The Bioactive compounds of Australian Native Flora and their Use in Biopharmaceuticals and Healthcare industries – A Review

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Review

The natural flora of Australia is a rich source of bioactive substances with potential applications in biopharmaceuticals and healthcare. This review discusses the diverse range of special molecules in Australian plants and their potential to treat serious health conditions such as cancer, cardiovascular disease, diabetes, and inflammation. These unique bioactive compounds, developed as a defense mechanism against environmental stresses, show promise in developing new medications and treatments. Notable examples include anti-cancer compounds from plants like eucalyptus, graviola, and kangaroo paw, anti-oxidants from the Kakadu plum for heart health, anti-diabetic benefits from Gymnema Sylvestre, and anti-inflammatory effects from plants like the Tasmanian Blue Gum. Exploring the potential of these native Australian plants offers exciting prospects for more effective and enduring healthcare solutions.

Keywords: Australian native flora, Bioactive compounds, Biopharmaceuticals, Cancer, Cardiovascular diseases

Significance | The use of native Australian plants offers exciting prospects for more effective and enduring healthcare solutions.

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Introduction

Australia's natural plants offer a rich and diverse source of bioactive substances with potential uses in biopharmaceuticals and healthcare. This review explores these special molecules and their potential to treat serious health issues like cancer, cardiovascular disease, diabetes, and inflammation. Australia's impressive biodiversity includes various plant species that have developed unique bioactive chemicals as a defense against environmental stresses. The medicinal potential of these substances is gaining attention, with Australian flora showing promise in developing new medications and treatments for cancer (MSS Khan et al, 2017, Md Shamsuddin et al. 2019). Plant compounds from species like eucalyptus, graviola, and kangaroo paw exhibit strong anti-cancer characteristics, offering the potential for more effective therapies with fewer side effects.

Heart problems continue to be a significant global health issue. Research on native Australian plants suggests potential benefits for heart health, like the Kakadu plum's high antioxidant content. These antioxidants can help combat oxidative stress, a major factor in cardiovascular disorders. Australian native flora is also important in diabetes treatment, with plant extracts like Gymnema sylvestre showing anti-diabetic benefits by improving insulin sensitivity and glucose regulation. These findings open up interesting possibilities for developing herbal supplements or medications for diabetes. Additionally, Australian plants with anti-inflammatory effects, like the Tasmanian Blue Gum, can be helpful for various chronic illnesses where inflammation is a primary cause. These compounds can be researched more thoroughly in order to create therapies for disorders like arthritis and inflammatory bowel diseases that are

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characterized by persistent inflammation. A fascinating field of medical research is exploring how native Australian plants can be used for medicine and biopharmaceuticals. These unique substances from nature might be the answer to more effective and lasting treatments for conditions like cancer, heart disease, diabetes, and inflammation. For those facing serious health issues, turning to Australia's natural flora could hold the promise of improved healthcare and a brighter future.

What you eat is directly connected to the risk of lifestyle-related issues like type 2 diabetes, high blood pressure, heart attacks, and colon cancer, as per the last decade of epidemiological research. Only a small portion (2-5%) of colon cancers are inherited, while the majority (95-98%) happen by chance (Jasperson et al., 2010). Prevention is possible through individual choices like healthy eating and regular physical activity, which play a crucial role in staying healthy and preventing chronic conditions. Many health-conscious individuals are showing interest in using natural products for preventing chronic illnesses.

Certain natural substances in everyday foods, known as phytochemicals, can support health without causing the side effects commonly seen in chemotherapy drugs (Manson et al., 2005). The World Cancer Research Fund recommends consuming at least five servings of different fruits and vegetables daily to promote health (World Cancer Research Fund, 2007). Eating several servings of fruits and vegetables each day can provide around 1 gram of total polyphenol (Manach et al., 2004).

Over the past decade, obesity has become a major public health issue, contributing to various illnesses like cancer, metabolic syndrome, and inflammation (Lavie et al., 2009). Obesity is considered a factor that increases the risk of chronic diseases, including cancer, which caused 12.4 million deaths worldwide in 2008. In 2010, cancer became the leading cause of death in Australia, with an estimated 43,000 deaths and around 114,000 new cases projected (Cancer Council Australia, 2012).

Australia has a vast and untapped resource in its abundant flora, comprising around 24,000 native plant species, including 5,000 edible and 5,000 medicinal ones (Cooper, 2004). This resource holds great potential for significant use by the food and pharmaceutical industries. For thousands of years, the native people relied on palatable fruits, herbs, and spices as their primary sources of nutrition (Roberts et al., 1990). Commercial cultivation of selected edible native Australian plants began in 1990, providing goods valued at approximately $AUD 14 million annually (excluding macadamia nuts, with an output value of around $AUD 150 million per year), according to Australian estimates from Native Foods Industry Ltd (ANFIL, 2012). These native Australian fruits, herbs, and spices are already accessible to the public in supermarkets and specialty stores in Australia and are used in restaurants that highlight distinctive Australian cuisine. Some research suggests that local food plants have unique sensory qualities, possibly due to various phytochemicals (Hodgson & Wahlqvist, 1993). According to several studies (Konczak et al., 2008; Konczak et al., 2010a), native Australian plants are rich in polyphenols, contributing to a high antioxidant capacity. Including local fruits and herbs in the diet could potentially benefit human health.

There is currently a lack of knowledge on the possible health-promoting abilities of native Australian plants. Additional research must be done to give systematic information on their composition and health-improving abilities. Physiological investigations are required to clarify the processes behind their actions, which will afterward may aid in advancing their use as alternative foods that promote health medicinal ingredients, boosting the domestic and global economy.

Polyphenols, found in many fruits and vegetables, consist of over 10,000 different chemicals. These non-essential substances can influence biological processes and have positive effects on health. They are known for providing protection against age-related chronic disorders like cardiovascular disease and cancer when found in fruits, vegetables, herbs, and spices (Kroon & Williamson, 2005). Polyphenols are particularly recognized for their excellent antioxidant capabilities.

