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A Brief Overview of *Syzygium Australe's* Morphology, Traditional Uses, Phytochemistry, and Pharmacological Potential

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Abstract

The evergreen tree *Syzygiumaustrale* J.C. Wendl. ex Link.B. Hylandcommonly known as Brush Cherry; is extensively dispersed over the subtropical and tropical regions. The tree is grown for its wood, eatable fruit, and aesthetic appeal. Its diverse leaves and fruits preparations are used in folk medicine for their anaesthetic, antibacterial and antifungal activities. It has also been proposed as a food that promotes health. This review's objectives are to present a comprehensive and up-to-date overview of the active constituents in different *S. australe*organs, including phenolics, flavonoids, triterpenoids, and tannins, along with their anti-inflammatory, antimicrobial, anticancer, and antioxidant capacities.

Keywords: Antioxidant, Antibacterial, Anthocyanins, Brush Tree, Ethnopharmacological uses, *Syzygium australe*, Volatile oil.

1. Introduction

Historically, a variety of ailments have been treated with plants. In traditional therapy, plants' preparations are still used to treat microbial infections like eczema, malaria, and respiratory disorders [1].One of the largest families in the plant kingdom, the Myrtaceae, with between 3,800 - 5,800 species spread acrossaround 140 genera [2]. Key chemical constituents in Myrtaceae include terpenoids, flavonoids, and phenolic compounds, which contribute to their various biological activities [3]. Myrtaceae plants specially of *Eucalyptus, Syzygium, Eugenia and Melaleuca* genera, are rich sources of essential oils with potent antimicrobial activity [4, 5].The family is therefore crucial for pharmaceutical studies because of its well-known antibacterial, anti-inflammatory and antioxidant properties [6]. *Syzygium* is the sixteenth largest genus of perennial blossoming plants in Myrtaceae[7, 8]. It grows in tropical forests such as mud pond forests, bamboo-growing forests and coastal jungles [9]. Itis a highly diverse genus that is farmed for a variety of products, including vibrant, tasty, and juicy fruits [10, 11]. There are 1,100–1,200 species of *Syzygium*[9, 12]which are spread across the world's tropical and subtropical climates [13, 14] and cultivated for their edible fruits and medicinal properties [7, 8]. They are native to Southern East Asia, the Pacific, and Madagascar in Africa [15]. Chemical constituents commonly found in *Syzygium* species include essential oils and tannins, which have been studied for their medicinal properties [16]. These constituents enable them to have antifungal and antimicrobial activities, which help in inhibiting food spoilage and microorganisms[17]. Many studies proved antibacterial activity for several *Syzygium* species. Specially, *S. australe* and *S. leuhmannii* extracts have good antimicrobial and antioxidant activity. Moreover, *S. aromaticum* (clove) has antibacterial, antifungal activities and used in traditional medicine as anaesthetic due to its volatile oil content [18] Furthermore, a characteristic shared by *Syzygium spp.*is their potent antioxidant capacities, which attribute their pharmacological activities in cancer, heart disease, neurological problems, and related to antidiabetic activities like obesity reduction [19-22]. Among *syzygium* species, *S. australe* and *S. luehmannii* produce extremely delicious fruits. The fruits can be consumed straight from the tree or processed to create sauces, jams, and cordials. *S. australe*has been suggested as a health promoting foods. Its tree is farmed for wood, nutritious fruit and beauty value [23]. *S. australe* is cultivated in Egypt, but no detailed review has been conducted on it. Therefore, this research aims to present a full and updated assessment on morphology, ethnomedicinal applications, phytochemical and pharmacological studies of different *S. australe* organs to aid in further researching. To fullfill the objective of this study, a systematic search for literature was performed using the Google Scholar, Egyptian Knowledge Bank, Scopus, PubMed Web of Science, and Elsevier databases. This search was performed using all MeSH terms and covered all structures of isolated compounds, ethnopharmacological uses, biological activities, clinical investigations, and mechanisms for *S. australe*. The review search period was from 1982 to 2024.

