylon cinereum* Lam (Sapotaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cells and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture.	Epigallocatechin, Quercetin, Linoleic acids	[42]
41	*Sideroxylon puberulum* A.DC (Sapotaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture.	Not reported	[42]
42	*Sideroxylon sessiliflorum* (Poir.) Capuron ex Aubrév (Sapotaceae)	Anti-inflammatory activity	Organic extract was prepared using maceration method.	Leaves' extract decreased concanavalin-A-induced T-cell and lipopolysaccharide-induced B-cell proliferation in C57BL/6 mice spleen culture.	Not reported	[42]
43	*Stillingia lineata* subsp. *Lineata* (Euphorbiaceae)	In vitro enzyme inhibitory activity Antidiabetic	Organic extract was prepared using maceration method and aqueous extract prepared using decoction method.	Leaves' extract inhibited *α*-glucosidase activity. Leaves' extract inhibited the in vitro movement of glucose across the dialysis tubing membrane.	Not reported	[45]
44	*Sygygium latifolium* (Poir.) DC. (*Myrtaceae*)	Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract inhibited the growth of *Staphylococcus epidermidis* (ATCC 12228), *Staphylococcus aureus* (ATCC 29213), *E. coli* (ATCC 25922), and *Propionibacterium acnes* (ATCC 6919). Leaves' extract inhibited tyrosinase enzyme.	Not reported	[62]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
45	*Syzygium coriaceum* Bosser & J. Guého (Myrtaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method, and essential oils were extracted using hydro distillation method.	Leaves' extract inhibited the growth of human epithelial breast cancer (MDA-MB-231) cells with an IC_{50} value of 53.41 µg/mL 48 h post extract treatment. The extract was proposed to induce apoptosis in MDA-MB-231 via the downregulation of anti-apoptotic Bcl-2 and BIRC5 genes. Moreover, the extract decreased the gene expression of microtubule-associated protein 1 light chain 3 (LC3) and beclin as well as telomerase reverse transcriptase (TERT) in MDA-MB-231 cells. The leaves' extract further inhibited the growth of human liposarcoma cells (SW872, IC_{50} = 35.3 µg/mL), human lung carcinoma cells (A549, IC_{50} = 46.4 µg/mL), and human hepatocellular carcinoma cells (HepG2, IC_{50} = 24.2 µg/mL) as well as immortalised human ovarian epithelial (HOE, IC_{50} = 63.7 µg/mL) cells. The extract caused the rupture of cell membrane integrity, resulting in extracellular leakage of lactate dehydrogenase enzyme in HepG2 cells. The leaves extract upregulated intracellular reactive species production, decreasing intrinsic catalase and glutathione peroxidase enzyme activity, in HepG2 cells. The extract further induced a decrease in the mitochondrial membrane potential, caused G0/G1 cell cycle phase arrest, induced mild DNA damage, as well as inhibited the colony-forming ability of HepG2 cells. The extract is reported to induce both apoptosis and necrosis in HepG2 cells. Essential oil from the leaves inhibited the growth of a human malignant melanoma cell line (UCT-MEL1, IC_{50} = 95.37 µg/mL) as well as that of a human keratinocyte non-tumorigenic cell line (HaCat, IC_{50} = 34.17 µg/mL). Essential oil from the leaves inhibited the growth of *Mycobacterium smegmatis* (ATCC MC (2) 155), *Cutibacterium acnes* (ATCC 6919), *Candida albicans* (ATCC 10231), *Candida tropicalis* (ATCC 750), *Staphylococcus epidermidis* (ATCC 12228), *Staphylococcus aureus* (ATCC 25923), methillin-resistant *Staphylococcus aureus* (MRSA), *Bacillus spizizenii* (ATCC 6633), and *Enterococcus faecalis* (clinical isolate). Leaves' extract inhibited growth of *Staphylococcus epidermidis* (ATCC 12228, ATCC 14990), *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922) and *Propionibacterium acnes* (ATCC 6919), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 25923), and *Bacillus cereus* (ATCC 10876). Leaves' extract inhibited acetylcholinesterase, butyrylcholinesterase, α-amylase, and α-glucosidase enzymes. The leaves essential oil inhibited elastase and anti-collagenase enzymes.	*(E)*-*β*-ocimene, *(Z)*-*β*-ocimene, α-guaiene (12.6%), *β*-selinene, myrcene, δ-guaiene, selin-11-en-4 a-ol, α-selinene. Hexahydroxydiphenyl- galloyl hexoxise, galloyl hexoside derivatives, gallic acid, gallotannin, methyl gallate, quercetin glycoside, kaempferol glycosides, quercitrin, quercetin 3-*O*-*β*-*D*-xylopyranosyl-(1→2)-α-L-rhamnopyranoside, tellimagrandin I, 3,4,6-tri-*O*-galloyl-*D*-glucose, quinic acid, gluconic acid, shikimic acid, citric acid, chebulic acid, flavogallonic acid, flavogallonic acid methyl ester, balanophotannin, ethyl-p-trigallate, ellagic acid, *O*-galloylglycerol, docosenamide.	[32–34,52,53,62]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
46	*Syzygium commersonii* J. Guého & A.J. Scott (Myrtaceae)	Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract inhibited the growth of *Staphylococcus epidermidis* (ATCC 12228), *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922), and *Propionibacterium acnes* (ATCC 6919). Leaves' extract inhibited tyrosinase activity. The extract downregulated the tyrosinase gene expression in mouse melanocyte (B16-F10) cells.	Not reported	[62]
47	*Syzygium glomeratum* (Lam.) DC. (Myrtaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Extract inhibited the growth of Dd2 *Plasmodium falciparum.*	Not reported	[43]
48	*Syzygium guehoi* Bosser & Florens (Myrtaceae)	Antimicrobial activity	Organic extract was prepared using maceration method.	Extract inhibited the growth of Dd2 *Plasmodium falciparum.*		[43]
49	*Syzygium petrinense* Bosser & J. Guého (Myrtaceae)	Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	The extract inhibited the growth of *Staphylococcus epidermidis* (ATCC 12228), *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922), and *Propionibacterium acnes* (ATCC 6919). Leaves' extract inhibited tyrosinase activity.	Not reported	[62]
50	*Terminalia bentzoë* (L.) L.f. subsp. *Bentzoë* (Combretaceae)	Anticancer activity Antimicrobial activity	Organic extract was prepared using maceration method.	Leaves' extract inhibited the growth of human liposarcoma cells (SW872, IC_{50} = 45.4 µg/mL), human lung carcinoma cells (A549, IC_{50} = 96.8 µg/mL), human hepatocellular carcinoma cells (HepG2, IC_{50} = 22.8 µg/mL), and human ovarian carcinoma (OVCAR-4, IC_{50} = 30.1 µg/mL and OVCAR-8, IC_{50} = 38.5 µg/mL) cells. The extract induced DNA damage and G0/G1 cell cycle arrest in HepG2 cells. Moreover, the extract inhibited the colony-forming ability of HepG2 cells. Both apoptosis and necrosis were observed as the mode of induced cell death in HepG2 cells. Leaves' extract showed antibacterial activity against clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*.	*α*/*β*-punicalagin, isoterchebulin, terflavin A, 3,4,6-trigalloyl-*β*-*D*-glucopyranose, 2′-*O*-galloyl-orientin, 2′-*O*-galloyl-isoorientin, 2′-*O*-galloylvitexin, ellagic acid	[35,47]
51	*Tambourissa cordifolia* Lorence (Monimiaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 15 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = 37 µg/mL). Leaves 'extract showed antibacterial activity, *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Salmonella enterica* (ATCC 14028), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes	Quercetin	[40]