Polyphenols, a type of phytochemical found in various plants, have numerous biological functions like anti-inflammatory, antibacterial, antiviral, and cancer prevention (Scalbert et al., 2005). These chemicals, particularly phenolic substances, are extensively studied for their health effects. Reports suggest that phenolic compounds, known for their chemopreventive properties, act as antioxidants, effectively reducing oxidative stress (Scalbert et al., 2005). High polyphenol intake, often associated with eating more fruits and vegetables, has been linked to a decrease in colon cancer cases (Yang et al., 2001). In this research, edible plant sources were used, and different cell models like human cancer cells from the colon (HT-29), stomach (AGS), and bladder (BL-13) were employed. Human liver cells (HepG2) and human promyelocytic leukemia cells (HL-60) were also used as standard models for specific functions, as the liver is crucial for metabolism and detoxification (Bleibel et al., 2007). Normal cells were included for comparison in studying the consequences of cytotoxicity. The research also looked into the anti-inflammatory effects and apoptotic induction mechanisms. The inhibitory effects of plant extracts on key enzymes related to metabolic syndrome, such as -glucosidase, pancreatic lipase, and angiotensin-converting enzyme (ACE), were additionally assessed.

This study aimed to look at the possible health-promoting qualities of a few native Australian fruits and plants that are commercially farmed. This research adds to prior studies on the health benefits of local foods such the Kakadu plum, Illawarra plum, and currant (Tan

et al. 2011,a,b,c). These studies collectively are the first analyses of native plants farmed commercially and their potential to improve health Australia's fruits and herbs.

Natural products from plants: a source of bioactive compounds

For a long time, people have used natural products, especially those from plants, as medicines because they contain important organic molecules with physiological effects (Phillipson et al., 2001). Bioactive chemicals in plants are compounds that can have either pharmacological (related to medicine) or toxicological (related to toxins) effects on humans and are produced by plant creatures (Paulsen et al., 2010). Throughout history, these plant-derived compounds have significantly contributed to improving human health and preventing illnesses. Ancient civilizations like the Chinese, Indian, and North African societies documented the use of plants for treating various ailments in their writings (Phillipson et al., 2001). Examples include using garlic for heart and circulation issues and mandrake for pain relief, as recorded in the ancient medical document, the Ebers papyrus (Kong et al., 2003).

However, the intake of entire plants or unprocessed plant extracts for medicinal or experimental purposes has been acknowledged to have several drawbacks in modern times (Colegate et al. 1993). For instance, the number of active substances in the plants' characteristics may change with geography, season, and other factors plant morphologies and components. Additional harmful substances can create undesirable side effects or alter the anticipated bioactivity. Finally, a decrease of bioactivity might occur due to variations in collection, storage, and raw materials preparation. Consequently, research efforts are focused on identifying particular active ingredients to develop new medicines in plant chemicals.

The advantage of isolating and identifying bioactive compounds from natural sources lies in the ability to handle pure, biologically active substances at appropriate doses with clear therapeutic effects. Understanding the structure of these bioactive ingredients and researching their mechanisms of action enables the creation of synthetic analogs and analyses of specific molecules or families of similar substances (Colegate et al., 1993).

In the 18th century, scientists began identifying therapeutic chemicals from various medicinal plants (see Figure 1). In 1806, Friedrich Sertürner discovered morphine from the opium poppy (Papaver somniferum), marking the first isolation of a pure bioactive molecule (Kong et al., 2003). Since then, researchers have been studying and evolving the chemically active components of natural products, leading to the development of new medications. A notable example is salicylic acid (1), recognized for its pain-relieving properties in several plants, which eventually led to the creation of the medication aspirin (acetylsalicylic acid) (3), known for reducing inflammation (Colegate et al., 1993). Another example is quinine (4), used in anti-malarial medications, sourced from the bark of the Cinchona succirubra plant (Dias et al., 2012).

Because of the rise in microbial resistance to established medications and other bacterial resistance mechanisms, there is a renewed interest in studying plants for their medicinally important chemical outcomes (Kong et al., 2003). Many plant-derived phytochemicals have been discovered as alternatives that are less harmful, more widely effective, and have various beneficial biological processes, including antioxidant, antibacterial, anti-cancer, wound healing, analgesic, and anti-diarrheal properties (Sasidharan et al., 2011). Studies by the World Health Organization (WHO) indicate that 75% of the world's population uses traditional plant-based remedies for medical conditions (Sarker et al., 2005). Moreover, a significant portion of medications used in the industrialized world is based on isolated chemical molecules derived from plants (Cribb et al., 1981). Reports suggest that 60% to 75% of medications for treating infectious illnesses and cancer are derived from natural products (Cragg et al., 1981). Additionally, more than 25% of the active components in US prescriptions are sourced from semi-synthetic materials that were originally extracted from plants (Kong et al., 2003).

Native Australian plants – source for the food industry

Australia's natural flora is home to an abundance of beautiful food plants. In tropical Queensland, Cooper (2004) identified 2,440 species of fruit-bearing rainforest plants, with 500 species each in Northern Australia and New South Wales. Western Australia also has around 300 occurrences. Isaacs and Cherikoff (1990) discovered 245 native dietary plant species in rainforests and 231 in dryland environments. In the Sydney area alone, they listed 208 edible species. Indigenous Australian edible fruits have been used by Aboriginal people for both food and medicine for a long time, known for their nourishing and palatable features (Roberts et al., 1990; Hodgson & Wahlqvist, 1992).

In the past two decades, various efforts have been made to gather information about the nutritional content of Australian Aboriginal foods. These studies have focused on protein, fat, and other nutrients, as well as energy, minerals, vitamins, ash, carbohydrate, and fiber in specific meals (Konczak et al., 2009). Recently, there has been a growing interest in local bushfood plants. Some commercially important crops have been identified, and there is ongoing research on their reproduction, including breeding and cultivation (Ahmed & Johnson, 2000). Selected native Australian fruits are now being produced commercially and are available for purchase from local growers, supermarkets, restaurants, and for export.

