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Review

Antioxidative and therapeutic potential of selected Australian plants: A review

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ABSTRACT

Ethnopharmacological relevance: Numerous common pharmaceuticals, including anti-cancer, antiviral and anti-diabetic drugs, are derived from traditional plant-derived medicines. With approximately 25,000 species of flora occurring in Australia that are adapted to the harsh environment, there is a plethora of novel compounds awaiting research in the context of their medicinal properties. Anecdotal accounts of plant-based medicines used by the Australian Aboriginal and Torres Strait Islander peoples clearly illustrates high therapeutic activity.

Aim: This review aims to demonstrate the medicinal potentials of selected native Australian plants based on scientific data. Furthermore, it is anticipated that work presented here will contribute towards enhancing our knowledge of native plants from Australia, particularly in the prevention and potential treatment of disease types such as cancer, microbial and viral infections, and diabetes. This is not meant to be a comprehensive study, rather it is meant as an overview to stimulate future research in this field.

Methods: The EBSCOhost platform which included PubMed, SciFinder, Web of Knowledge, Scopus, and ScienceDirect databases were searched for papers using the keywords: medicinal plants, antioxidative, antimicrobial, antibacterial, anticancer, anti-tumor, antiviral or antidiabetic, as well as Australian, native, traditional and plants. The selection criteria for including studies were restricted to articles on plants used in traditional remedies which showed antioxidative potential and therapeutic properties such as anticancer, antimicrobial, antiviral and antidiabetic activity.

Results: Some plants identified in this review which showed high Total Phenolic Content (TPC) and antioxidative capacity, and hence prominent bioactivity, included *Tasmannia lanceolata* (Poir.) A.C. Sm., *Terminalia ferdinandiana* Exell, *Eucalyptus* species, *Syzygium* species, *Backhousia citriodora* F.Muell., *Petalostigma* species, *Acacia* species, *Melaleuca alternifolia* (Maiden & Betche) Cheel, *Eremophila* species, *Prostanthera rotundifolia* R.Br., *Scaevola spinescens* R. Br. and *Pittosporum angustifolium* Lodd. The majority of studies found polar compounds such as caffeic acid, coumaric acid, chlorogenic acid, quercetin, anthocyanins, hesperidin, kaempferol, catechin, ellagic acid and saponins to be the active components responsible for the therapeutic effects. Additionally, mid to non-polar volatile organic compounds such as meroterpenes (serrulatanes and nerol cinnamates), monoterpenes (1,8-cineole and myodesert-1-ene), sesquiterpenes, diterpenes and triterpenes, that are known only in Australian plants, have also shown therapeutic properties related to traditional medicine.

Conclusion: Australian plants express a diverse range of previously undescribed metabolites that have not been given full *in vitro* assessment for human health potential. This review has included a limited number of plant species of ethnomedicinal significance; hundreds of plants remain in need of exploration and detailed study. Future more elaborate studies are therefore required to screen out and purify lead bioactive compounds against numerous other disease types. This will not only improve our knowledge on the phytochemistry of Australian native flora, but also provide a platform to understand their health-promoting and bioactive effects for pharmaceutical interventions, nutraceuticals, cosmetics, and as functional foods. Finally, plant-derived natural compounds (phytochemicals), as well as plant-based traditional remedies, are significant sources for latent and

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novel drugs against diseases. Extensive investigation of native medicinal plants may well hold the key to novel drug discoveries.

1. Introduction

Increasing rates of non-communicable diseases (NCDs) such as cancer, diabetes, and cardiovascular diseases, alongside the emergence of new antimicrobial-resistant viruses and bacterial strains are becoming a growing concern globally. The World Health Organization (WHO) reports 41 million deaths worldwide in 2016 were collectively attributed to NCDs, equivalent to 71% of all global deaths (World Health Organisation, 2018). Similarly the death toll from communicable diseases has also increased especially due to the current COVID-19 pandemic, caused by the coronavirus SARS-CoV-2, which has claimed many lives and is projected to worsen as infection rates continue to increase worldwide (https://www.who.int/emergencies/diseases/novel-coronavirus-2019). Offsetting and treating these disease types using plant-derived compounds has been viewed as a potential therapeutic option alongside western medicine. This has been proposed by numerous literature and is extensively practiced by traditional healers belonging to various cultures (Konczak et al., 2010; Murhekar et al., 2017; Netzel et al., 2007; Oliver, 2013; Richmond et al., 2019). Natural therapeutic medicines are becoming an attractive option as they are perceived to have a lesser incidence of adverse reactions and lower costs associated with remedy preparations when compared to synthetically produced pharmaceuticals (Cock, 2012a). Natural compounds already are an important part of commercial drugs. For example, approximately 45% of all anticancer drugs have been derived from plant sources, of which 12% are unmodified natural products and 32% are synthetic derivatives of plant-based compounds (Vuong et al., 2014). It is also worth noting that half the drugs that were approved for use between the years 1981–2014 were derived from or structurally resembled natural compounds (Newman and Cragg, 2016). One estimate suggests that 80–85% of the global population depends on traditional medicines and remedies for their health care needs (Bhat, 2017), with the majority of these being prepared directly from the plant parts or their active ingredients and/or compounds.

Australian plants may offer promising prospects for the isolation and characterization of prophylactic and/or therapeutic phytochemicals, particularly those that are novel anti-cancer and antiviral agents (Vuong et al., 2014). The variable climate of Australia has given rise to over 25,000 plant species (Richmond et al., 2019), which have evolved to suit the often-harsh growing conditions. Apart from primary biomolecules and metabolites such as carbohydrates, lipids, proteins, and nucleic acids that play an important role in plant physiological functions, plants also synthesize specialised metabolites. Specialised metabolites, which include alkaloids, phenolics, sterols, essential oils and lignins, serve to improve the plant's survival by protecting them against external stressors (such as ultraviolet radiation, extreme temperature fluctuations, salinity, drought, wind, soil type and acidity) and herbivores (Richmond et al., 2019). The expression of specialised metabolites in plants is often affected by exogenous non-genetic influences, such as climatic and agronomic factors. Ephemeral climates and insect herbivory are important stimulants of the expression of bioactive specialised metabolites that are referred to as phytochemicals, which are also active against single-celled organisms such as pathogenic bacteria, or in mammalian systems against cancerous growths, modulated by antioxidation and cytotoxicity (Cock, 2014; Jamieson et al., 2014; Ota and Ulrih, 2017).

Hence, some of these metabolites are beneficial as part of a healthy diet or are suitable for industrial applications and contemporary or alternative medicine (Juri et al., 2020). Bioactive compounds derived from certain Australian plants have already been connected to significant health benefiting outcomes (Cock, 2008, 2012a, 2014; Cock and Matthews, 2016; Murhekar et al., 2017; Sautron and Cock, 2014). Anecdotal evidence suggests that Indigenous communities have used a wide variety of plants for medicinal purposes before the arrival of European settlers (Richmond et al., 2019). However, there is limited literature available that provides in-depth understanding and/or evidence about the medical application of Australian plants and plant-derived remedies (Locher et al., 2013). There is some contemporary literature that mainly focuses on the northern and western Indigenous populace (Wigmore et al., 2016). Some plant genera identified to be widely used by the Australian Aboriginal and Torres Strait Islander peoples for medicinal purposes include *Acacia*, *Eucalyptus*, *Eremophila, Syzygium*, and *Melaleuca* (Cock, 2011). These genera are amongst the largest in Australia and their species are mostly spread across the continent, hence explaining their extensive use. One such group of plants are the Eucalypts, which are iconic Australian forest trees covering 77% of Australia's total native forest area. They include approximately 800 species in the three genera *Angophora, Corymbia* and *Eucalyptus* and are found in all states and territories (Australian Bureau of Agricultural and Resource Economics and Sciences, 2019).

Hence, this review aims to encapsulate and consolidate the existing scientific data and documented evidence available which highlights the phytochemistry and bioactivity of selected native Australian plants. Furthermore, it is anticipated that work presented here will contribute towards enhancing our knowledge of native plants from Australia, particularly in the prevention and potential treatment of disease types such as cancer, microbial and viral infections, and diabetes. This is not meant to be a comprehensive study, rather it is meant as an overview to stimulate future research in this field.

2. Methodology

Published literature in the last twenty years on the developments and research on native Australian plant species as sources of bioactive compounds with potential antioxidative, antimicrobial, anticancer, and anti-diabetic properties, were sourced and examined for this review. Information was extracted from original research and review articles and cross-references found on numerous databases from the host platform 'EBSCOhost' which includes the PubMed, SciFinder, 'Web of Knowledge', Scopus, and ScienceDirect databases with search terms: (Medicinal, antioxidative, antimicrobial, antibacterial anticancer, antitumor, antiviral OR antidiabetic) AND (Australian, native, traditional OR plants). The selection criteria for including studies were restricted to articles on plants used in traditional remedies which showed antioxidative potential and therapeutic properties such as anticancer antimicrobial, antiviral and antidiabetic.

3. Results and discussion

3.1. Ethnomedicinal practices

Australian Aboriginal and Torres Strait Islander peoples have established a profound connection with the land and implicit knowledge of the native flora and fauna (Locher et al., 2013). As one of the world's oldest surviving cultures, the Australian Aboriginal and Torres Strait Islander peoples have utilized plants as therapeutic agents and as interventions for their general wellbeing, which is believed to have contributed to their long-standing survival (Richmond et al., 2019). Nevertheless, many native Australian plant species and traditional plant-based remedies currently being utilized and practiced by Indigenous communities remain unexplored from a scientific perspective and, as such, provide a large scope to investigate their bioactivity and

chemical constituents. The ethnomedicinal knowledge entailing various plant sources, collection times, and preparatory methods are passed down from one generation to the next, mostly in the form of oral lore and preserved through songs, paintings, and dances (Locher et al., 2013). Francis Bodkin (known as Aunty Fran), a botanist and Aboriginal elder, wrote the book "Dharawal Pharmacopeia" on the taxonomic identification, medicinal and ceremonial uses of thousands of native Australian plants by the Dharawal people (Akhtar et al., 2016). Dharawal people are Indigenous Australians from Sydney and Illawara which is in the coastal region of South Sydney. It is stated that the Dharawal Indigenous people have a special importance for plants from the genus *Eucalyptus* and often use these plants for their anti-inflammatory activity effects. Another famously used plant in traditional "bush" medicine is the *Scaevola spinescens* R. Br. In 1935 an Aboriginal man named Albert Neebrong from Western Australia was diagnosed with tongue cancer and reportedly cured himself using *S. spinescens.* Later methanol extract of the plant was sent to the National Cancer Institute (NCI) in the United States and although significant anticancer activity was noted, scientific interest in this plant decreased due to lack of selective toxicity for different cell types (Kavelin, 2007).

Aboriginal and Torres Straight Island people recognise different chemotypes within a species as distinct botanical entities as opposed to modern taxonomy. For instance, modern taxonomy recognises *Eremophila longifolia* as a single species, while indigenous people recognise tetraploids and diploids as different species. Chemical analysis agrees with this and the primary characteristic that enables differentiation between these entities is smell. Much of Australia's flora is characterized by chemical drift within single species. *Prostanthera* is one of the most highly varied in terms of its volatile chemistry. *Prostanthera rotundifolia* is made up of many unnamed taxa that are lumped into the *P. rotundifolia* heterogeneous species aggregate. Therefore, implying that the elucidation of chemical variation prior to connections to traditional therapeutic use is paramount in ethnopharmacological studies. Often specific chemotypes are used medicinally for different things, but recognised by the one binomial name in modern taxonomy (Heinrich and Jäger, 2015).