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2. Taxonomy

Based on phenotypic system of classification of flowering plants, the systematic position of *S. australe*is outlined as follows [24]

Domain	Eukaryopta
Kingdom	Plantae
Subkingdom	Viridaeplantae
Phylum	Tracheophyta
Subphylum	Euphyllotina
Infraphylum	Radiatopses
Division	Magnoliophyta
Class	Magnoliopsida
Clade	Dicotyledon
Subclass	Rosidae
Superorder	Myrtanae
Order	Myrtales
Family	Myrtaceae
Genus	*Syzygium*
Species	*australe*

Synonyms

-*Eugenia australis* J.C. Wendl. ex Link(basionym)
- *Eugenia myrtifolia*Sims nom. illeg.
- *Eugenia simmondsiae*F.M.Bailey
- *Jambosa australis* (J.C.Wendl. ex Link) DC.
- *Jambosamyrtifolia*Heynh.
- *Jambosathozetiana*F.Muell.
- *Myrtus australis* (J.C.Wendl. ex Link) Spreng.

Common Names

- Brush Cherry
-Magenta Cherry
-Purple Monkey Apple.
- Scrub Cherry [23, 25, 26]

3. Origin/distribution

S. australe thrives in coastal habitats, often found in rainforest margins and wet sclerophyll forests. It is indigenous to Eastern Australia's coastal regions, which stretch from Central Queensland to New South Wales' South Coast [27].

4. Botany Description

As shown in **fig. 1 (a)** it is an erect, evergreen shrub (3–5 m tall) up to 25 m with small leaves having small oil dots. The oblong to oval, petiolate, opposite leaves measure 1-3 cm in width and 3-10 cm in length. Their lower surface is paler, having visible lateral and intramarginal veins. The apex is shortly acuminate; the base is cuneate and stem is 4-winged. Summertime is when flowering occurs most frequently. Terminal and axillary inflorescences are usually 3–7 flowered, with four yellow–white spatulate petals that are 4-6 mm long, free-flowing, and packed with stamens. The 15–20 mm long, creamy white and many stamens are present. Edible fruits **fig. 1 (b)** are produced in summer and fall in bunches of three to six. They are ovoid, measuring 15 to 25 mm in length by 15 mm in diameter, and range in color from reddish pink to red (although purple, purplish red, bluish and carmine have also been seen). The flesh is white, juicy and has a crisp, refreshing texture. It often produces solitary seeds and solitary, smooth-cotyledon embryos. Bark is flaky; outer blaze cream, pink, rarely red, fibrous in texture [27, 28].

Figure 1: Photograph of leaves (a) and Ripe fruits (b) of *S. australe*
Magnification scale of fig 1 (a) is 3.6 and of fig 1 (b) is 1.

5. Ethnobotany and medicinal uses

Traditionally, *Syzygium* species have been used to treat a wide range of illnesses, such as colds, coughs, diarrhea, dysentery, fevers, toothaches, pain, inflammation, pneumonia, wounds, hemorrhages, ulcers, and as a general tonic [29]. They are used against skin microorganisms and skin sores, while essential oils of clove are used to flavor food [18, 30-32]. Although *S. australe* is not frequently used in traditional medicine, it is beneficial due to its anesthetic properties[33].

6. Phytochemistry

6.1. Phytochemical screening

Using conventional assays, a qualitative phytochemical analysis was conducted on crude methanolic extract (ME) and its fractions to determine the existence of flavonoids, phytosterols, cardiac glycosides, phenolic substances, triterpenoids and tannins [34-36]. Results of the phytochemical screening are represented in **Table 1**.

Table 1: Preliminary screening of *S. australe* leaves and fruits extracts

	Leaves extracts					**Fruits extracts**				
Active constituents	Methanol	Water	Ethyl acetate	Chloroform	Hexane	Methanol	Water	Ethyl acetate	Chloroform	Hexane
Polyphenolics -Total & Insoluble (modified Folin–Ciocalteu procedure)	+++	+++	++	-	-	+++	+++	++	+	-
-Water soluble phenolics (modified Folin–Ciocalteu procedure)	+++	+++	+	-	-	+++	+++	+	-	-
Phytosterol (Leiberman–Buchard test) & Triterpene (modified Salkowski test)	+	+	-	-	-	+	-	-	-	-
Flavonoid (modified Kumar test)	+++	++	++	-	-	+++	+++	+	-	-
Tannin (modified ferric chloride test)	+	+	-	-	-	+	+	-	-	-
Alkaloids (Mayer's and Wagner's reagent test)	-	-	-	-	-	-	-	-	-	-
Anthraquinones (modified Kumar and Ajaiyeoba tests)	-	-	-	-	-	-	-	-	-	-

_: no response, +: weak response, ++: moderate response, +++: strong response [34-36]

6.2. Physiochemical evaluation

According to extractive values obtained as shown in **Table 2**, the largest yields of leaves and fruits were obtained from ME which were 360 mg%, for both followed by chloroform extract which were 265 and 247 mg%, respectively.The smallest yields of leaves and fruits were from hexane extract which were 50, 62 mg%, respectively. Furthermore, the fruit extract contained chemical values such total anthocyanin and total phenolic. The fruits acidified ME had a total phenolic content of 12.55±0.59 (µmol GAE/g FW)[36-38].