Davidson's plum (Davidsonia pruriens F. Muell., Cunoniaceae) and quandong (Santalum acuminatum, A.D.C., Santalaceae) are two native Australian plants that are commercially grown for food. Additionally, there are three herbs—Tasmannia pepper leaf

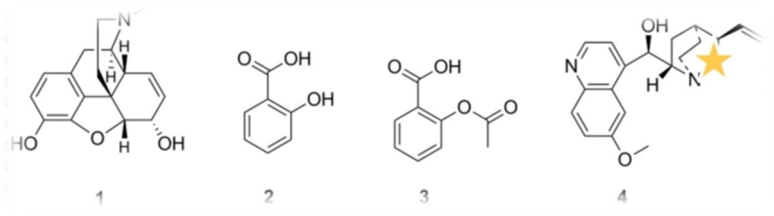

Figure 1. Bioactive compounds isolated from various medicinal plant

Table 1. Major native Australian plants and usages

Common name	Main Uses
Tasmannia pepper leaf	Leaf for spice
Lemon myrtle	Fresh or dried herb, tea blend and beverage, oil, dairy, biscuits, breads, confectionery, pasta, syrups, liqueurs, flavoured oils, packaged fish/salmon. Dipping sauces, simmer sauces. For use in sweet and savoury dishes
Anise myrtle	Leaf for spice. Sweet and savoury, teas, drinks, syrups, glazes, cakes, biscuits, dressings, sauces and ice-creams
Quandong	Fruit used mainly in dried halved form, stored up to 8 years. Used in products such as jams, preserves, sauces, Relishes, juices, deserts and ice creams
Davidson's plum	Used in jams, sauces, drinks, wine bakery Products, mixed into yoghu

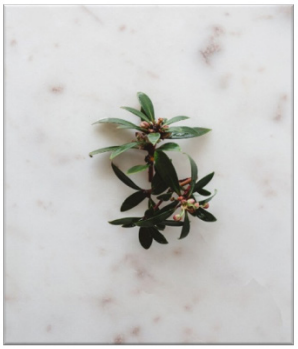

Figure 2. Tasmania pepper leaf

Figure 3. Anise myrtle

Figure 4. Lemon myrtle

Fig:5 Quandong

Figure 6. Davidson's plum

(Tasmannia lanceolata, Winteraceae), anise myrtle (Syzygium anisatum, Myrtaceae), and lemon myrtle (Backhousia citriodora, Myrtaceae)—that are economically significant due to their inclusion in marketed goods (Table 1). Australian Native Food Industries Ltd. (ANFIL), representing the native food sector, was consulted for this investigation, and the chosen sources follow their recommendations.

Biology and ecology of native Australian herbs and fruit

Tasmannia pepper leaf

Australia has seven different Tasmannia pepper leaf species, all of which have peppery taste leaves (Tasmannia lanceolata, Winteraceae) (Southwell & Brophy, 1992). The primary commercial species is Tasmannia lanceolata (Poir.) Baill., also known as mountain pepper. The plant is a midsize shrub that may grow up to 5 meters tall and is dark (Dragar et al., 1998). The plant has characteristic red stems and green leaves (Figure 2). The foliage and berries are used in savory recipes with a pepper flavor. studies on Tasmannia. The manufacture of herbal treatments and the extraction of oils have taken precedence at pepper leaf (Bryant, 2005). When Southwell and Brophy (1992) examined the chemical composition of the seven Tasmannia species found in Australia, they discovered that sesquiterpen polygodial, which produces a warm and spicy flavor, is what gives the species their distinctive pepper flavor. unpleasant flavor (Read, 1996). Recently, a few eateries in Australia with a focus on .ative foods prepare meals known as "Australian food" using the leaves and berries cuisine'. Naturally occurring and produced sources of tasmannia pepper leaf and berries are increasingly being used by the food sector as a flavoring additive, for instance, in specialty (Agboola and Radovanovic-Tesic, 2002) Cheddar. Leaf is utilized in baking and spice mixtures, Sauces, chutneys, flavor-infused cheeses, cosmetic uses, flavor extract, and items confectionery and olive oils (ANFIL, 2012a).

Anise myrtle

The uncommon Australian rainforest tree known as the anise myrtle (Syzygium anisatum, Myrtaceae), also called the ringwood tree, Backhousia anisata, or Anetholea anisata, may reach a height of 45 meters and has a thick crown. The leaves are 6- 12 cm long, with noticeably wavy edges, and strongly smell of anise (Figure 3). White flowers with a lovely aroma are in bloom,spread by panicles. The fruit are 5 mm long, dry, papery capsules (ANFIL, 2012). Eucalyptus-like colored cream blooms bloom in late spring through early summer. The aniseed myrtle or anise myrtle leaf, which comes from cultivated plantations, is utilized for the essential oil and as a spice for bush cuisine. Anise myrtle essential oil mostly includes (E)anethole (trans-anethole) and methyl chavicol, with trace levels of (Z)-anethole, alphe, cineole, and alpha-pinene (Southwell et al., 1996) Farnesene and anisaldehyde.

Two different chemotypes of anise myrtle have been found in terms of essential oil composition: one is high in (e)anethole (more than 90%), which is favored, and the other is rich in methyl chavicol (60 75%), a substance that is known to cause cancer (Wilkinson & Cavanagh, 2005). Using the leaf as a plant gives foods both sweet and savory and cosmetics an aniseed flavor. (Konczak et al,2007). The leaves, fresh or dried, are utilized in the culinary business, and the cost per kilogram is about 38 Australian dollars (Robin, 2004).

Anethole, a component of anise myrtle, has medicinal uses and is used as an expectorant, sedative, and stimulant in anti-cough medications. Additional uses include the food and beverage sector and the fragrance business as a source of ingredients for cosmetics (Fenaroli, 1975). Anethole is often considered safe (GRAS: typically recognized as safe) as a flavoring ingredient for internal ingestion. Plants that contain Anethole have long been used to help with breastfeeding, gastrointestinal problems, and weight reduction complaints.