The traditional knowledge of plant use as therapeutics is rapidly being lost as Indigenous cultures merge into mainstream western societies (Oliver, 2013); as such, formal recordings and documentation are therefore warranted to protect and preserve this wealth of information. Consequently, there are collaborative efforts between Indigenous community elders, ethnobotanists, ethnopharmacologists and natural product chemists to explore and establish the characteristic biochemical properties of traditional Indigenous medicinal plants and remedies, providing much-needed scientific justification and protection of this crucial communal and cultural knowledge (Locher et al., 2013). Anecdotal information and previous academic research on ethnomedicinal, endemic, and native Australian plants have prompted an extensive investigation in the past few years. Table 1 contains selected endemic and native plant species that have been reportedly used by the Australian Indigenous communities as ethnomedicines in treating various ailments.

Plants are spiritually and culturally significant to the Australian Aboriginal and Torres Strait Islander peoples. Many plants which they value are totemic, with information on the use of these plants being confined to the village elders or those initiated into a tribe (Ahmed and Johnson, 2000). Hence, in order to investigate the traditional knowledge of these plants, approvals from traditional owners and polices on Indigenous ecological knowledge and property rights must be adequately addressed. In addition to this, ethnomedicinal knowledge of plants and remedies vary in different aboriginal communities. At times, these predicaments can impede the extent of research and the availability of information on native plants, thus explaining the relative scarcity of documented ethnomedicinal knowledge about plants used by the Australian Aboriginal and Torres Strait Islander peoples.

3.2. Bioactive phytochemicals

Phytochemicals are active plant chemicals that protect plants from disease and damage, and at the same time contribute to plant color, aroma, and flavor (Koche et al., 2016). Phytochemicals accumulate in different parts of the plant such as the roots, stems, flowers, fruits, and seeds, in quantities that depend on the plant variety and the climatic growing conditions. A detailed classification of the phytochemicals is described in Fig. 1. The different moieties of these chemical compounds may provide pharmacophores for drug development. It has been found that quinone, naphthoquinone anthraquinones, and benzoquinone are amongst the most abundant groups among different chemical moieties (Goyal et al., 2017). The three major groups of specialised metabolites are terpenoids, phenolic compounds, and alkaloids (Fig. 1). Terpenoids (example: menthol, abietic acid, solanine and abscisic) are largely produced from the products of glycolysis via the mevalonate pathway or the methylerythritol phosphate (MEP) pathway, whereas phenolic compounds are a ubiquitous class of non-volatile secondary plant metabolites and are derived mainly from the shikimic acid pathway through aromatic carboxylic acids – cinnamic or benzoic (Holopainen et al., 2018; Matkowski, 2008). Some examples of phenols include quercetin, kaempferol, catechins, and anthocyanins. On the other hand, alkaloids are derived from amino acid precursors (Holopainen et al., 2018). Flavanols and their oligomeric forms called condensed tannins or proanthocyanidins, flavone, and flavonols and anthocyanins are flavonoids with the strongest antioxidant properties (Matkowski, 2008).

Polyphenols are the largest group of phytochemicals with phenolic structural features and is a term used collectively for several sub-groups of phenolic compounds (Tsao, 2010). These natural compounds are bioactive with antioxidative properties, albeit to varying degrees, which protect cell constituents against oxidative damage potentially through scavenging the reactive oxygen species (ROS) and free radicals. Consequently this averts the deleterious effects of ROS on nucleic acids, proteins, and lipids (Cock, 2014; Konczak et al., 2010; Netzel et al., 2007). Therefore antioxidants such as polyphenols (example: phenolic acids, lignans and hydrolysable tannins) can be broadly defined as compounds that inhibit or delay oxidation of substrates even if their occurrence is significantly lower than the oxidized substrate (Matkowski, 2008). Normal cellular metabolism generates ROS and free radicals as by-products of aerobic metabolism, namely superoxide, hydroxyl, peroxyl, peroxynitrite, and nitric oxide. The balance between formation and removal of the ROS is essential in maintaining regular cellular physiological functions. Elevated levels of ROS causes damage to nucleic acids, proteins and membrane lipids, potentially leading to health problems such as cardiovascular diseases and carcinogenesis (Wang et al., 2010). Hence the strong antioxidant properties of most polyphenols which are attributed to their hydroxyl group have preventive effects against the development of degenerative NCD diseases such as cancer, cardiovascular diseases, neural degeneration, diabetes, and obesity (Cassidy et al., 2020; Konczak et al., 2010; Matkowski, 2008). Generally more hydroxylated compounds express larger free radical scavenging capacity, whereas the methylation of the hydroxyl group partially decreases this effect (Matkowski, 2008).

On the other hand, synthetic antioxidants such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), tert-butyl hydroquinone (TBHQ) and propyl gallate (PG), have widely been used in hampering lipid oxidation. However the safety of these synthetic antioxidants has recently been questioned due to their toxicity and possible carcinogenicity (Shahidi, 2000; Wang et al., 2010). Subsequently the negative health effects of synthetic antioxidants have prompted increased interest and research in achieving antioxidative effects from natural sources such as plant materials.

Moreover, phenolic compounds such as phenolic acids, flavonoids and tannins are the most effective and salient antioxidants since they can chelate metal ions, prevent lipid peroxidation and free radical scavenging capacity (Guleria et al., 2013). The metal ion chelating property

Table 1
Ethnomedicinal uses of selected native Australian plants, arranged by family.

Scientific names	Family	Common names	Location	Ethnobotanical uses	References
Acacia aulacocarpa Benth.	Fabaceae	Brown Salwood, Hickory Wattle, Golden-flowered Salwood, Wattle or Wattle Black	Northern Qld to northern NSW	Bark, leaves, pods, and seeds- used for treating coughs, diarrhea, and dysentery. Also used for cases of internal bleeding. As a wash (applied externally)- used to treat wounds and other skin problems, hemorrhoids, perspiring feet, some eye problems, and mouth wash.	(Fern, 2019; Symmons and Symmons, 1997)
Allocasuarina littoralis (Salisb.) L.A.S. Johnson	Casuarinaceae	Black sheoak, bull oak, waytuck	Qld, NSW, WA, ACT, Vic and Tas	Antibacterial and antifungal.Used as an astringent and to treat diarrhea, dysentery, headache, and fever	(Cock, 2008, 2012a)
Backhousia citriodora F. Muell.	Myrtaceae	Lemon myrtle	Queensland coastal forests	Treating headaches	Gardening Australia (2011)
Buckinghamia celsissima F. Muell.	Proteaceae	Ivory curl	Northeast Qld	Antibacterial	Cock (2012b)
Callitris endlicheri (Parl.) F. M. Bailey and *Callitris glaucophylla* Joy Thomps and L.A.S. Johnson	Cupressaceae	Black Cypress White Cypress	Throughout Australia.	Aqueous or lipophilic animal fat extracts- used for treating scabies, sores, or rashes. Smoke fumigation of pine needles- treats coughs and colds.	Sadgrove et al. (2014)
Citrus australasica F.Muell.	Rutaceae	Finger limes	Southeast Qld, northern NSW	Antiseptic to infected sores and boils (pulp and juices)	Richmond et al. (2019)
Duboisia hopwoodii (F. Muell.) F.Muell.	Solanaceae	Pituri, pitchuri thornapple or pitcheri.	NSW and south-east Qld	Used to treat diarrhea, congestion, motion sickness and as a sedative.	Kavelin (2007)
Eremophila longifolia (R. Br.) F.Muell.	Scrophulariaceae	Weeping emu bush	Arid and semi-arid regions of all mainland states	Leaves used to treat sores, scabies, cuts, and boils. Also used for treating general pain and illness such as respiratory infections, colds, and fever and used as an eyewash and treating headaches and insomnia.	(Fern, 2019; Locher et al., 2013; Singab et al., 2013)
Eucalyptus spp.	Myrtaceae	Gum trees or stringybark trees	Temperate regions of Australia	Gum- treat diarrhea and fill tooth cavities. Leaves- used as antiseptics, cure colds and treat wounds and eye infections Leaves sun-dried and then infused in boiling water-treat colds, fever, internal and pain. Inner bark or leaves are brewed with water then used to treat sores and scabies.	(Akhtar et al., 2016; Vuong et al., 2014; Wigmore et al., 2016)
Geijera parviflora Lindl *Geijera salicifolia* Schott	Rutaceae	Tree wilga and lavender bush	NSW and southern Qld	Inner bark of trees- used for microbial and fungal infections, topical treatment of wound infections.	Sadgrove et al. (2014)
Hakea spp.	Proteaceae	needlewoods or corkwoods, or as pincushion, cricket ball or frog Hakeas	South-west of WA and along the eastern coast of Australia	Antiseptic properties - mixed with animal fat has been used as emollient to treat burns	Wigmore et al. (2016)
Leptospermum scoparium J. R.Forst. & G.Forst	Myrtaceae	Tea tree, broom tea tree, manuka	Eastern Australia	Leaf vapor-used for colds and coughs. Gum exudate-for scalds and burns. Aqueous bark and seed extracts- for infections and inflammation. Leaves- for urinary complaints. Derived honey- good antibacterial agent	Cock (2013)
Melaleuca alternifolia (Maiden & Betche) Cheel	Myrtaceae	Narrow-leaved Tea Tree	NSW and Qld.	Antiseptic properties of essential oils obtained by steam distillation of plant foliage recently discovered in the 1920s. inhalation of the volatiles from essential oils or crushed leaves used to treat coughs, colds, wounds, sore throat, and skin aliments.	(Wigmore et al., 2016; Wright et al., 2015)
Mentha australis R.Br.	Lamiaceae	River mint	Widespread throughout Australia. Usually found by rivers and creeks	Treat colds and coughs. Inhaling crushed mint relieves headaches. Also used as an abortifacient by the Aboriginal community	Tang et al. (2016)
Petalostigma banksii Britten & S.Moore	Picrodendraceae	Quinine Bush	NT, north-eastern Qld, and central-eastern Qld	Toothache and mouth inflammation	Deo et al. (2016)
Pittosporum angustifolium Lodd.	Pittosporaceae	Gumby gumby or gumbi gumbi, or weeping pittosporum	In land areas of Australia.	Leaf or fruit extracts as poultice or a decoction: external ailments such as bruising, muscle aches, eczema, and other forms of pruritis. Infusions from leaves- treat cough and cold, cramps, eczema, and skin disease and induce lactation in mothers of newborn.	(Bäcker et al., 2014; Blonk and Cock, 2019; Sadgrove and Jones, 2013)
Prostanthera cuneata Benth. *Prostanthera rotundifolia* R.Br.	Lamiaceae	Mintbush or mint bush	Vic, NSW, and ACT	Antiseptics. Antibacterial, antifungal, and carminative. Used externally in the treatment of colds and headaches	(Gardening Australia, 2011; Tang et al., 2017; Wigmore et al., 2016)