Table 1. *Cont.*

	Species	Bioactivity	Type of Extraction Method Employed	Mechanism of Action	Phytochemical Identified	References
52	*Tambourissa peltata* Baker (Monimiaceae)	Anticancer activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method and aqueous extract prepared using decoction method.	Leaves' extract inhibited human hepatocellular carcinoma cells (HepG2, IC_{50} = 590 µg/mL) and human colorectal carcinoma cells (HT29, IC_{50} = 820 µg/mL). Leaves' extract inhibited acetylcholinesterase, butyrylcholinesterase, tyrosinase, α-amylase, and α-glucosidase enzymes.	Isocitric acid, Prodelphindin dimer B, Procyanidin trimer B-type, Gallocatechin, Dihydroxybenzoic acid derivatives, Epigallocatechin, Catechin, Roseoside, Epicatechin, Myricetin glycoside, Quercetin glycoside, Mearnsetin glycoside, Kaempferol glycoside, Isohamnetin glycoside.	[63]
53	*Turraea rigida* Vent. (Meliaceae)	Anticancer activity Antimicrobial activity In vitro enzyme inhibitory activity	Organic extract was prepared using maceration method.	Leaves' extract selectively inhibited human breast cancer (Hs578T, IC_{50} = 30 µg/mL) cells as opposed to the non-malignant human breast (Hs578BsT, IC_{50} = not obtained at highest concentration tested). Leaves' extract showed antibacterial activity, *Escherichia coli* (ATCC 25922), *Klebsiella oxytoca* (ATCC 43086), *Salmonella enterica* (ATCC 14028), and *Bacillus cereus* (ATCC 11778). Leaves' extract inhibited acetylcholinesterase and xanthine oxidase enzymes	Epigallocatechin, Kaempferol	[40]