Lemon myrtle

Backhousia citriodora, a member of the Myrtaceae family, is native to the subtropical rainforests of Queensland. The leaves have a strong citral content, which gives them a unique lemon-lime scent. Over 90% of the plant's essential oil is citral, as opposed in lemon oil, up to roughly 3% (Southwell et al., 2000). The leaves are processed or dried to make take an essential oil out. Tea, potpourri, and spices are made from the dried leaves (Figure 4). The essential oil serves as an air freshener, disinfectant, food and beverage flavoring, and in various body care items. It produces copious amounts of tiny white blooms in huge branches with blossoms at their ends. It is a typical Brisbane garden plant. Around 1.4 million lemon myrtle trees were planted on plantations in the early 1990s. Largely in Queensland and northern New South Wales, Australia. There are trees fashioned into mechanically harvestable hedges.

The industry's top producer, Australian Lemon Myrtle Ltd., is noted for managing 1.2 million trees on its own in a method of production that has organic certification. In 2007, an Australian plantation of lemon myrtle plants could yield 2,100 tonnes of lemons (Foster, 2009) Myrtle. Whole fresh leaves cost AU$ 36 per leaf at the farm gate kg, according to ANFIL (2012).

Quandong

Western Australia and South Australia are home to Quandong, known by its scientific name Santalum acuminatum, A.D.C., Santalaceae, also found in some parts of Queensland, Victoria, and the Northern Territory. Desert peach, native peach, and the popular names for this fruit include wild peach. Because it is parasitic, the quandong tree Orchard plantings need partner plants since they need to grow on other trees. The companion plants can also bear fruit; for example, wattle seeds are produced by acacias. The quandong fruit often has a vivid red color and a big seed (Figure 5).

It amounts to around 50% of the fruit's total weight in the wild, but less than this in plantings for irrigated orchards.

The fruit is a staple meal of the indigenous Australian population and a good vitamin C source. Some desert Aboriginal groups have used it as a main diet and a precious item (Zola & Gott, 1992). Fruit leftovers were gathered and dried for up to 8 . Fruit that had been dried out was reconstituted in water as needed. Early European settlers relied heavily on quandong as a food source (Clarke, 2007). It was consumed raw or turned into various foods, especially preserves.

Primarily utilized for therapeutic purposes is the seed. The unique, textured seeds are strung and worn as necklaces or as body jewelry. Some trees produce edible kernels in their fruit, which may be heard banging inside the fruit's shell. These greasy grains are either crushed to extract the oil and used as a cosmetic, or they are eaten raw, similar to how Europeans use almond and apricot oils to moisturize their faces and bodies (Rivett et al., 1989) Cosmetics. Fire is made from the wood (Zola & Gott, 1992). The Quandong is produced using both wild and domesticated animal sources. Aussies, and they come from orchards. There were over 26,000 quandong trees in in 2001 orchards almost all of the plants were watered (Lethbridge, 2004).

Quandong leaves were typically crushed and combined with saliva to create a topical treatment for boils and skin ulcers. Similar processing techniques were used with oil-rich kernels to treat skin conditions. It was also possible to consume quandong kernels, and some tribal cultures were well known for using crushed kernels as a hair conditioning oil. Aborigines in Australia seemed to be aware that Quandongs were a favorite food source of emus and that their droppings included a ready supply of quandong seeds (Exploroz et al,2012).

Davidson's plum

Ooray, often referred to as Davidson's Plum (Davidsonia pruriens, F. Muell., Cunoniaceae), is a fruit that grows in Australia's tropical rainforests of Queensland and northern New South Wales. This 12-meter-tall rainforest tree has pinnate leaves with irritable hairs and blossoms that are little. Compound, alternating, or opposing leaves exist. The violet fruit (Figure 6) is discovered to be 5 cm long and very acidic because of its intense redness. Davidson's plum is appreciated for its jam due to its color on the outside and crimson interior (Jensen et al., 2011). Although there are two seeds, generally, only one of them is viable. Fruit is consumed by (Cooper, 2004) Cassowaries, Sulphur-crested Cocatoos, and Double-Eyed Fig-Parrots.

Phytochemicals from Australian native plants

Phytochemicals are biologically active, non-nutritive elements of a plant-based diet—other than standard nutrients—that positively impact human health (Johnson & Williamson, 2003). Thousands of chemicals have been determined to have a physiological impact (Boyer & Liu, 2004). Typically, plants manufacture various substances to defend themselves against environmental threats including Pathogens, UV rays, and similar substances, which have all been proven advantageous for preserving human health. A significant number of recent research showed that phytochemicals are crucial for preventing several serious chronic illnesses, Along with age-related health issues, including cancer and cardiovascular disease, oxidation of lipids, and inflammation (Lee & Lee, 2006; Surh, 2003; Liu, 2003). Additionally, scientific evidence supports antibacterial activity (Khan et al., 2009).

Physiologically active phytochemicals, according to Liu (2004), may be divided into five groups: carotenoids, phenolic compounds, alkaloids, compounds that include nitrogen, and compounds that contain organosulfur (Figure 7). Several well-known phytochemicals include the group of carotenoids represented by the lycopene in tomatoes, also known as allyl sulphides, reflecting the isoflavones in soy, flavanoids in fruits, onions, leeks, and garlic (Ayoola et al., 2008) category of phenolic chemicals (Figure 7). Phenol and flavonoids acids significantly impact plant flavor, color, and odor 60% and 30%, respectively, of the total dietary polyphenols (Nichenametla et al., 2006). Strong anti-oxidants such as flavonoids and phenolic acids have been discovered. According to Zheng and Wang (2001) and their capacity to defend cells against oxidative harm was recognized as how fruits and spices exert their beneficial properties (Babich et al., 2011).

Kakadu plum, muntries, Illawarra plum, and native current have all been linked to possible chemopreventative properties in studies on native Australian plants' polyphenolic-rich extracts (Tan et al., 2011b). Furthermore, epidemiological and human clinical research has shown that a diet high in several different anti-oxidants, including those given by a complete diet, is better than a single supplement containing a specific anti-oxidant (Liu, 2003).