(*continued on next page*)

Table 1 (*continued*)

Scientific names	Family	Common names	Location	Ethnobotanical uses	References
Santalum acuminatum (R. Br.) A. DC.	Santalaceae	Quandong, Sweet Quandong, Wild Peach, Desert Peach, Native Peach, Guwandhuna, Gutchu, Wanjanu, Mangata, Goorti, Wadjal	Arid and semi-arid regions of all Australian mainland states	Oil used as cosmetics to smooth skin of face and body. Some kernels more toxic and avoided.	Richmond et al. (2019)
Scaevola spinescens R. Br.	Goodeniaceae	currant bush, maroon bush, or prickly fanflower	All mainland Australia states and territories.	Roots: treat stomach pain and urinary disorders. Crushed stem: treat boils, rashes, and skin disorders. Whole plant burnt and the fumes inhaled to treat colds. Leaves and twigs steamed: exposure to the steam treated sore.	Cock & Matthews (2016)
Solanum centrale J.M. Black	Solanaceae	Bush tomato	NT and SA	Plant roots baked in ash and then peeled- used to treat toothache. Plant may have contraceptive qualities.	Slow Food in Australia (2017)
Syzygium anisatum (Vickery) Craven & Biffin	Myrtaceae	Anise myrtle, Aniseed myrtle, Ringwood	Northern NSW	Antimicrobial uses Used as a medicine for abdominal pain	(Gardening Australia, 2011; Sautron and Cock, 2014)
Syzygium australe (J.C. Wendl. ex Link) B. Hyland	Myrtaceae	Bush cherry, lilly pilly	NSW, Qld and WA	Antimicrobial uses. Pulp of *S. leuhmannii* (riberry) was applied to sore ears.	(Richmond et al., 2019; Sautron and Cock, 2014)
Tasmannia lanceolata (Poir.) A.C. Sm.	Winteraceae	Mountain pepper, Tasmanian pepper, Native pepper, Pepper berry or Pepper leaf	South-eastern Australia	Treatment of skin disorders, venereal diseases, colic, stomachache, and as a quinine substitute. Used for stomach disorders, as an emetic, in a general tonic, used for curing skin disorders, venereal diseases, colic, quinine substitute and scurvy treatment (bark)	(Cock, 2014; Maen and Cock, 2015; Richmond et al., 2019)
Terminalia ferdinandiana Exell	Combretaceae	Kakadu plum, billy goat plum, green plum, salty plum, wild plum, murunga, marnybi, manmohpan, kullari plum, gubinge	WA, Qld, and NT	Whole fruits- cure headaches, colds, and flu. Pounded fruit- antiseptic and a soothing balm for aching limbs. Sap and bark - treat skin condition (wounds, sores, and boils), fungal (ringworm), and bacterial infections (leprosy sores). Drunk as tea- for colds, flus, backaches, and sore feet.	(Gorman et al., 2019; Richmond et al., 2019)

occurs through the deprotonation of the phenolic hydroxyl group, which generates an electronegative oxygen (O-) center in the resulting phenoxide ion as shown in reaction 1 (Hider et al., 2001). The resulting O^{-} ions have potential to interact with several bacterial and fungal peptides, which may result in protein deactivation and loss of function (Singab et al., 2013). Therefore, this suggests that the potent

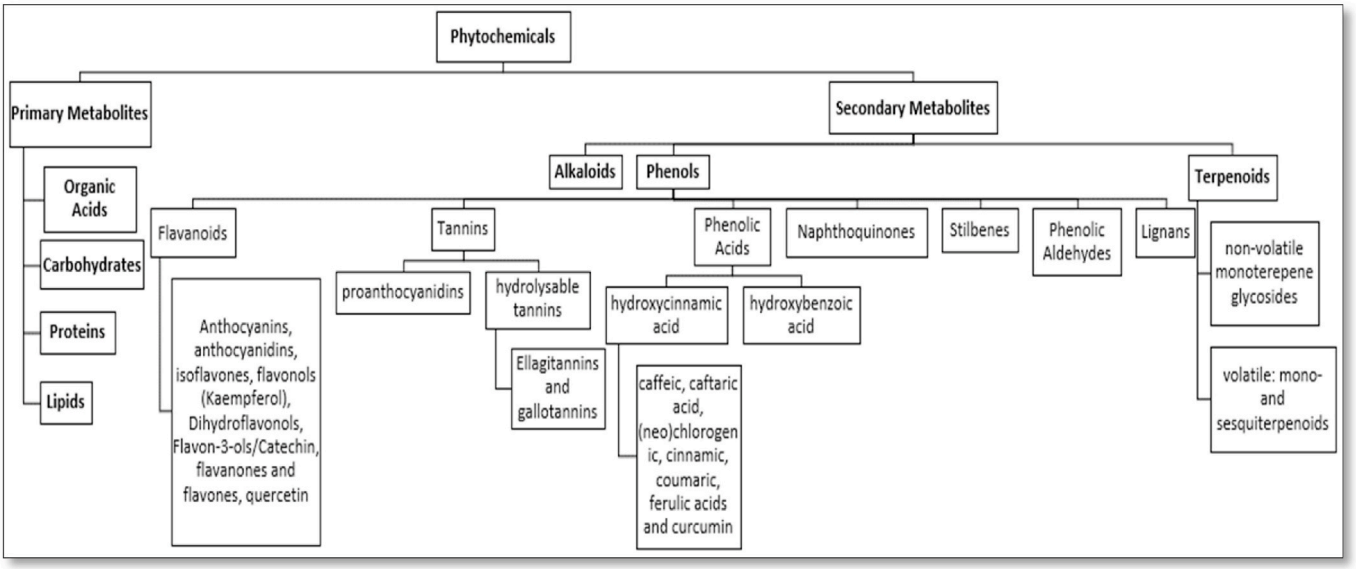
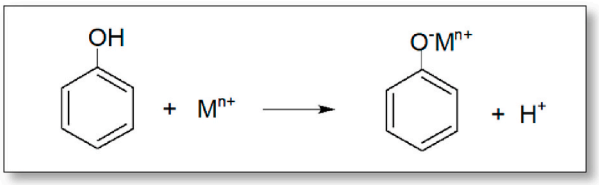


Fig. 1. Classification of phytochemicals.

antibacterial activity of some plant compounds may be mainly due to their reactive phenolic OH group.



Tannins have shown anticarcinogenic and antimutagenic as well as antimicrobial properties (Amarowicz et al., 2004). Some flavonoids such as flavonols, quercetin, and catechin have also been reported to have antioxidant activity and may therefore be beneficial for human health (Djordjevic et al., 2011; Matkowski, 2008). According to Wright et al. (2015), many studies have also reported potent antibacterial activities for a wide variety of flavonoids and several tannins have been shown to inhibit the growth of a broad spectrum of bacterial species (Wright et al., 2015). It was also noted that *Eucalyptus* spp. extracts contained relatively high levels of flavonoids and tannins (Wright et al., 2015). However, the chemical composition and bioavailability of nutrients and antioxidants vary between species and varieties of plants. Abiotic and biotic stressors, such as climate or geographical location and evolution, can influence activity levels; however the extraction and processing conditions can also impact the activity of analytes studied (Bhat, 2017). Terpenes and terpenoids have been used for treating various ailments, food and beverages, and form key components of rituals in many major religions, for instance, terpene scents such as myrrh and frankincense are mentioned in biblical texts and used as holy incense in sacred temples (Pichersky and Raguso, 2018). Volatile terpenoids impart specific flavors to food and drinks, such as the ginger flavor caused by zingiberene and grapefruit flavor caused by nootkatone. They can also preserve food due to their microbicidal and insecticidal properties. More complex terpenoids such as paclitaxel and vinblastine have been used in the treatment of cancer (Pichersky and Raguso, 2018). In general, monoterpenoids and sesquiterpenoids are volatile when not conjugated to polar or large (>200 Da) moieties, while higher order terpenoids are generally non-volatile. Some examples of plant terpenoids isolated from Australian plants are given in Fig. 2.

The distinct significance of bioactive phytochemicals in the food and beverage, pharmacology and medical industries and traditional and religious societies is widely appreciated. Numerous studies have and are continuously being carried to explore phytochemicals in plant species occurring throughout the world. There is however scarce information in the literature on Australian plants. Nonetheless, Tang et al. (2016) identified and quantified phenolic compounds in methanolic (MeOH) extracts of Australian native mint *Mentha australis* using HPLC with photodiode array detector, liquid chromatography high-resolution mass spectrometry, tandem mass spectrometry, and nuclear magnetic resonance spectroscopy. The major compounds identified were rosmarinic acid (160.4 ± 0.85 μg mg^{-1} purified extract), neoponcirin (145.0 ± 0.42 μg GAE mg^{-1}), narirutin (30.3 ± 0.02 μg GAE mg^{-1}), chlorogenic acid (15.4 ± 0.05 μg mg^{-1}) and biochanin A (9.6 ± 0.06 μg GAE mg^{-1}, while caffeic acid, apigenin, hesperetin, and naringenin were minor compounds (Tang et al., 2016). Tang et al. (2017) also performed similar studies on the Australian native herb *Prostanthera rotundifolia* and found the major compounds to be verbascoside (48.8%), 4-methoxy cinnamic acid (36.4%), p-coumaric acid glucose ester (9.2%) and 1-*O*-β-D-glucopyranosyl sinapate (5.6%), while compounds present in trace amounts were caffeic acid, p-coumaric acid, hesperidin and naringenin (Tang et al., 2017). These compounds are shown in Fig. 3.