Table 2: Phytochemical evaluation of *S. australe* leaves and fruits and chemical values of fruits

Extract type	Extractive values (mg%)	
	Fruit	Leaf
Methanolic	360	360
Water	240	180
Ethyl acetate	110	88
Chloroform	247	265
Hexane	62	50
Chemical values of fruits		
TPC	12.55±0.59µmol GAE/g FW	
TPC	2.14 ±0.10mg GAE/g DW	
Total anthocyanins	3.17±0.06µmol CE/g FW	

CE/g FW: cyanidin 3-glucoside equivalent / gram of fresh weight, GAE/g FW: gallic acid equivalent / gram of fresh weight, GAE /g DW: gallic acid equivalent / gram of dry weight, TPC: total phenolic compounds.

6.3. Analysis by GC-MS headspace

The aqueous and methanolic extracts (AE and ME) of *S. australe* leaves were examined using GC-MS headspace [36]. The main compounds found in the *S. australe* extracts were 1-vinylheptanol (5.8 and 12.1%), 2-ethyl-1-hexanol (6.5 and 8.7%), 2-heptyl-1,3-dioxolane (2.6 and 2.8%) and 1-methyloctyl butyrate (6.3 and 3%). Also, there were terpinen-4-ol (0.19 and 0.42%), caryophyllene oxide (0.6 and 0.2 %). linalool (1.1 and 0.1%), exo-fenchol (3.3 and 0.1%). 1-terpineol (2.8 and 3.6 %) and L-camphor (0.1 and 0.1%) were also detected. They were each given a relative abundance percentage in the ME and AE, respectively. Also, they contained terpenoids such as endo-borneol, isoneral (0.25 and 0.2% in the AE, respectively) and isoborneol (9.5% in the ME) as shown in (**fig. 2)** The ME showed two additional peaks (borneol and terpineol) that were not present in the AE. Both chromatograms also showed a number of minor peaks [36].

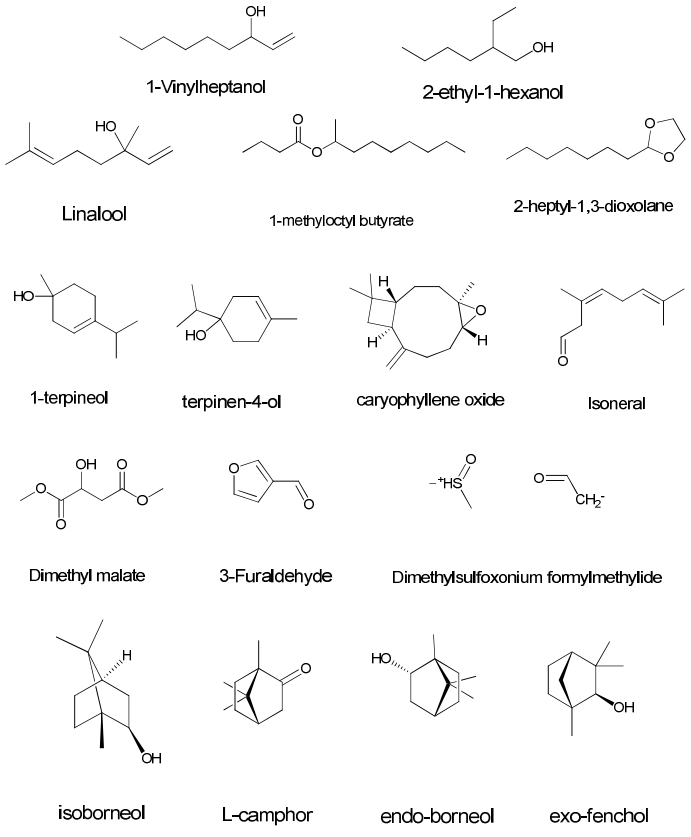

Figure 2: Terpenoids structures identified by Headspace GC/MS-MS of *S.australe*leaves.