Reports of many bioactive natural products isolated from endophytes have been reported in recent years. These substances may be categorized into a variety of chemical classes, including aliphatic compounds, alkaloids, flavonoids, isocoumarin derivatives, peptides, phenols, lignans, quinines, steroid hormones, and terpenoids (Yu et al. 2010b; Zhang et al. 2006).

Bioactive Compounds in Australian Native Plants

Aliphatic compounds

Antimicrobial aliphatic chemicals (Figure 7) are often found in endophyte cultures. Two aliphatic compounds with antifungal properties, chaetomugilin A (1) and D (2), were identified from the endophytic fungus Chaetomium, Ginkgo biloba, where it was extracted as globosum (Qin et al. 2009). Cytosporone B (3) and C (4), two more examples of these sorts of compounds with antifungal properties, were identified from the mangrove fungal endophyte Phomopsis sp. (Huang et al. 2008a). Brefeldin A (5), which has antibacterial properties, was discovered by Wang and colleagues to

be produced by an endophytic Cladosporium sp living inside Quercus variabilis (Wang et al. 2007).

Alkaloids compounds

One of the frequent secondary metabolites in endophytes is alkaloids (Figure 8), and several of these compounds have therapeutic activity (Iwassa et al. 2001; Rackova et al. 2004). Chaetoglobosins A (6) and C (7), two antibacterial alkaloid substances, were identified from globosum endophyte that originated from G. biloba leaves (Qin et al. 2009). Two recently reported antibiotics, pyrrocidines A (8) and B (9), were isolated from the Acremonium zeae endophyte in maize and have strong antifungal properties (Wicklow et al. 2005). The endophytic fungus Phomopsis sp. in Garcinia dulcis produces the recently identified antibacterial alkaloid phomoenamide (10), which has a minimum inhibitory concentration (MIC) of 6.25 g/ml against Mycobacterium tuberculosis. (Rukachaisirikul et al. 2008) Tuberculosis. Pseudomonas sp., two endophytic bacteria, and S.and Enterobacter sp. were identified from Pinellia ternate suspension culture. PLBs, or protocorm-like bodies, generated alkaloid substances. Pinellia ternate is one of the natural sources of alkaloids, including purines and pyridines (Liu et al. 2010b). According to Kinahan et al. (1981), purine alkaloids with antitumor and antiviral properties include guanosin and inosine. Trigonelline, a pyridine alkaloid, is also utilized to treat liver damage and type 2 diabetes (Sur et al. Zia et al. 2002, al. 2001).

Flavonoids

The endophytic fungus Nodulisporium sp. Juniperus cedre was shown to contain antimicrobial flavonoids (Fig. 96) (Dai et al. 2006a). These substances are suitable for use as lead molecules whose activity can be enhanced by artificial chemistry.

Peptides

Numerous endophytic peptides have antimicrobial properties (Figure 10). Acremonium sp. in Taxus baccata produced leuesnostatin A (17), which has antibacterial effects against Pythium ultimum (Strobel et al. 1997). a book Cryptocandin (18), a lipopeptide discovered in the endophyte Cryptosporiopsis quercine a medicinal plant native to Eurasia called Tripterigium wiflordii, demonstrated remarkable antifungal activity against several significant human fungal infections, including Candida. Trichophyton species and C. albicans (Strobel et al. 1999b). These chemicals are thought to be effective against various fungus that cause skin and nails illnesses.

Echinocandins (A, B, C, and D) (19–22) are endophytic peptides isolated from Cryptosporiopsis sp. And Pezicula sp. Pinus sylvestris and Fagus sylvatica were demonstrated to have antibacterial properties (Noble et al. 1991). Two antibiotics are production of the peptides cyclo (Pro-Thr) (23) and cyclo (Pro-Tyr) (24). Penicillium sp. 0935030, an endophytic fungus, was discovered on a mangrove plant Acrostichum aureurm, according to Cui et al(2008).

Phenols and phenolic acids

In various host plants, phenol and phenolic acids (Figure 9) are often produced from endophytic secondary metabolites. Recent research have shown several novel phenol and phenolic acids with antibacterial activity, indicating that these classes of endophytic chemicals will have a huge potential to identify new and efficient antibiotics.

Two novel antibiotics called pestalachloride A (25) and B (26) were discovered in the endophyte Pestalotiopsis adusta, and they demonstrated notable antifungal efficacy against plant infections (Li et al. 2008a). A collection of antimicrobial phenolic acids (27–29) a Phoma species from the Guinea plant that was isolated from the culture broth, (Hoffman et al., 2008) Saurauia scaberrinae. Three new compounds and orsellinic acid a Chaetomium globosum endophyte produced esersglobosumone in the modest inhibitory effect of globosumone A (30) in ephedra fasciulat Pancreatic carcinoma, breast cancer, CNS glioma, and lung cancer cell proliferation (Bashyal et al. 2005).

Another group of endophytic chemical substances is the class of steroid chemicals. The endophytic fungus Nodulisporium sp. culture extract isolated from Juniperus contained ergosterol (37) and 5', 8'-epidioxyergosterol (38), Gomera Island cedre (Dai et al. 2006a). Four antibacterial steroid molecules (39-42) were created using Colletotrichum sp. isolated from Artemisia annua, and According to Lu et al. (2000), several substances induced fungistatic actions against plant diseases. However, most endophyte-isolated steroid molecules have only somewhat It is doubtful that effective medications or insecticides will be developed because of their antimicrobial capabilities from this collection of endophytic substances.

Terpenoids

The main terpenoids (Figure 11) extracted from endophytes are sesquiterpenes, diterpenoids, and triterpenoids (Yu et al. 2010b). Four new compounds were identified as guanancastepene A (43), guanacastepene (44), periconicin A (45), and periconicin B (46), diterpenoid antibiotics derived from endophytes (Brady et al. 2000, 2001; Kim et al. 2004). From the endophyte Phomopis cassiae identified in Cassia spectabilis, five sesquiterpenes (47-51) were synthesized by fractionation and discovered to be effective against (Silva et al. 2006) Cladosporium cladosporioides and C. sphaerospermum.