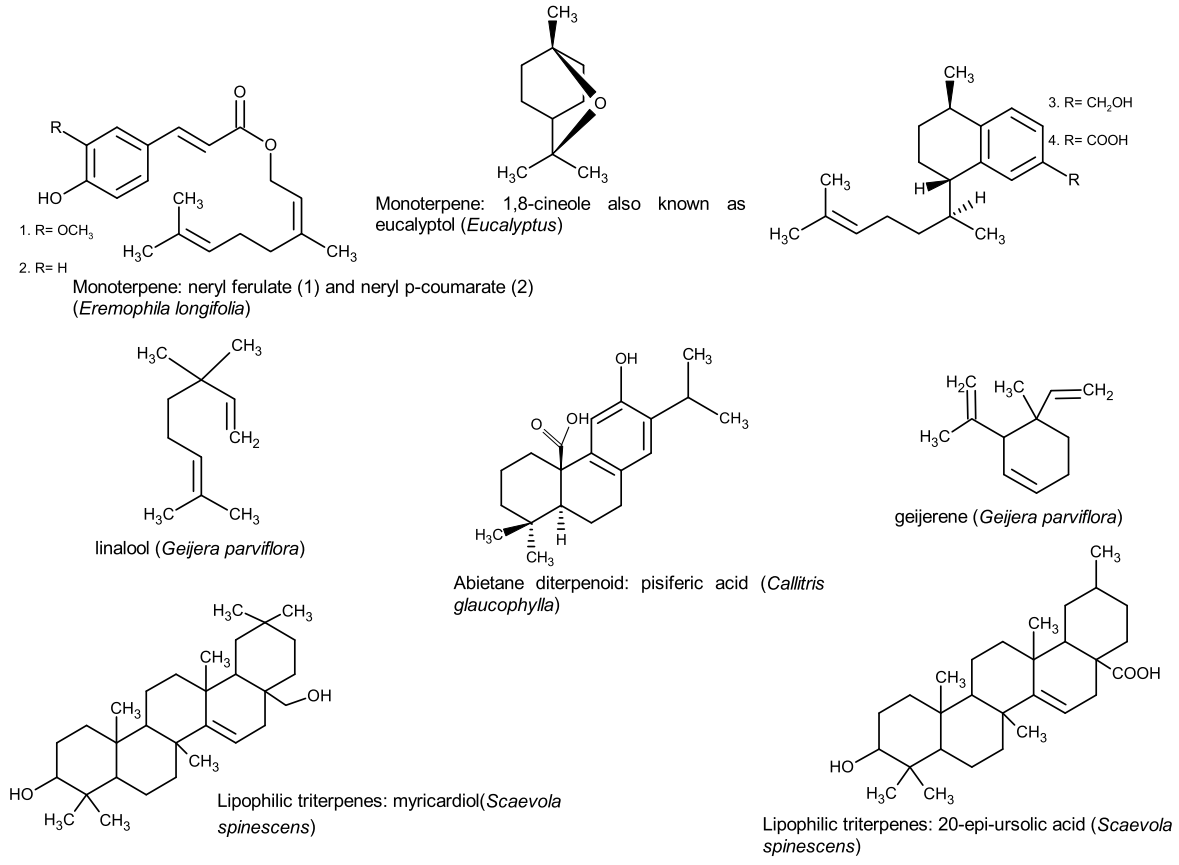


Fig. 2. Some terpenoids isolated from Australian plants.

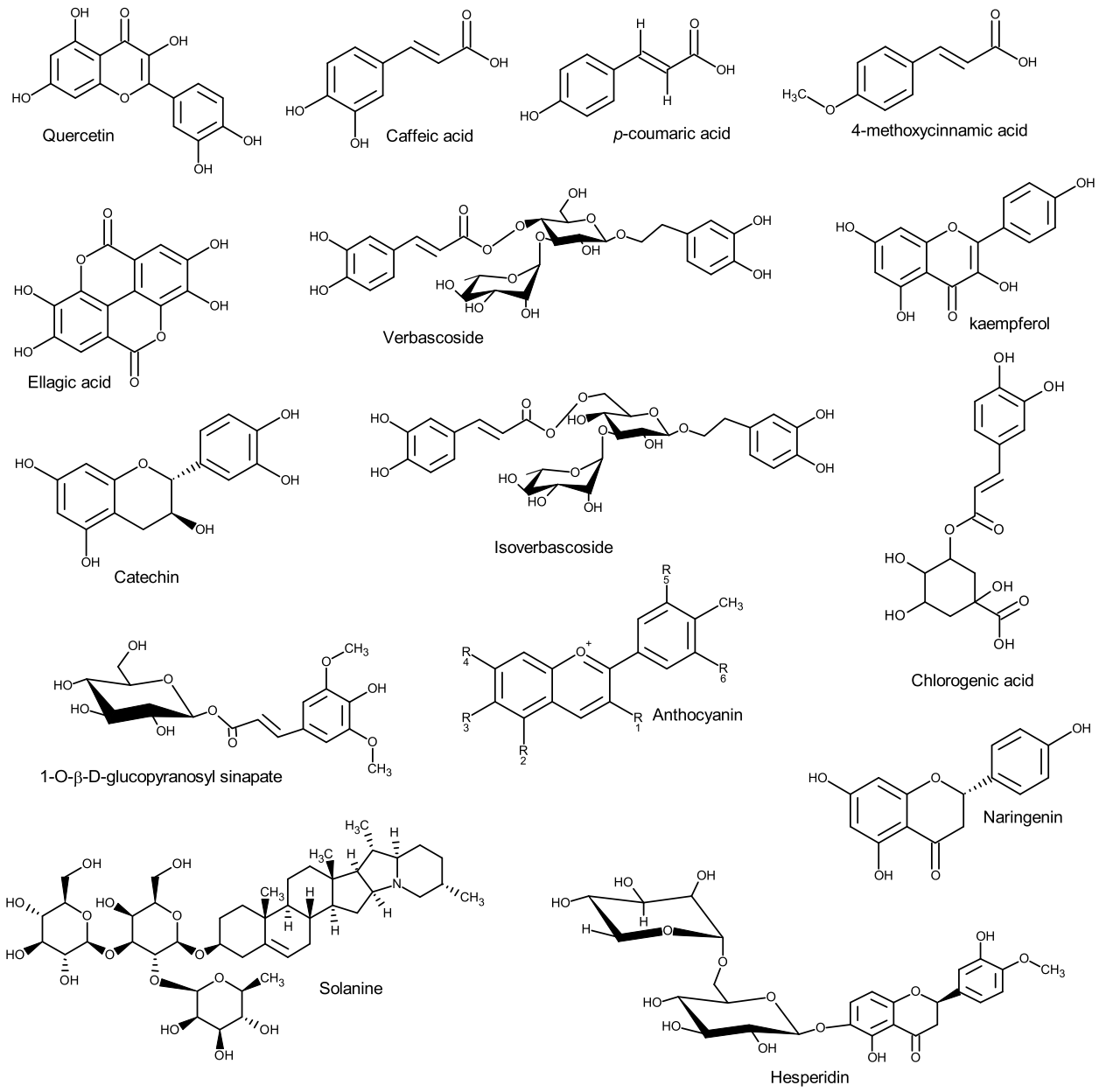


Fig. 3. Common plant phenolic compounds adopted from (Tang et al., 2017).

3.3. Therapeutic potential of native Australian plants

3.3.1. Anticarcinogenic effect

The treatment and prevention of several types of cancers have been linked to high level of antioxidant phytochemicals. Sakulnarmrat et al. (2013) reported the cytoprotective and pro-apoptotic activities of the polyphenolic-rich extracts of Australian herbs, *Tasmannia lanceolata* (Poir.) A.C. Sm., *Syzygium anisatum* (Vickery) Craven & Biffin and *Backhousia citriodora* F.Muell. As such, *T. lanceolata* extracts demonstrated the highest cellular antioxidant activity which was assessed based on the effective reduction of free radical 2,7-dichlorofluorescein (DCF) introduced into HepG2 cultured cells. The effective cellular antioxidant activity depends on successful uptake, distribution and metabolism of phenolic compounds occurring in the extract. *Tasmannia lanceolata* extracts contained the highest total phenolic content (TPC), comprising of monomeric compounds such chlorogenic acid, p-coumaric acid and quercetin/derivatives, which are readily absorbed by cells, therefore explaining its superior cellular antioxidant activity. On the other hand, *S. anisatum* extract exhibited the greatest cytotoxic effects against all tested cancer cell lines with the lowest IC_{50} values (HT-29 (colorectal adenocarcinoma) $IC_{50} = 760 \pm 30$ μg/mL), AGS (gastric adenocarcinoma) $IC_{50} = 590 \pm 50$ μg/mL, BL13 (bladder cancer) $IC_{50} = 560 \pm 50$ μg/mL and HepG2 (hepatocellular carcinoma) $IC_{50} = 380 \pm 20$ μg/mL) (Table 2). *S. anisatum* extracts had the highest total antioxidant capacity (TAC) compared to *T. lanceolata* and *B. citriodora* (Table 2), explaining its greater cytotoxic activity. The study used cancer cell lines associated with the digestive system as these cells are directly exposed to phytochemicals from food components after the digestive process (Sakulnarmrat et al., 2013).

Terminalia ferdinandiana Exell was another plant of interest, with substantial amounts of TPC and TAC as compared to other plants mentioned in Table 2. Its cytotoxic effects against promyelocytic leukemia HL-60 cells due to induced apoptosis via DNA fragmentation and caspase activation, and direct DNA damage in colon adenocarcinoma cells (HT-29) have also been previously demonstrated (Tan et al., 2011). In addition to its polyphenolic compounds such as quercetin, hesperetin,

Table 2
Phytochemical content, anticancer and antimicrobial activity of selected native Australian plants.

Species	Common names	Extraction Method/Solvent	Compounds identified	TPC (mg GAE/g DW)	TAC (FRAP) (mg TE/g)	Anticarcinogenic effect IC_{50} (μg/ml)	Cytotoxic effect (Toxicity towards normal cells)	Antimicrobial (fungal/bacteria) effect	References
Acacia aulacocarpa Benth.	Wattle seeds	80% aqueous MeOH/1.0% HCl (v/v).	Trace amounts of Chlorogenic acid, Quercetin hexoside, Rutin hexoside, Kaempferol/ luteolin hexoside	0.76 ± 0.12	0.99 ± 0.07 (FRAP - mg Fe^{+2}/g)	Not determine d	ND	Activity against *A. hydrophilia P. fluorescens* and *B. cereus*	(Cock, 2012a; Konczak et al., 2010)
Angophora hispida (Sm.) Blaxell	Eucalyptus	100 mL of water and heated at 85 °C for 15 min.	ND	107.85 ± 1.46	98.81 ± 0.15	87.28 (MIA PaCa-2)	SI: 0.44	Not determined	Bhuyan et al. (2017)
Angophora floribunda (Sm.) Sweet				47.81 ± 0.58	70.51 ± 1.52	75.58 (MIA PaCa-2)	SI: 0.90	Not determined	Bhuyan et al. (2017)
Corymbia citriodora (Hook.) K.D. Hill & L.A.S. Johnson				57.02 ± 0.92	87.85 ± 2.68		CPE: 83.73 μg/mL	Not determined	Bhuyan et al. (2017)
Corymbia maculata (Hook.) K.D. Hill & L.A.S. Johnson				47.60 ± 1.43	80.37 ± 2.64	~462.90 (MIA PaCa-2)	0.14		Bhuyan et al. (2017)
Backhousia citriodora F. Muell.	Lemon myrtle	MeOH	**Flavonoids:** Flavonol glycosides (Hesperidin rhamnoside, Hesperidin pentoside, and Hesperitin hexoside) and Myricetin	660.5 ± 58.8	280.6 ± 12.1 (mg Fe^{+2}/g)	Cytotoxic effect of acidified MeOH against HT-29 (IC_{50}: 1350 ± 140), AGS (IC_{50}:1250 ± 530), BL13; IC_{50}:1120 ± 350) and HepG2 (IC_{50}: 1360 ± 80) cancer cells	ND	Inhibitory activity against *A. hydrophilia, P. fluorescens, B. cereus* and *B. subtilis*	(Cock, 2012a; Konczak et al., 2010; Sakulnarmrat et al., 2013)
Davidsonia pruriens F. Muell.	Davidson's plum	MeOH, aqueous and EtOAc	Anthocyanin compounds (cyanidin 3-sambubioside, delphinidin 3-sambubioside, peonidin 3-sambubioside and petunidin 3-sambubioside)	48.60–949	37.41–516.97 (mg Fe^{+2}/g)	Fruit: HeLa- 276 (MeOH) 316 (aqueous) 305 (EtOAc) CaCo2-169 (MeOH) 354 (aqueous) 372 (EtOAc) Leaf: HeLa- 376 (MeOH) CaCo2-212 (MeOH) 295 (aqueous)	Fruit: SI: 23.34 (MeOH) SI: 9.12 (aqueous) Leaf: no toxicity at any dose tested.	Not determined	(Jamieson et al., 2014; Richmond et al., 2019)
Eremophila alternifolia R. Br.		MeOH and EtOAc	8, 19-dihydroxyserrulat-14-ene, 8-hydroxyserrulat-14-en-19-oic acid, Pinobanksin, Pinobanksin-3-acetate, Pinobanksin-3-cinnamate.	ND	ND	Not determined	ND	Antifungal activity against *Cryptococcus* spp. (Zone of inhibition: 7–12.5 mm).	Hossain et al. (2019)
Eremophila longifolia (R. Br.) F.Muell.		EtOH and MeOH	flavonoids, lignins and phenylpropanoids, and enriched with sesqui- and di-terpenes	ND	ND	Not determined	ND	E: inhibits *Streptococcus mutans* and *Streptococcus sobrinus.*	Hayhoe & Palombo (2011)
Eucalyptus spp.		100 mL Analytical MeOH (≥99.9%) with 15 h of mechanical shaking.	ND	ND	ND	Not determined	ND	Leaf extracts show activity against *B. cereus, B. subtilis, L. monocytogenes, M. luteus, S. aureus, E. coli, K. pneumoniae, P. aeruginosa, S. Typhimurium, L. monocytogenes, M. luteus, S. aureus*	Wigmore et al. (2016) Cock (2012a)