2.2. Mauritian-Endemic Plants in Combatting Antimicrobial Resistance

The use of herbal formulations in the management of infectious diseases in Mauritius is well established [64]. The ethnomedicinal uses of Mauritian-endemic plants in the management of microbial diseases have been previously summarised [29]. An effort to compile the in vitro antimicrobial activities of indigenous plants, including endemic species, published up to 2019 was made by Suroowan et al. [65]. The inference from the scientific literature published by several independent research groups revealed that thirty-six Mauritian-endemic plant species, when applied in the form of leaves' extracts, imposed in vitro growth-inhibitory activity against a broad spectrum of microbial strains, including both bacteria and fungi (Table 1).

Six leading deadly bacteria, notably *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, accounted for 73.4% of antimicrobial resistance-related death globally for the year 2019, with drug-resistant strains of *E. coli* claiming the highest number of death [10]. The lethality of these bacteria was also recognised by the WHO, and they are earmarked as high-priority pathogens for developing novel antibiotics capable of killing these bacteria [66]. The following literature, therefore, focuses on endemic species having reported antimicrobial activities against these six drug-resistant pathogens.

The 36 plant species showed selective antimicrobial activity against *E. coli* (n = 30), *P. aeruginosa* (n = 23), *S. aureus* (n = 21), *K. pneumoniae* (n = 7), and *A. baumannii* (n = 2) (Table 1). No endemic plant extract showing activity against *S. pneumoniae* was reported. *Psiadia arguta* and *P. terebinthina* were of particular interest due to their reported wide-spectrum inhibitory activity against all of the six deadly bacteria except *S. pneumoniae*,. Moreover, *P. arguta* and *P. terebinthina* are reported to inhibit biofilm formation against *E. coli* and *S. epidermidis* via the quenching of the efflux pump in the organism [56]. Other Mauritian-endemic plants that exhibited antibacterial activity against at least three of the above-mentioned bacteria include *Aloe purpurea*, *A. tormentorii*, *D. populifolius*, *P. lithospermifolia*, *P. viscosa*, *S. coriaceum*, and *T. bentzoë* (Table 1). Apart from the leaf's crude extracts, essential oils derived from the leaves have also been investigated for their inhibitory potential against a panoply of pathogens. The essential oils have demonstrated inhibitory activity either with their sole application or have potentiated the activity of conventional clinical antibiotics. For instance, essential oil from *P. arguta* leaves potentiated the inhibitory effect of gentamicin against *E. coli* and *S. epidermidis* [57]. Likewise, essential oil from *S. coriaceum* leaves synergistically boosted the effect of the standard antibiotic, i.e., ciprofloxacin, against *P. aeruginosa* and also gave an additive effect against *S. aureus* when combined with the drug streptomycin [52]. These plants are of particular interest for further investigation due to their potential to suppress the growth of numerous bacterial species (Table 1).

2.3. Key Challenges and Future Work

Attempts to discover potent bioactive extracts from the island's indigenous floral diversity, with the ambition to establish potential clinical concoctions or purified molecules, have been the epicentre of investigation for various research groups in the past decades. In the search for promising drug candidates, some investigators have allowed their research work to be guided by the medicinal uses of endemic plants, intending to elucidate the active ingredients and validate their purported therapeutic claims [37,39,46–50,54,55,61,67,68]. Meanwhile other scientists have randomly screened the unexplored unique floral reserve, aiming to evaluate the health benefits of these endangered plant species before their permanent loss due to extinction [32–34,51,63]. Yet, a pre-clinical drug candidate budding from the endemic resources of Mauritius is beyond the horizon. Drug research in Mauritius is associated with numerous challenges and limitations. The subsequent text depicts the key limitations of the so-far published research work and recommends prospective studies.