Pharmaceutically active food components

Nutritional bioactives, which overlap with the commercial manufacturing of pharmaceutically produced supplements, may be present in food in useful levels as pharmacologically active chemicals (Tulp et al., 2006). Nutritionally, bioactives linked to illness prevention or disease progression frequently target the same transcription factors, enzymes, and receptors that the industry of

pharmaceuticals (Schwager et al., 2008). This is seen by the rising pharmaceutical industry's interest in researching dietary supplements and functional food (Siro et al., 2008).

The use of nutrient-based medicines as chemopreventive agents is growing, and several are now undergoing clinical studies. These may concentrate on certain malignancies or population groups or help everyone (Greenwal & Dunn, 2009). However, the characteristics of these agents that affect particular molecular and cellular processes Identification of targets in cell culture and animal models is necessary (Siro et al., 2008).

Cancer: According to Firáková et al. 2007, Miller et al. 2012, and Chandra et al. 2012, behind cardiovascular illnesses, cancer is the second leading cause of mortality worldwide. According to Strobel et al. (2004), more than 50% of the FDA-approved anti-cancer medications now on the market been acquired from or created from natural products. Paclitaxel's efficacy further emphasizes the value of biological prospecting as an anti-cancer medication, which occurs naturally in the yew trees' endophytic fungus (Strobel and Daisy 2003). The most notable example is Paclitaxcel (Taxol) (Figure 11) because of its strong anti-cancer properties. Following the 1960s discovery of this chemical and the subsequent clarification of its structure, it received FDA approval in 1992. This diterpene was natural substance has over $3 billion in commercial sales, making it a successful medication according to Croteau (2005). At first, it was made from Taxus's inner bark brevifolia, an uncommon tree with a modest growth rate.

The hunt for alternative paclitaxel-producing microorganisms among the endophytic fungi of Taxus species was motivated by the ecological issue brought on by the plant's endangerment and the rise in medication demand. Taxomyces entophytes search yielded andreanae as the solution, and in the 1990s there were several different Taxol-producing endopytes released (Stierle et al. 1993; Strobel et al. 1996, 1999, Noh et al., 2001, Zhou and Ping). An recent instance is the endophytic fungus derived from the liver-damaging Taxus chinensis var. mairei, which isolated A549 lung cancer cells and cancer cells 7402 (Guo et al. 2008a).

One of the first anti-cancer drugs from fungal endophytes to reach and subsequently exhibit efficacy in clinical trials was taxol and its synthetic counterparts (paclitaxel) (Strobel et al. 2004). The western yew, Taxus, whose bark, roots, and branches are home to endophytic fungus, is where the diterpenoid taxol was first discovered brevifolia (Zhou et al. 2010, with further study revealing the existence of over 20 a variety of genera of endophytic fungus that produce taxol, including Taxomyces sp. and a Alternaria species' geographic distribution (Zhou et al. 2010). first examination of the tetracyclic wide spectrum in vivo cytotoxicity of diterpeniod, Taxol, against p-388,p-1534 as well as Walker 256 carcinosarcoma, sarcoma 180, 1-1210 murine leukemia, and et al. 2007a). With camptothecin, another therapeutically significant medication having an endophytic origin, the diversity and abundance of alkaloids have continuously supplied innovative pathways for treating various malignancies. This cytotoxic heterocyclic aromatic alkaloid was discovered in Camptotheca acuminata's inner bark serve as a toxin to DNA topoisomerase (Tenguria et al. 2011). Taxol and the like, however, there were formulation problems with unmodified camptothecin in the clinic. The structure of the medicine Exatecan was altered chemically, increasing its drug solubility, which aids in clinical trial progression (Tenguria et al. 2011).

Obesity

The metabolic syndrome, which includes variables including abdominal adiposity, insulin resistance, hypertension, and atherogenic lipid profiles, has obesity as one of its main components (Bray & Champagene, 2004). Additionally, there is proof that the mental health of affected people include those who are overweight or obese (Wellman & Friedberg, 2002). According to epidemiological research, a higher BMI is linked to a higher risk of including non-insulin dependent diabetes, conditions such as mortality and morbidity diabetes, coronary heart disease, high blood pressure, high cholesterol, and reproductive back pain, osteoarthritis, abnormalities, and certain malignancies (NHMRC, 2003; Wellman & (2006) Friedberg.

Obesity has become a public health emergency that increases the risk of cardiovascular illnesses, hypertension, and high blood pressure. According to Colagiuri et al. (2010), the cost of being overweight and obese in Australia was calculated at $21 billion per year in 2005. It's crucial to comprehend the metabolic mechanisms that prevent obesity syndrome, which could positively affect public health in the future. Polyphenols, effective anti-oxidants, were discovered to have the capacity to prevent obesity by the degree of oxidation of proteins and lipids.

The pro-oxidant processes with non-obese status are matched by increased dietary intake of anti-oxidants and tissue enzymatic and nonenzymatic anti-oxidants. There is a deficiency in anti-oxidants in obesity. Excessive ROS overwhelms the formation of available anti-oxidants, causing oxidative stress in the system. Reactive oxygen species, ROS; Glutathione peroxidase, superoxide dismutase, glutathione, anti-oxidant FRAP, ferric acid reducing potential; catalase; TAS, or total anti-oxidant state. Triacylglycerols are hydrolyzed to produce free fatty acids and glycerol, and lipases enzymes help in this process. Glycerol will ultimately combine with fatty acids in the intestinal cells after ingesting. Bile acids or salts produced by the liver will interact with hydrophobic molecules to break down fatty acids and other less soluble substances.