(*continued on next page*)

Table 2 (*continued*)

Species	Common names	Extraction Method/Solvent	Compounds identified	TPC (mg GAE/g DW)	TAC (FRAP) (mg TE/g)	Anticarcinogenic effect IC_{50} (μg/ml)	Cytotoxic effect (Toxicity towards normal cells)	Antimicrobial (fungal/bacteria) effect	References
								and P. aeruginosa (MIC_{50}:1–0.5 μg/mL)	
Melaleuca alternifolia (Maiden & Betche) Cheel	Tea tree	MeOH and aqueous	MeOH extracts: Flavonoids (+++), saponins (++) and tannin (+++).	MeOH and aqueous +++	ND	Not determined	Leaf MeOH extract: LC_{50}: 1287 μg/mL	MeOH and aqueous extracts: no inhibitory effect against *Bacillus anthracis*. MeOH leaf extracts: inhibition against *L. monocytogenes* (MIC: 500 μg/mL*), M. luteus* ((MIC: 60 μg/mL*), S. aureus* (MIC: 500 μg/mL) and *P. aeruginosa* (250 μg/mL).	Wright et al. (2015) (Wigmore et al., 2016)
Petalostigma pubescens Domin *P. triloculare* Müll.Arg.		MeOH, aqueous, EtOAc $CHCl_3$ and hx leaf and fruit extracts	M, W and E extracts: Saponins, flavonoids, tannins and free anthraquinones acetic acid; 2,2-dimethoxybutane; 4-methyl-1,3-dioxane. decane; undecane; 2-furanmethanol; 1,2-benzenediol; 1,2,3-benzenetriol; and benzoic acid	**Leaf** MeOH +++ Aqueous + EtOAc – $CHCl_3$ – Hx + **Fruit** MeOH ++ Aqueous + EtOAc + $CHCl_3$ – Hx –	ND	Not determined	Non- toxicity or low toxicity. >1000 μg/mL at 24 or 48 h. Leaf and fruit EtOAc extract 600–1650 μg/mL at 24 or 48 h, showing low toxicity.	MeOH, aqueous, and EtOAc extracts displayed potent antibacterial activity against Gram-positive and Gram-negative bacteria in the disc diffusion assay, with MIC values generally <10 μg/ml. E extracts showed maximum potency, achieving MIC values < 1 μg/mL.	Kalt & Cock (2014)
Prostanthera rotundifolia R. Br.	Mint	MeOH (80%, v/v).	Main compounds: verbascoside, 4-methoxycinnamic acid, glucose ester of p-coumaric acid and 1-O-β-D-glucopyranosyl sinapate. Minor compounds: caffeic acid, p-coumaric acid, hesperidin, and naringenin.	260.4 ± 12.3	151.68 ± 7.00	Not determined	ND	Crude leaf extracts against bacteria such as *B. subtilis*, *L. monocytogenes*, *M. luteus* and *S. aureus* (MIC: 500 μg/mL)	(Tang et al., 2017; Wigmore et al., 2016)
Santalum acuminatum (R. Br.) A. DC.	Quandong	Possibly MeOH	**Flavanoids:** Anthocyanins (Cyanidin-3-glucoside and pelargonidin-3-glucoside), quercetin, rutinoside and kaempferol	32–543	25.35–180.08 (mg Fe^{+2}/g)	Anti-proliferative & pro-apoptotic activity against colorectal and gastric adenocarcinoma cells.	ND	Not determined	(Richmond et al., 2019; Vuong et al., 2014)
Scaevola spinescens R. Br.	Currant bush, maroon bush, or prickly fanflower	EtOAc and aqueous	20-*epi*-ursolic acid	ND	ND	ND	ND	Showed activity against *Streptococcus pyogenes* and *Staphylococcus aureus* (MIC: 1.87–7.5 μg/mL)	Mejin (2009)
Solanum centrale J.M. Black	Bush tomato	MeOH	**Phenolic acids**: Hydroxybenzoic acid, Ferulic acid, Chlorogenic acid, Caffeic acid, p-Coumaric acid. **Flavanoids:** Quercetin hexoside, rutinoside, Kaempferol and luteolin hexoside.	12.40 ± 0.9	11.52 ± 0.50 (FRAP - mg Fe^{+2}/g)	Not determined	ND	Not determined	Konczak et al. (2010)

(*continued on next page*)

Table 2 (*continued*)

Species	Common names	Extraction Method/Solvent	Compounds identified	TPC (mg GAE/g DW)	TAC (FRAP) (mg TE/g)	Anticarcinogenic effect IC_{50} (μg/ml)	Cytotoxic effect (Toxicity towards normal cells)	Antimicrobial (fungal/bacteria) effect	References
Syzygium anisatum (Vickery) Craven & Biffin	Anise myrtle	TPC and TAC: MeOH Anticancer and Antibacterial activity: MeOH (≥98%), EtOH (≥98%), aqueous and Hx (≥98.5%)	**Flavanoids:** Catechin, quercetin, hesperetin and myricetin. **Tannins:** ellagic acid and ellagitannins	728.9 ± 25.8	449.8 ± 17.0 (FRAP - mg Fe^{+2}/g)	Cytotoxic effect against HepG2 (IC_{50}: 380 ± 20), BL13 (560 ± 50), AGS (590 ± 50) and HT-29 (760 ± 30) cancer cell lines.	ND	Hx, MeOH and EtOH leaf extracts showed broad-spectrum activity against bacteria *Escherichia coli* and *Staphylococcus aureus*) and yeasts (*Candida albicans, Candida krusei, Dekkera anomala, Rhodotorula mucilaginosa, Saccharomyces cerevisiae and Schizosaccharomyces pombeStaphylococcus aureus* (inhibition zone 10–15 mm)	(Alderees et al., 2018; Konczak et al., 2010; Sakulnarmrat et al., 2013)
Syzygium australe (J.C.Wendl. ex Link) B.Hyland	Brush cherry	TPC and TAC: Acidified MeOH Anticancer/ antimicrobial bioactivity: MeOH, aqueous and EtOAc	**Anthocyanins:** pelargonidin 3-glucoside, peonidin 3,5-diglucoside, petunidin 3,5-Diglucoside and malvidin 3,5-diglucoside.	2.14 ± 0.10	4.58 ± 0.11	Fruit: HeLa- 134 (MeOH) 172 (aqueous) 58 (EtOAc) CaCo2- 279 (MeOH) 27 (aqueous) Leaf: HeLa- 187 (MeOH) 283 (aqueous) CaCo2-653 (MeOH) 325 (aqueous)	Anticancer bioactivity: Fruit SI: 14.02–45.97 Leaf SI: 0.86–1.57	MeOH fruit and leaf extracts showed activity against *Shewanella* spp. in liquid dilution assay (MIC: fruit 86–600 μg/mL and leaf 563–1100 μg/mL). Aqueous extracts showed higher MIC values in liquid dilution assays (MIC: fruit 375-150 μg/mL and leaf 281–2300 μg/mL). Fruit extracts MeOH and aqueous LC_{50} values > 1000 μg/mL Leaf extracts MeOH and aqueous LC_{50}: 294 and 244 μg/mL respectively	Netzel et al. (2007) Jamieson et al. (2014) Murhekar et al. (2017)
Syzygium luehmannii (F. Muell.) L.A.S. Johnson	Riberry	TPC and TAC: Acidified methanol Anticancer/ antimicrobial bioactivity: MeOH, aqueous and EtOAc	Possibly flavonoids, tannins, anthocyanins, and gallic acid.	2.23 ± 0.14	4.78 ± 0.42	Fruit: HeLa- 884 (MeOH) 86 (aqueous) CaCo2-791 (MeOH) 124 (aqueous) Leaf: HeLa- 165 (MeOH) 128 (aqueous) CaCo2-387 (MeOH) 43 (aqueous)	Fruit: SI: 0.47–3.85 Leaf: SI: 2.73–6.35	Leaf and fruit MeOH extract activity against *Shewanella* spp. (MIC: 500–4800 μg/mL) Leaf and fruit aqueous extracts activity against *Shewanella* spp. (MIC: 750–2800 μg/mL) LC_{50}:414–813 μg/mL	Netzel et al. (2007) (Jamieson et al., 2014) (Murhekar et al., 2017)
Tasmannia lanceolata (Poir.) A.C. Sm.	Tasmanian pepper	TPC and TAC: MeOH (≥98%), EtOH (≥98%), aqueous and hex (≥98.5%)	**Phenolic acids:** Coumaric acid, chlorogenic acid. **Flavonoids:** quercetin, quercetin 3-rutinoside, and anthocyanin (cyanidin 3-rutinoside)	911.9 ± 57.8	248.2 ± 6.8 (mg Fe^{2+}/g)	Acidified MeOH extracts cytotoxic effects against HT-29 (colorectal adenocarcinoma; IC_{50}: 1309 ± 30), AGS (gastric adenocarcinoma, IC_{50}:1880 ± 250), BL13 (bladder cancer IC_{50}: 560 ± 100) and HepG2 (hepatocellular carcinoma) (IC_{50}:1130 ± 190) cancer cells lines.	Level of necrotic cells did not increase indicating that the extracts at the applied concentrations were not cytotoxic	All leaf extracts except aqueous extracts showed anti-yeast activity against *Zygosaccharomyces bailii* and *Saccharomyces cerevisiae*, antifungal activity against *Sclerotinia libertiana*, *Mucor mucedo, Rhizopus chinensis, Aspergillus niger, Penicillium crustosum* and antibacterial activity against *Salmonella choleraesuis* (Inhibition zone- 8–44 mm)	Alderees et al. (2018) Sakulnarmrat et al. (2013).
Terminalia ferdinandiana Exell	Kakadu plum	TPC and TAC: Possibly MeOH	**Phenolics:** Quercetin, hesperetin, Kaempferol and luteolin glycosides	158.57	34.84 ± 0.30	Activity against human promyelocytic leukemia; Anti-proliferative & pro-apoptotic activity against colon cancer cells	ND	Fruit MeOH and leaf MeOH, aqueous and ethyl acetate extracts showed inhibitory effects against Methicillin-resistant *Staphylococcus aureus* with MIC values as low as 223 μg/mL.	(Cheesman et al., 2019; Tan et al., 2011)