6.4. Analysis by HPLC/ESI/MS-MS

HPLC/ESI/MS-MS was used to determine anthocyanin composition from fruits acidified ME. The overall anthocyanin content was 3.17±0.06 µmol CE/g FW. Malvidin 3,5-diglucoside was the main pigment with 76.3% of the total content. among the four anthocyanin compounds. Additional three minimal peaks were observed and accounted for 13.3%, 6.6% and 3.8% of the total anthocyanin content. They were assigned as petunidin 3,5-diglucoside, delphinidin 3,5-diglucoside and peonidin 3,5-diglucoside, respectively (**fig.3)**[37].

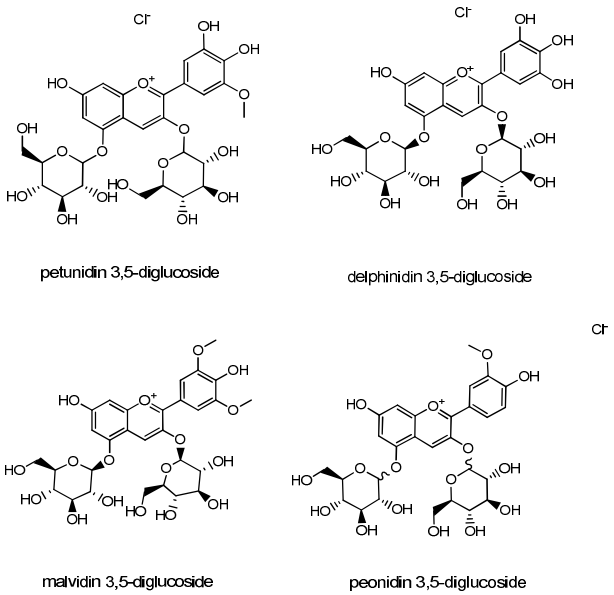

Figure 3: Anthocyanins' structures by using HPLC/ESI/MS-MS analysis on *S. australe* fruits.

7. Biological activity

7.1. Quantification of toxicity

7.1.1. Artemia nauplii bioassay

The *Artemia nauplii* bioassay was performed to evaluate the toxicity between 125 to 2000 µg/ml for *S. australe*leaves and fruits using potassium dichromate. Leaves extract showed hazardous properties with LC_{50} values $\leq 10^3$ µg/ml. In contrast, fruits extracts were considered non-toxic due to their values being higher than 10^3 µg/ml [39]. The concentrations of the ethylacetate, chloroform and hexane leaves and fruits extracts showed toxicity more than 50% thus, the toxicity values couldn't be determined against Artemia lethality assay and Normal human primary dermal fibroblast [36].

7.1.2. Therapeutic index (TI)

Leaves ME demonstrated substantial potential with treatment indices > 10 against all fungal infections. Additionally, this extract was found to have TI values of 35.2 when against *E. floccosum*, implying that it is a viable, safe therapeutic choice. The fruit ME had TI values of 11.9 and 13.5 for the clinical strains of *Candida albicans* and *E. floccosum*, respectively. The TI values of ethyl acetate, chloroform, and hexane leaves and fruits extracts against all fungal infections could not be determined. As they were found to be less than 50% at all concentrations tested, indicating that they were not hazardous [36].

7.2. Antioxidant activity

The strong antioxidant capabilities of *Syzygium*species are a common characteristic. The increased awareness of antioxidant plants is directly linked to the preventive benefits associated with lower incidence of neurological degenerative disorders, cancer, and cardiovascular diseases [19-22]. Additionally, it has been correlated to preventing diabetes, decreasing obesity, scavenging free radicals, and shielding cells from oxidative stress, which could result in lipid, protein, and nucleic acid damage [22]. By using the DPPH assay [34, 35, 40], the total antioxidant capacity was estimated and expressed as mg ascorbic acid equivalent (AAE) / g of plant material. The antioxidative potential of aqueous, ethyl acetate and methanolic leaves extracts were (2.6, 25, 40 mg AAE, respectively) and that of fruit were (55, 41, 9.2 mg AAE, respectively). Chloroform and hexane extracts of both organs were below the detection threshold. Using the Trolox Equivalent Antioxidant Capacity Assay (TEAC) and the Photochemiluminescence (PCL) assay, the antiradical characteristics of the fruits acidified ME were studied. The fully ripened fruits extract has a 26.95±0.64 µmol TE/g FW and 3.28±0.19 µmol TE/g FW antioxidant capacity