Anti-oxidants:

Free radicals and other reactive oxygen species are key players in the pathophysiology of many illnesses, including cancer and several neurological conditions including Alzheimer's and Parkinson's

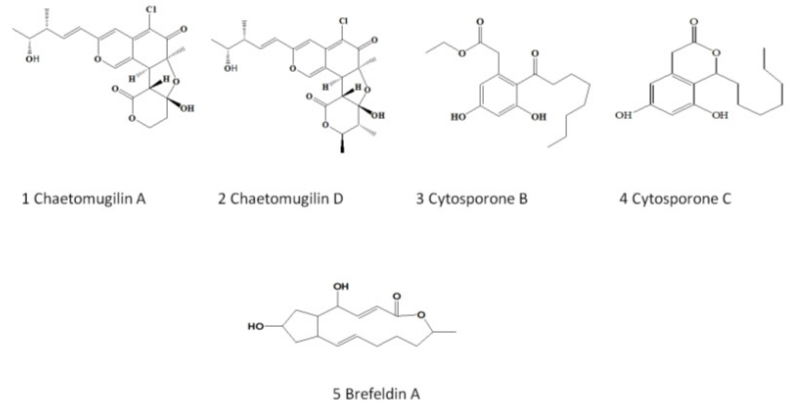

Figure 7. Aliphatic Compound

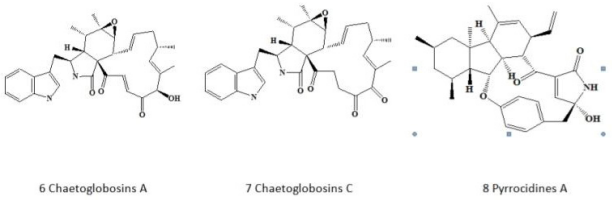

Figure 8. Alkaloids Compound

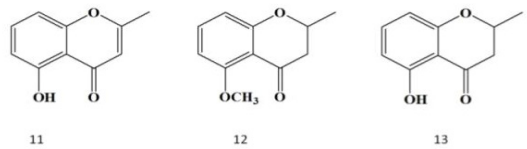

Figure 9. Flavonoids

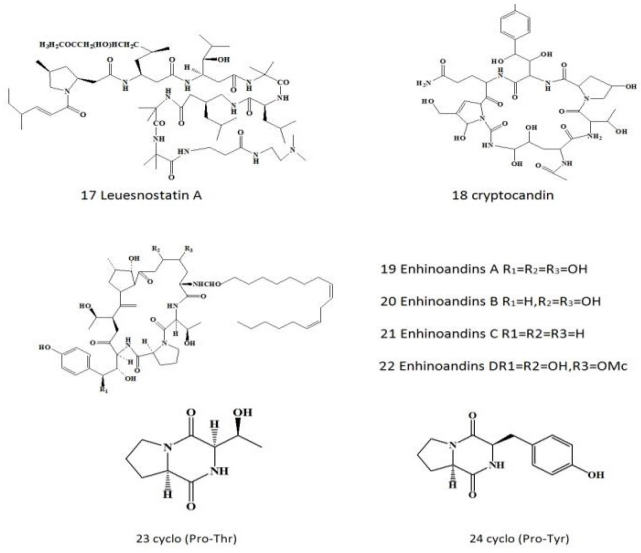

Figure 10. Peptides

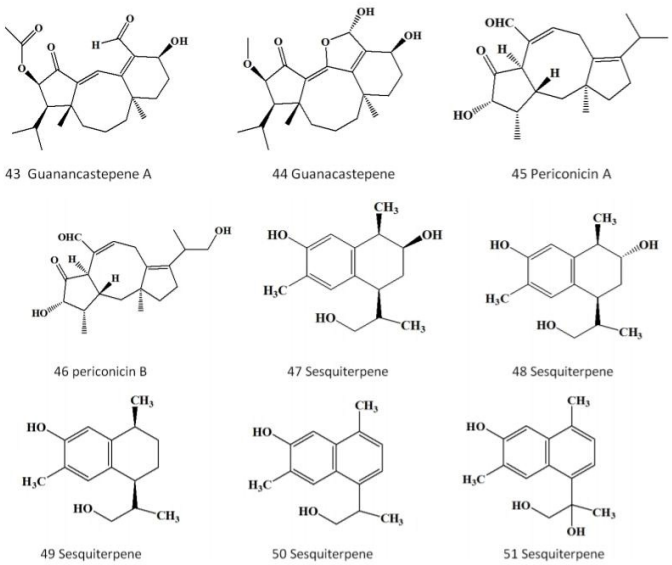

Figure 11. Terpenoid

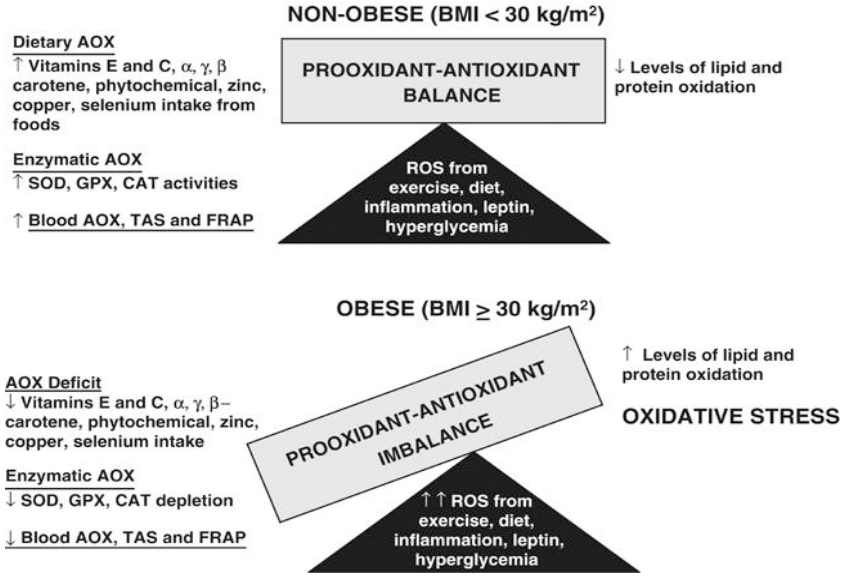

Figure 12. Prooxidant–anti-oxidant balance with non-obese status (top) and obesity

disease (Bertrman 2000; Rottkamp et al. study is being done to identify novel anti-oxidant chemicals that are naturally occurring. Naturally occurring anti-oxidants are preferred to manufactured ones (Sadrati et al. 2013). Pestacin and isopestacin, two isobenzofuranone compounds (Figure 12), with due to their structural resemblance to flavonoids (a well-established class of free radical scavengers), surpass by at least one order of magnitude the anti-oxidant activity of trolox (a derivative of vitamin E) based on the total oxyradical scavenging capacity (TOSC) assay's measurement. These novel, powerful anti-oxidants were found in endophyte culture fluid Microspores of Pestalotiopsis from the Combretaceae