EtOH: Ethanol, MeOH: Methanol, $CHCl_3$: Chloroform, Hx: hexane, EtOAc Ethyl acetate, TPC: Total Phenolic, TAC: Total Antioxidant Capacity.
+++ indicates a large response, ++ indicates a moderate response, + indicates a minor response, − indicates no response.
LC_{50}: 50% Lethal concentration, LC_{50} > 1000 at 24 or 48 h, suggesting no or very low toxicity toward *Artemia nauplii* lethality bioassay. CPE: Cytopathic Effect, IC_{50}: 50% Inhibitory concentration, SI: selectivity indices (SI=CPE/IC_{50}), SI > 20 indicates low cytotoxicity. MIC: Minimum inhibitory concentration. ND: No Data.
Acidified MeOH (80% MeOH, 19% H_2O and 1% acetic acid, v/v/v).

kaempferol and luteolin glycosides (Richmond et al., 2019; Vuong et al., 2014), the plant's anticarcinogenic properties are also linked to high levels of ascorbic acid (Tan et al., 2011). Ascorbic acid acts as a free radical scavenger and reduces oxidative stress due to its redox properties; thus, potentially preventing carcinogenesis. *Eucalyptus* species (*Angophora floribunda* and *Angophora hispida*) crude aqueous extracts showed anticancer activity (IC_{50}: 75.58 and 87.28 μg/mL, respectively) against primary pancreatic cancer cell line (MIA PaCa-2), comparable to gemcitabine (0.0118 μg/mL), a synthetic chemotherapeutic drug (Bhuyan et al., 2017). The authors claimed that these values were promising and are likely to display lower IC_{50} values similar to gemcitabine, once purified.

Syzygium australe (J.C.Wendl. ex Link) B.Hyland fruit extracts (MeOH), water, and ethyl acetate) in MTS ((3-(4,5-dimethylthiazol-2-yl)-5-(3- carboxymethoxyphenyll-2-(4-sulfophenyl)-2 H-tetrazolium, inner salt)/phenazine methosulfate) cell viability assay were seen to have promising potency against cervical cancer (HeLa) and colon carcinoma cancer (CaCo2) cell lines, with selectivity index (SI) values ranging from 14.02 to 45.97 (Jamieson et al., 2014). Leaf extracts of *Syzygium australe* (J.C.Wendl. ex Link) B.Hyland also showed potency against these cancer cell lines, however, very low SI values (0.86–1.57) were obtained. Similarly *Davidsonia pruriens* F.Muell. Fruit and leaf extracts evaluated against HeLa and CaCo2 cells showed MeOH fruit extract to be most effective against both cell lines as compared to the water extracts (Table 2). The MeOH fruit extracts also showed a high SI (23.34) as opposed SI of the fruit water extracts (9.12), whereas leaf extracts showed no toxic effects. Generally, SI values > 20 are considered to have low cell toxicity (Astani et al., 2010), making them ideal candidates for pharmaceutical drug development. Whilst *Prostanthera rotundifolia* R.Br. has also shown high TPC and TAC values (260.4 ± 12.3 and 151.68 ± 7.00 respectively) (Tang et al., 2017), there are no data on their anticancer activities.

More importantly, studies have shown the antiproliferative activity of compounds isolated from Australian *Pittosporum angustifolium* (Bäcker et al., 2013; Bäcker et al., 2014). Triterpene saponins isolated from the seeds of *Pittosporum angustifolium* showed antiproliferative effects (IC_{50}: 1.74–34.1 μM) against cancer urinary bladder carcinoma (cell line 5637), breast cancer (MCF7) and glioblastoma, grade IV (LN18) (Bäcker et al., 2014). Backer et al. (2013) also evaluated triterpene saponins isolated from the leaves of *P. angustifolium* against cell line 5637 and found that only compounds with an angeloyl-residue at C-22 of the aglycone displayed antiproliferative activities (IC_{50}: 2.1–17.9 μM).

This review found that the extraction solvent and plant parts evaluated, although belonging to the same plant, generally presented varying results. Methanol was the most commonly used extraction solvent, with extracted compounds displaying greatest potency against the cancer cell lines in many cases (Ahmed and Johnson, 2000; Jamieson et al., 2014; Konczak et al., 2010). Moreover, phytochemical build up and retention may differ in different parts of the plant, hence testing potency of various plant parts may be critical for future studies.

3.3.2. Antimicrobial activity

There is increasing interest in the antibacterial potential of Australian plants due to the growing urgency to find antibacterial agents against the evolving super-resistant bacterial strains (Bai, 2017). Globally, the traditional medicinal use of *Syzygium* species has been well reported due to its anesthetic, antibacterial and antifungal properties (Arora and Kaur, 2007; Duraipandiyan et al., 2006; Guleria et al., 2013). Some Australian *Syzygium* species are being used by native Australians as therapeutic agents, however, information about their phytochemical profiling and medicinal properties remain scarce. Netzel et al. (2007) mentioned that *Syzygium luehmannii* (F.Muell.) L.A.S. Johnson and *Syzygium. australe* (J.C.Wendl. ex Link B.Hyland) fruits grown in the NSW regions have therapeutic potential due to their extremely high antioxidant content. *S. australe* MeOH fruit extracts in liquid dilution assays showed potency against various *Shewanella* spp. with lower minimum inhibitory concentrations (MIC) ranging from 86 to 600 μg/mL, compared to MeOH leaf extracts (MIC: 563–1100 μg/mL). Whereas the aqueous extracts of both leaf and fruits (MIC range: 281–2300 μg/mL) were higher in comparison to the MeOH extracts. On the contrary, *S. luehmannii* fruit and leaf aqueous extracts showed greater inhibition (MIC: 750–2800 μg/mL), compared to MeOH extracts (MIC: 500–4800 μg/mL). The lethal concentration (LC_{50}) values of *S. australe* fruit were greater than 1000 μg/mL towards *Artemia franciscana nauplii* after 24 h exposure, suggesting no toxicity. Whereas its leaf extracts (LC_{50}:244–294 μg/mL) and *S. luehmannii* fruit and leaf extracts (LC_{50}: 414–813 μg/mL) showed toxicity. LC_{50} values > 1000 μg/mL at 24 or 48 h suggest no or very low toxicity toward *Artemia nauplii* in a lethality bioassay (Kalt and Cock, 2014). This study evidently showed that *S. australe* fruit extracts were more effective against the *Shewanella* spp. with low toxicity as opposed to its leaf extracts and *S. luehmannii* leaf and fruit extracts (Murhekar et al., 2017). *S. australe* MeOH leaves extracts inhibiting the growth of numerous bacterial species, including *Aeromonas hydrophilia*, *Alcaligenes faecalis, Citrobacter freundii*, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas fluorescens, Serratia marcescens*, *Bacillus cereus and Staphylococcus aureus* with MIC ranging between 200 and 3000 μg/mL have also been reported (Sautron and Cock, 2014).

Terminalia ferdinandiana was of interest due to its reported inhibitory activity against Methicillin-resistant *Staphylococcus aureus*, a common bacterium causing infections in various parts of the body. The MIC quantified by liquid dilution method showed values as low as 223 μg/mL, with nontoxic effects towards *Artemia nauplii* indicating its potential medicinal use (Cheesman et al., 2019). Furthermore, other native Australian plants that also exhibited antibacterial activities include *Acacia aulacocarpa* Benth., *Backhousia Citriodora* F. Muell, *Buckinghamia celsissima* F. Muell, *Allocasuarina littoralis* (Salisb.) L.A.S. Johnson, and members of the *Callistemon*, *Eucalyptus* and *Leptospermum* genera (Table 2). These plants are particularly worthy of further study due to their high potency against a wide range of bacteria. *Backhousia citriodora* (leaves) and *Callistemon citrinus* (both leaves and flowers) both belonging to the family Myrtaceae were the most versatile species, due to their ability to inhibit the growth of all four bacteria (*Aeromonas hydrophilia, Bacillus cereus, Bacillus subtilis,* and *Pseudomonas fluorescens*) that were tested (Cock, 2012a). The antimicrobial activity of a different species of *Callistemon* (*C. rigidus*) have also been previously reported, where the flower extracts of the plants were more potent inhibitors of bacterial growth than the leaf extracts (Cock, 2012a). The MeOH, water, and ethyl acetate extracts from species of the *Petalostigma* genus showed the lowest MIC (<10 μg/mL) values in this review against both gram-positive and gram-negative bacteria in the and were nontoxic against *Artemia nauplii* ($LC_{50} > 1000$ μg/mL). Comparatively, *Prostanthera ovalifolia* R.Br. crude leaf extracts showed inhibitory effects against bacteria such as *B. subtilis*, *L. monocytogenes*, *M. luteus* and *S. aureus* with higher MIC values (around 500 μg/mL) (Wigmore et al., 2016).

Parasitic infections in livestock hinders the productivity and sustainability of a farming systems. The anthelmintic activity of *Acacia baileyana*, *Acacia melanoxylon*, *Acacia podalyriifolia*, *Alectryon oleifolius*, *Duboisia hopwoodii*, *Eucalyptus gomphocephala* and *Santalum spicatum* water extracts against *in vitro* cyathostomin (*Nematoda, Strongylida)* larvae (IC_{50}:30.9–196 μg/mL) have also been reported (Payne et al., 2013). The study found tannins to likely be the bioactive compound responsible for the anthelmintic effects in most of the plants except for *A. melanoxylon* and *D. hopwoodii* since incubation of extracts with polyvinylpolypyrrolidone (PVPP) before the assays showed no inhibition of larval development. Similarly, Kotze et al. (2009) also found tannins to be the bioactive compound in 40% of native shrubs which showed anthelmintic effects against *Haemonchus contortus* larvae. The shrubs investigated mainly belonged to the genus *Eremophila, Myoporum, Rhagodia, Atriplex, Maireana* and *Acacia*.