The crude herbal extracts or essential oils tested are comprised of a mixture of structurally diverse molecules, making it difficult to successfully differentiate the bioactive components from the pool of inactive molecules [69]. Identifying principal bioactive com-

ponents present in the crude extracts and their purification is paramount to establishing their molecular mode of action and their pharmacokinetic and toxicity profile. Only three studies have attempted to delineate the bioactive compounds through bioassay-guided fractionation [33,35,61]. Future work aiming at the characterization of lead bioactive molecules present in promising extracts is warranted.

Great research effort has been devoted towards unravelling the bioactivities of endemic plants. However, as can be inferred from Table 1, most of the research conducted by local scholars was limited to in vitro assays only. In stark contrast, in vivo studies to corroborate the in vitro findings are scanty. Although the in vitro model allows for rapid and affordable preliminary screening of herbal extracts, the results generated are not conclusive, as limited insights in terms of the extract's behaviour in a multicellular organism are available [70]. As such, animal studies are required to corroborate the in vitro findings. Moreover, it is established that following administration, drugs including natural products are bio-transformed inside the body [71]. In vivo biotransformation considerably alters the clinical efficacy and safety profile of drugs [72]. Biotransformation may decrease as well as significantly increase the bioactivity of the parent compounds [72,73]. Forthcoming analysis in this area should also focus on the microbial and cellular metabolism profiles of promising extracts.

From a mechanistic point of view, limited insight is provided regarding the mode of action of the extracts. Promising anticancer extracts are reported to induce cell cycle arrest in malignant cells. However, the molecular cascade of events is yet to be elucidated. Likewise, the antibacterial mechanism of action of the two *Psaidia* species is restricted to their ability to modulate the efflux pump in the organism. More rigorous investigation of the targeted signalling pathways, gene modulations, and alterations in the cellular microenvironment is prescribed.

The toxicological aspect of endemic plants has vaguely been explored, with the only available reports being restricted to preliminary studies conducted on brine shrimp eggs. A greater understanding of the safety window of the extracts for human administration is of utmost importance and needs to be thoroughly investigated before any attempt at clinical studies.

3. Materials and Methods

Literature searches were performed on electronic databases such as PubMed and Science Direct as well as the Google search engine to identify publications that report the bioactivities of Mauritian-endemic terrestrial flora. Only articles in English published from 1981 up to January 2023 were considered and critically assessed for data extraction. The various electronic databases were searched using relevant keywords including bioactivities of Mauritius extract, anticancer extracts from Mauritius, antimicrobial from Mauritius, antidiabetic from Mauritius, clinical trials in Mauritius, Mauritius-endemic plants, and specific binomial names of endemic plant species. The Plants of the World Online (https://powo.science.kew.org, accessed on 15 January 2023) database of the Kew Royal Botanic Gardens was consulted for acquiring the authenticity of the botanical names and endemicity of the plants discussed in this review.

A total of 2190 peer-reviewed articles' titles were obtained following the initial generalised search of the scientific databases. After title screening, 95 articles relevant to this review were recognised, and after eliminating duplicates, 61 articles were selected. Following abstract consultation, a final 33 articles were considered for this study. The inclusion criteria consisted of the following parameters: (1) Plants must be endemic to Mauritius; (2) the plant's sample must have been collected in Mauritian mainland territory; and (3) the article must report the biological bioactivities of the extract. The collected information was tabulated, and the biological activities, reported/proposed mechanism of action, and major phytoconstituents present in the plants are specified.

4. Conclusions

The current review is a repertoire regarding the reported bioactivities of Mauritius-endemic plants. With these findings, it can be inferred that Mauritian-endemic flora is indeed a fertile source to probe for drug candidates with potential application in the combat against drug resistance. The current data provided a solid basis for future in-depth mechanistic studies directed toward the molecular mechanism of action of the endemic extracts related to their anticancer and antimicrobial activities and also allow investigation the pharmacokinetics and metabolism profile of the bioactive compounds. Moreso, the bioactivity of the promising extracts needs to be evaluated in animal models and preferably in clinical trials to gauge their clinical efficacy and safety profile.

Although over 50% of pharmaceutical compounds rely on biological resources, the process of including these promising plants in biomedicine is multi-stepped and long, requiring appropriate expertise and pharmaceutical infrastructure. In addition, consideration of population biodiversity, specifically the within-taxa diversity of ecotypes, phenotypes, and chemotypes, is vital. Furthermore, appropriate frameworks should be implemented to drive sustainable exploration and the use of products developed from this biodiversity.

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