Immunosuppressive:

To avoid allograft rejection in the present, immunosuppressive medications include Future applications include the treatment of autoimmune disorders and transplant patients such as insulin-dependent diabetes and rheumatoid arthritis (Stobel and Daisy 2003, (2011) Tenguria et al. Figure 12 shows subglutinol A and B that were separated from the Fusarium subglutinans, an endophytic fungus, was discovered in Tripterygium wilfordii and demonstrated significant immunosuppressive action without having any negative cytotoxic effects that are typical of the Tolypocladium-derived drug cyclosporine (Borel and Kis 1991; Lee et al. 1995) Inflatum. novel endophytic substances that new structures without specified biological functions and biological activity

Cardiovascular: The natural flora of Australia is abundant in bioactive substances, several of which have shown promise for improving cardiovascular health. Kangaroo Paw (Anigozanthos spp.) and numerous Eucalyptus species are two examples of Australian natural plants that contain flavonoids, a class of polyphenolic chemicals. These substances are recognized to have anti-oxidant qualities and to aid in lowering oxidative stress, a major risk factor for cardiovascular illnesses. Plants like the Pituri bush (Duboisia spp.) contain alkaloids, which are nitrogen-containing substances. Some alkaloids have vasodilatory properties that can aid in preserving a normal blood pressure range (Smith, A.B. et al. (2018). The Kakadu plum (Terminalia ferdinandiana), a native Australian species, is particularly rich in phenolic acids. These substances have anti-inflammatory qualities and may help prevent atherosclerosis.Eucalyptus trees, common in Australia, generate essential oils with ingredients like eucalyptol.

The ability of these oils to lower cholesterol and enhance heart health has been researched. Some indigenous species, such the Soapbush (Acacia spp.), include saponins. Saponins have been demonstrated to decrease cholesterol and may help to avoid heart disease. These plants include flavonoids and phenolic acids that can help fight oxidative stress and lower the risk of heart disease. Blood pressure control: Alkaloids and other substances may help to keep blood pressure levels in a healthy range, which lessens the stress on the heart. Phenolic acids and other anti-inflammatory substances may aid in preventing inflammation in blood vessels, lowering the risk of atherosclerosis: Essential oils and saponins have demonstrated potential in controlling cholesterol levels, an important aspect of heart health (Jones, C.D. et al. (2019).Numerous research have looked at the cardiovascular advantages of native Australian plants. Research has shown the anti-oxidant capacity of Kangaroo Paw extract, for instance, and has highlighted the cholesterol-lowering properties of Eucalyptus essential oils. Investigations examining the conventional usage of these plants by Indigenous cultures also provide light on the plants' possible health advantages.

Challenges and Future recommendation

Searching for bioactive substances in Australian native flora for biopharmaceuticals and healthcare is like going on a botanical treasure hunt. However, it's not a simple quest; numerous obstacles add to the adventure's intensity and complexity. The vast variety of Australian plant species, exceeding 30,000, poses a fascinating challenge. Each plant could hold the key to discovering new medications. The difficulty doesn't just lie in finding these plant treasures but also in documenting and understanding their complex chemical makeups.

These undiscovered manuscripts are like hidden stories containing bioactive substances that could revolutionize healthcare. However, finding and sharing these stories is challenging. Preserving biodiversity adds another exciting challenge, especially as we explore the uncharted territory of native Australian plants. Extracting bioactive substances requires extreme care to protect the environment, as overharvesting or unsustainable methods may endanger the very species we aim to learn from. The journey into the realm of biopharmaceuticals is also filled with regulatory obstacles. Developing pharmaceuticals from natural ingredients involves rigorous testing and adherence to complex rules and regulations, making it as challenging as scaling a botanical mountain.

Several suggestions are on the horizon to make this tour through the wild terrain of Australian native flora even more thrilling and rewarding:Discover Hidden Gems Establish a network of professionals, amateurs, and researchers who work together to explore local flora. Sharing resources and exchanging ideas may make the journey more effective and entertaining.Use ethical methods to harvest bioactive substances. Create regulations that guarantee the preservation of local flora, enabling us to profit from nature's pharmacy responsibly.We should arm ourselves with cutting-edge technology, or technological adventurism. This treasure hunt might become a high-tech adventure using sophisticated analytical tools and automation, hastening the finding process.Seek investments from the public and commercial sectors using investment expeditions. Explorers can use incentives, grants,

and assistance as treasure maps to lead them to the abundant sources of bioactive chemicals. To manage the complicated regulatory landscape, forge connections with regulatory agencies. Collaborative efforts can speed up the process from discovery to market. Rouse public enthusiasm for and interest in the beauty of native Australian plants. Everyone may become a fellow explorer via education and outreach initiatives, safeguarding and appreciating our botanical riches.

Exploring native Australian flora for bioactive chemicals is an exciting journey filled with challenges, making the discovery even more captivating. The vast diversity, the need for biodiversity protection, and complex regulations add extra layers of interest to this botanical adventure. To turn this trip into an epic adventure, we can establish cooperative networks, support sustainable practices, embrace technology, attract funding, simplify laws, and spark public curiosity. Ultimately, the value we seek lies not only in preserving Australia's unique biodiversity but also in developing groundbreaking biopharmaceuticals. This is a journey that captivates not only scientists and explorers but anyone enchanted by the wonders of nature. As we progress, let's remember that we are caretakers of the botanical riches that make our environment incredibly fascinating and beautiful while searching for healthcare treatments for cancer, cardiovascular diseases, diabetes, and inflammation.

Author contribution

A.M.S.A.M. wrote, drafted, reviewed and edited and C.P. reviewed the paper.

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Competing financial interests

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