A few studies have reported on the antimicrobial activity of compounds isolated from genus *Eremophila.* Serrulatane compounds 8,19-

dihydroxyserrulat-14-ene (1) and 8-hydroxyserrulat-14-en-19-oic acid (2) isolated from *Eremophila neglecta* J.M.Black showed antibacterial activity against all Gram-positive test strains and antimycobacterial activity against isolates of *Mycobacterium fortuitum* and *Mycobacterium chelonae* by broth microdilution assays. Compound 1 was found to be significantly more active as compared to compound 2. However, the cytotoxic evaluation against Vero cells (CCL-81, African Green Monkey) revealed that compound 1 was also most toxic (Anakok et al., 2012). Similarly, *Eremophila duttonii* F. Muell. isolates belonging to the serrulatane class namely Serrulat-14-en-7,8,20-triol (3), Serrulat-14-en-3,7,8, 20-tetraol (4) and 4-Hydroxyngaione (5) showed MIC in the range of 23–1500 μg/mL against Gram-positive bacteria (*S. aureus* ATCC 29213, *S. epidermidis* ATCC 12228 and *S. pneumoniae* ARL 10589). Compound 3 exhibited the strongest activity (MIC: 23–94 μg/mL) against the tested strains with *S. epidermidis* and *S. pneumoniae* being the most susceptible strains (Smith et al., 2007). Sadgrove et al. (2014) have reported on significant antimicrobial activities (MIC: < 100 μg/mL) of isolated compound (−)-genifuranal (5,6-dihydro-4H-cyclopenta [c] furan-4-ylacetaldehyde) from *Eremophila longifolia*. This compound was only observed in the plant leaves after being subjected to a heating or smoking process and is believed to be derived from hydrolysis and rearrangement of geniposidic acid or a related glycoside (Sadgrove et al., 2014a,b). Antibacterial nerol cinnamates: neryl ferulate (1) and neryl *p*-coumarate have also been previously identified using bioassay guided fractionation (Galappathie et al., 2017).

Moderate antimicrobial activities of solvent extracts of essential oils obtained from pine needles of *Callitris endlicheri* (Parl.) F.M.Bailey and *Callitris glaucophylla* J.Thomps. & L.A.S.Johnson were reported against *P. aeruginosa*, *S. aureus*, *B. subtilis* and the yeast *Candida albicans*. Abietane diterpenes such as pisiferal, pisiferol and ferruginol occurred in high concentration in the fresh needle solvent and smoked extracts and were responsible for their bioactivity (Sadgrove and Jones, 2014). In a later study pisiferic acid was identified as the major compound responsible for antimicrobial effects (Sadgrove et al., 2020). Hydrodistilled essential oils from *E. longifolia* dominated by hydrocarbon monterpenes and monoterpenols had moderate antimicrobial activity for both Gram-positive and Gram-negative bacteria. Whereas oils with higher ketones demonstrated less activity. On the contrary, very high antifungal activity against *T. interdigitalis, T. rubrum* and *T. mentagrophytes* were noted (Sadgrove et al., 2011). Moreover, essential oil from *Geijera parviflora Lindl* chemotype containing linalool, geijerene/pregeijerene, 1,8-cineole and bicyclogermacrene, also demonstrated promising antimicrobial and free radical scavenging activity (Sadgrove et al. (2014)). Similarly, antimicrobial activity was observed for myodesert- 1- ene, isolated from *Eremophila dalyana*, which is an aromatic Australian desert species used in the treatment of cold, chest infections and *Sarcoptes scabiei* infestation (Sadgrove et al., 2016). Potential antibacterial activity of an isolated compound, 20-*epi*-ursolic acid from *Scaevola spinescens* R. Br. against *Streptococcus pyogenes and Staphylococcus aureus* at low MIC values ranging from 1.87 to 7.5 μg/mL have also been previously reported (Mejin, 2009). Meroterpenes marcrocarpals B-G consisting of a phloroglucinol dicarbaldehyde part and diterpene part, isolated from leaves of *Eucalyptus macrocarpa* were found to be active compounds against *Bacillus subtilis* and *Staphylococus aureus* (Yamakoshi et al., 1992).

Whilst the extracts investigated appear to be promising antimicrobial agents, caution is needed before the plant extracts can be applied for medicinal purposes or as food additives to inhibit spoilage (Cock, 2012a). For instance, the high toxicity levels (LC_{50}: 455 μg/mL) of *Eucalyptus* spp. extracts make it unsafe for ingestion (Wright et al., 2015). Alternatively, the extracts may be useful for external application as ointments, inhibitory agents, disinfecting contaminated sites, and sterilizing surfaces in contact with microbes (Wright et al., 2015). Additionally, the effects of antioxidants are dose-dependent – whilst in low doses they behave as antioxidants, in high doses they induce oxidative stress thereby becoming highly toxic (Jamieson et al., 2014). Furthermore, the purification and identification of bioactive components in the plant extracts in future studies is paramount, as this will help to further understand its biological and chemical mechanisms of apoptosis, antiproliferative, cytotoxicity or microbial inhibitory effects. As most studies have been conducted *in vitro*, further work on the isolation and identification of compounds may prove useful for *in vivo* and clinical testing. More rigorous investigations into the bioactivity of Australian native plants are warranted, particularly those with high phenolic contents.

3.3.3. Antiviral activity

Viral infections are one of the main causes of morbidity and mortality globally, with one example being the current spread of the SARS-CoV-2 causing the COVID-19 disease. Viruses are small infectious agents with genomes of either RNA or DNA surrounded by a shell of protein. Unlike free-living bacteria, viruses are obligate intracellular parasites of the eukaryotic cells, utilizing several host cell's metabolic processes to propagate new viruses (Liu and Du, 2012; Perez, 2003). The emergence of new viruses and viral strains resistant to commonly used antiviral agents calls for the need to explore the possibility of antiviral effective compounds in medicinal plants (Mani et al., 2020).

The secondary plant metabolites such as essential oils, odors and volatile products have a wide application in folk medicines throughout the world including the Aboriginal communities. The main constituents of essential oils such as monoterpenes and sesquiterpenes and phenylpropanoids including carbohydrates, alcohols, ethers, aldehydes, and ketones are responsible for the biological properties of aromatic and medicinal plants (Astani et al., 2010). An estimate of 44% of the approved antiviral drugs between 1981 and 2006 were derived from natural products, semi-synthetic natural product analogs, or synthetic compounds based on natural product pharmacophores (Liu and Du, 2012). Several studies have been done on the antiviral activity of ethnomedicinal plants globally, however, the great scope for antiviral potential in native Australian plants have still not been explored.

In one recent study, the antiviral activity of the *Scaevola spinescens* R. Br. was investigated using the MS2 bacteriophage plaque reduction model system (Cock and Matthews, 2016). It reported potent antiviral activity in all *S. spinescens* extracts (methanolic, water, ethyl acetate, chloroform, and hexane extracts) which inhibited 47–100% of plaque formation. The methanolic and chloroform extracts exhibited the maximum potency with plaque formation reductions of 95.2 ± 1.8% and 100 ± 0% respectively. All extracts were also found to be non-toxic in the *A. franciscana* bioassay, implying potential control of RNA viruses at therapeutically safe concentrations. This study putatively identified several compounds (ammarin, nodakenetin, scaevoloside, alidyjosioside, ursinic acid, vanillactic acid, eudesmic acid and chlorogenic acid) by metabolomic profiling using non-targeted HPLC separation coupled with high-resolution quadrupole time of flight mass spectrometry (Cock and Matthews, 2016). Furthermore, *Petalostigma pubescens* Domin and *Petalostigma triloculare* Müll.Arg. methanol, water, and ethyl acetate extracts also displayed inhibitory effects in the MS2 plaque reduction assay (Kalt and Cock, 2014). The methanol extract inhibited 26.6–49.0%, water extracts inhibited 85.4–97.2% and all ethyl acetate extractions inhibited 100% of MS2 plaque formation, with all extracts showing low or no toxicity. The fruit extracts were generally found to be more potent inhibitors. Moreover, RP-HPLC showed that the *P. triloculare* Müll.Arg. ethyl acetate fruit extract was the least complex of the bioactive extracts and the subsequent analysis of this extract by GC-MS revealed 9 main compounds present (acetic acid; 2,2-dimethoxybutane; 4-methyl-1,3-dioxane; decane; unadecane; 2-furanmethanol; 1,2-benzenediol; 1,2,3-benzenetriol; and benzoic acid) (Kalt and Cock, 2014).

Although the antiviral activity of Australian native tea tree and eucalyptus species is limited, Astani et al. (2010) reported on the antiviral activity of *Eucalyptus* oil, tea tree (*Melaleuca* spp.) oil, and monoterpenes which commonly occur in *Eucalyptus* and tea tree oil. The *in*

vitro study using herpes simplex virus type 1 (HSV-1) found that at maximum noncytotoxic concentrations plaque formation was significantly reduced by >96% by *Eucalyptus* oil, tea tree oil and thyme oil, whereas monoterpenic constituents were able to suppress viral infection by >80% (Astani et al., 2010). Hence essential oils and plant monoterpenes may be suitable antiviral agents. Although the screening and isolation of compounds in essential oils are important, the mixtures of different compounds in essential oils may likely be preferable to single compounds due to synergistic activity of the constituents. For instance, whilst terpinen-4-ol was the major compound in tea tree oil and showed a lower antiviral activity compared to α-terpinene and γ-terpinene, the oil complex had a higher antiviral activity (Astani et al., 2010).

A study by Semple et al. (1998) was worth noting as 40 different plant species used in traditional medicine by the Australian Aboriginal people were screened for their antiviral activity against poliovirus and Ross River Virus (RRV), both RNA viruses, and Human cytomegalovirus (HCMV), a DNA virus. Ethanol plant extracts were tested *in vivo* using human embryonic lung (HEL) cells for HCMV, baby hamster kidney (BHK-21) cells for RRV, and Buffalo green monkey kidney (BGM) cells for poliovirus. The most active plants were Dianella longifolia var. grandis (roots) and *Pterocaulon sphacelatum* (Labill.) F.Muell. (green aerial parts) which showed 75% inhibition against poliovirus at effective concentrations (EC) of 31–250 and 6–52 μg/mL, respectively, followed by Euphorbia australis Boiss. (whole plant) (50% inhibition of HCMV, EC: 6–24 μg/mL). *Eremophila latrobei* subsp. glabra (stems) and Pittosporum angustifolium Lodd. var. microcarpa (leaves) showed 25% inhibition against RRV (EC: 25–102 and 35–70 μg/mL respectively) and *Scaevola spinescens* R. Br. (leaves) showed 25% inhibition of HCMV (EC: 68–136 μg/mL) (Semple et al., 1998).

Moreover, the inhibitory concentrations (IC_{50}) were imperative in determining the effectiveness of the natural products against the viral strains. The recommended IC_{50} values are below 100 μg/mL for extracts and below 25 μM for pure compounds (Astani et al., 2010). Nonetheless, the SI is considered the most important predictive value for future application of plant isolates. Amoros et al. (1992) recommended a selectivity index of at least 4 as appropriate, however, drugs with a higher selectivity are preferable (Astani et al., 2010). Also, the high antiviral activity of essential oils and isolated monoterpenes was observed when herpes virus was incubated with these drugs before host cell infection, thereby suggesting these compounds directly inactivate the virus and might interfere with the virion envelope structures or mask viral structures, preventing adsorption or entry into host cells (Astani et al., 2010). Hence, establishing the mode of antiviral infection is also recommended in determining when the extract/essential oils/drug is most effective and should be extensively investigated in future studies.

3.3.4. Antidiabetic activity

Diabetes is another major health concern globally which often coincides with conditions such as obesity, hypertension, hyperlipidemia, and cardiovascular diseases and has long term negative effects on various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels (Gulati et al., 2015). In Australia, around 1.7 million people live with diabetes and the rates of diabetes and uncontrolled blood sugar levels are three to five times higher in Australian Aboriginal and Torres Strait Islander peoples as compared to the non-Indigenous Australians (Deo et al., 2016; Diabetes Australia, n.d.). Type I diabetes is an autoimmune disease, which results in irreversible loss of function of the pancreatic beta cells, responsible for producing insulin. The loss of these cells results in insulin deficiency and hyperglycemia. In contrast, type II diabetes is the result of an insulin deficit or insulin resistance and is often referred to as a lifestyle disease due to its high prevalence in obese populations (Ota and Ulrih, 2017). The main pathogenesis in type II diabetes is oxidative stress and other stresses (endoplasmic reticulum stress, lipotoxicity and glucotoxicity) and overnutrition, that induce inflammatory responses (Ota and Ulrih, 2017).

Evidence has shown that prolonged exposure to elevated glucose induces the production of free radicals, particularly ROS through glucose autoxidation and protein glycation (Deo et al., 2016). Consequently, the therapeutic approach is the use of antioxidants to counter or overcome the effects of excess ROS and the use of phytochemicals to lower glucose absorption by inhibiting intestinal carbohydrate-hydrolyzing enzymes α-amylase and α-glucosidase (Ota and Ulrih, 2017), pancreatic lipase and angiotensin-converting enzyme (ACE) (Sakulnarmrat and Konczak, 2012). Antidiabetic drugs stimulate glucose uptake either by synthesis enhancement of insulin-independent (basal) glucose transporter GLUT-1 or by increasing expression or translocation of the insulin-dependent/sensitive glucose transported GLUT-4 (Gulati et al., 2015). Although the majority of the anti-diabetic drugs treat one of the key symptoms which is hyperglycemia (elevated blood glucose concentration), they exacerbate weight gain and obesity which further contributes to the progression of type II diabetes (Gulati et al., 2015). Anti-diabetic agents that stimulate glucose uptake by adipose or muscle cells but, unlike thiazolidinedione or insulin, do not induce obesity or the other side effects are ideal. Other pharmacological approaches via different modes of action include acarbose, miglitol, and voglibose which inhibit α-amylase and α-glucosidase activity, aminoguanidine for antiglycation in alleviating diabetic complications, and ramipril and perindopril which inhibit ACE for the treatment of hypertension (Deo et al., 2016). However, since these strategies are replete with severe side effects, the development of new types of anti-diabetic drugs that are either hypoglycemic or antihyperglycemic and lack side effects are highly desirable.

Alternative treatments which include the use of traditional medicinal plants are now becoming an attractive option. Plants are rich sources of phytochemicals (carotenoids, resveratrol, quercetin, silymarine, sulphoraphane, and indole-3-carbino) that can protect one from chronic diseases such as diabetes, by targeting multiple cell signaling pathways (Gulati et al., 2015). Many contemporary medications used are structurally derived from compounds found in traditional medicinal plants. For instance, the development of the antihyperglycemic drug metformin can be traced to the traditional use of *Galega officinalis* for the treatment of diabetes (Ota and Ulrih, 2017). Similarly, ingestion of leaves of *Nerium indicum*, an Indian plant, reduces postprandial (after eating a meal) blood glucose level in humans and has been used as a folk remedy for type II diabetes (Sakulnarmrat and Konczak, 2012). *Cassia auriculata* (Leguminosae), a Sri Lankan endemic plant, has shown inhibitory effects against α-glucosidase which were comparable to that of therapeutic drug acarbose (Sakulnarmrat and Konczak, 2012). While Australia is one region with a rich flora and fauna, Australian native plants have not been extensively investigated for their use in the treatment of diabetes.

Nevertheless, Gulati et al. (2015) investigated the anti-diabetic mechanism of Australian native plants by glucose uptake in the 3T3-L1 murine pre-adipocytes and assessed the inhibition of lipid accumulation in these well-characterized cell lines. Their findings suggested that *Acacia tetragonophylla* F.Muell. stem extract exerted its anti-diabetic properties by stimulating glucose uptake in adipocytes with substantial inhibition of adipogenesis (lipid accumulation). On the other hand, *Acacia kempeana* F.Muell. and *Santalum spicatum* A. DC. extracts showed stimulation of glucose uptake and *Beyeria lechnaultii* (DC.) Baill. and *Euphorbia drummondii* Boiss. only showed substantial inhibition of adipogenesis (Gulati et al., 2015). Notably *A. tetragonophylla* may well be useful in the treatment of type II diabetes, having glucose-lowering potential and minimal adipogenic activity, both desirable traits of antidiabetic drugs. Intriguingly, among the numerous mechanisms of actions that were proposed, the dualistic glucose-dependent and independent actions were emphasized. However there was a lack of evidence about the *Opuntia* spp. fruit products as an alternative or complementary therapy in the reduction of risk or management of type II diabetes, with only the cladode showing promise in potential glucose-lowering effects, indicating that further investigation is required (Gouws et al., 2019).

Furthermore, Deo et al. (2016) investigated the inhibitory activity of

selected Australian medicinal plant extracts (*Petalostigma pubescens* Domin, *Petalostigma banksia* Britten & S.Moore, *Memecylon pauciflorum* Blume, *Millettia pinnata* (L.) Panigrahi and *Grewia mesomischa* Burret) against protein glycation, ACE and digestive enzymes linked to type II diabetes. They found that the leaf extracts of *P. banksii* showed the strongest inhibition of α-amylase ($IC_{50} = 166.50 \pm 5.50$ μg/mL) whereas *P. pubescens* showed strong inhibition of both α-amylase and α-glucosidase ($IC_{50} = 160.20 \pm 27.92$ μg/mL and 167.83 ± 23.82 μg/mL, respectively). The antiglycation potential of *P. banksia* root and fruit extracts were noteworthy ($IC_{50} = 34.49 \pm 4.31$ μg/mL and 47.72 ± 1.65 μg/mL, respectively) given that the IC_{50} values were significantly lower ($p < 0.05$) compared to the other extracts. Subsequently, ACE inhibition IC_{50} values of the plant extracts were found to range between 266.27 ± 6.91 to 695.17 ± 15.38 μg/mL. In addition to their antihypertensive properties, ACE inhibitors are effective in controlling diabetic nephropathy through the suppression of renal monocyte chemoattractant protein 1 (MCP-1) (Deo et al., 2016). The study also concluded that the inhibitory effects of the extracts on α-amylase, α-glucosidase and the antiglycation showed no correlation with the total phenolic and total flavonoid contents and FRAP or DPPH (Deo et al., 2016). Similarly, work by Sakulnarmrat and Konczak (2012) on native Australian herbs established that *Tasmannia lanceolata* (Poir.) A.C. Sm. leaf extracts inhibited α-glucosidase ($IC_{50} = 0.83$ mg/mL) and pancreatic lipase ($IC_{50} = 0.60$ mg/mL), whereas *Syzygium anisatum* (Vickery) Craven & Biffin and *Backhousia citriodora* F.Muell. fractions had pronounced α-glucosidase- inhibitory activities ($IC_{50} = 0.30$ and 0.13 mg/mL, respectively) and were less effective against lipase. Various levels of correlation with the levels of total phenolics and antioxidant capacities and enzyme-inhibitory activities of plant extracts was evident (Sakulnarmrat et al., 2013) as opposed to the findings of Deo et al. (2016) mentioned earlier.

Jaeger et al. (2018) recently found that ethanol extracts from *Acacia ligulata* Benth. (Fabaceae) leaves and pods also have inhibitory effects on α-amylase and α-glucosidase with IC_{50} values between 9.7–34.8 and 12.6–64.3 μg/mL, respectively. Moreover, Ota and Urih (2017) stated that in the majority of the herbal products and specialised metabolites used in treating diabetes, the mechanism of action involved regulation of insulin signaling pathways, translocation of GLUT-4 receptor and/or activation of nuclear receptor peroxisome proliferator-activated receptor-γ (PPARγ) and that several flavonoids inhibit glucose absorption by inhibiting intestinal α-amylase and α-glucosidase. Hence, a collation of some common plants with their active phytochemicals which have antidiabetic properties, as described in a review by Ota and Urih (2017), included *Aegle marmelos* (L.) Corrêa (Aegelin, coumarins, alkaloids), *Allium cepa* L. (Allyl sulfide), *Aloe vera* (L.) Burm.f. (Aloin, aloe-emodin, pseudoprototinosaponin AIII, prototinosaponin AIII), *Arctium lappa* L. (Sitosterol-beta-D-glucopyranoside), *Cannabis sativa* L. (Cannabinoids, cannabinol), *Lycium barbarum* L. (Polysaccharide), *Morus alba* L. (Moran A), *Olea europaea* L. (Triterpenoids), *Oryza sativa* L. (Glycan), *Psidium guajava* L. (Vescalagin, strictinin, isostrictinin, pedunculagin), *Punica granatum* L. (Gallic acid, ellagic acid), *Stevia rebaudiana* (Bertoni) Bertoni (Stevioside)and *Ziziphus spina-christi* (L.) Desf. (Christinin-A). Nevertheless, the antidiabetic properties of the Australian plants are still not extensively explored and with a wide range of plant species there is potential for novel antidiabetic drug discoveries.

4. Conclusion

This review encompasses some ethnomedicinal plants native to Australia, which have been investigated for their phytochemical and therapeutic properties. Epidemiological studies have widely reported a link between plant phenolics and antioxidative capacities, useful in treating and preventing various illnesses. The high antioxidant containing plant extracts were found to have numerous types of phytochemicals such as phenolic acids (coumaric acid, cyanidin-3-glucoside, chlorogenic acid), flavonoids (quercetin, catechin, hesperetin, kaempferol and luteolin glycosides), tannins (ellagic acid and ellagitannins) and terpenoids (serrulatanes, monoterpenes, lipophilic diterpenes and lipophilic triterpenes). The prominent occurrence of TPC and antioxidative capacities evaluated in majority of the studies validate the ethnomedicinal claims of the native plants. Moreover *in vitro* studies have also shown promising evidence of potential bioactive compounds with medicinal properties. Whilst some studies have characterized the plant phytochemicals, majority have not isolated and purified the bioactive compounds. The *in vivo* bioactivity testing of Australian plant extracts is also limited. This review has included a limited number of plant species of ethnomedicinal significance; hundreds of plants remain in need of exploration and detailed study. In particular, limited information has been published on *in vivo* and human clinical studies. Future more elaborate studies are therefore required to screen out and purify lead bioactive compounds against numerous other disease types. This will not only improve our knowledge on the phytochemistry of Australian native flora, but also provide a platform to understand their health-promoting and bioactive effects for pharmaceutical interventions, nutraceuticals, cosmetics, and as functional foods. Finally, plant-derived natural compounds (phytochemicals), as well as plant based traditional remedies, are significant sources for latent and novel drugs against diseases. Extensive investigation of plant-based medicines and native plants may well hold the key to novel drug discoveries.

Ethic statement

This research did not include any human subjects or animal experimental work.

Declaration of competing interest

There are no conflicts of interest to disclose.

Authors contribution statement

The authors contributions are as follows; **Janice Mani**: conceptualization, methodology, formal analysis, investigation, data curation and original draft preparation. **Joel Johnson:** investigation, writing-review and editing, **Holly Hosking and Nanjappa Ashwath:** writing review and editing, **Paul Neilsen, Daniel A Broszczak and Kerry Walsh:** supervision, review and editing and **Mani Naiker:** investigation, supervision, writing-review and editing.

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