according to TEAC and PCL assays, respectively [36, 37]. The total antioxidant capacity of fruits acidified ME according to ferric reducing antioxidant power assay is 4.58 ± 0.11 mgTE/g [26]. According to Netzel et al. (2007) [37]*S. australe* fruits grown in New South Wales exhibit high antioxidant activity, which makes them possibly therapeutic. Additionally, fruits of *S. australe* were found to exhibit very high antioxidant activity in DPPH assay [37, 38]. *S. australe* fruits had an ascorbic acid content of 0.72 μmol/g, which was roughly 10–25 times greater (g/g) than blueberries. There are a lot of additional substances rather than ascorbic acid which are correlated to their strong antioxidant activity [37, 38].

7.3. Antimicrobial Activity

Many species of *Syzygium* exhibit antibacterial activity against a broad spectrum of microorganisms associated with inflammation and autoimmune disorders [18]. The AE and ME of *S. australe* greatly reduced the growth of *Klebsiella pneumoniae* according to a recent study using leaves and fruits extracts [41]. *Klebsiella pneumoniae* is the cause of ankylosing spondylitis (AS), thus inhibiting its growth will stop AS from developing. They also inhibited *S. pyogenes* growth [18]. The growth of many bacterial species, suchas *Aeromonas hydrophilia, Alcaligenes faecalis, Citrobacter freundii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas fluorescens, Serratia marcescens, Bacillus cereus,* and *Staphylococcus aureus,* are inhibited by the ME from *S. australe*leaves, with MIC values reported to range between 200 and 3000 μg/ml [18]. *S. australe* fruits extracts outperformed its leaves extracts in their ability to combat *Shewanella spp.* with low toxicity [42]. By liquid dilution assay ME and AE of fruits have MICs against *Shewanella spp.* (86-600 and 375-150 μg/ml, respectively). Likewise, the same extracts of the leaves have MICs (563-1100 and 281-2300 μg/ml, respectively) [26]. In the Artemia nauplii lethality test, fruits ME and AE have LC_{50} values $>10^3$μg/ml, indicating negligible toxicity. In contrast, leaves ME and AE have LC_{50} values of 294 and 244 μg/ml, respectively [18, 26, 43]. 73% of gram-negative bacteria and 67% of gram-positive bacteria were inhibited by leaves ME. When tested against *Salmonella salford, Bacillus subtilis, Saccharomyces cerevisiae, Enterobacter aerogenes*, and *Escherichia coli*, this extract exhibited no action [32]. ME and AE of fruits have mean MIC values of 769 and 636.9 μg/ml against *Proteus mirabilis*, respectively. Leaves ME and AE have also mean MIC values of 976.3 and 1328.4 μg/ml, respectively [26]. *C. albicans* and *S. cerevisiae* were unaffected by the extract's antifungal effects, while a nystatin-resistant strain of *A. niger* was affected [32]. Noteworthy, most of the fungi evaluated in those trials were fluconazole-resistant strains [44]. Consequently, *S. australe* was used to treat fungal skin conditions [45]. Furthermore, standard disc diffusion and liquid dilution MIC protocols were employed on a panel of human dermatophytes to test the fungal growth inhibiton capacity of plant extract [36, 42]. Consequently, *S. australe* leaves extracts with the highest TIs and fungal inhibitory activities by (MIC) were the most promising for phytochemical profile analysis [36].

7.4. Anti-inflammatory and analgesic activity

Extracts of *Syzygium* species and essential oils can reduce the symptoms of various disorders by inhibiting the last phase inflammatory processes. Modulating the immunological response once it is triggered, prevent the contact between the antigen and the immune system. Recent research showed that ME and AE of *S. australe* of both leaves and fruits were able to significantly inhibit *K. pneumoniae* growth [18, 41]. Since the preventative properties may be specific to each autoimmune disease, such as in the prevention of rheumatic and inflammatory conditions, further studies are required to assess the antimicrobial activity against the distinct microbial initiators[18, 46-48].

7.5. Anticancer activity

Fruit extracts (methanolic, water, and ethyl acetate) show possible cytotoxic effect. Not only against cervical cancer (HeLa) but also colon carcinoma cancer (CaCo2) cell lines using the MTS cell viability assay featuring selectivity index (SI) values between 14.02 and 45.97. The ethyl acetate extract of fruits showed higher anticarcinogenic activity against the Hela cell line than both AE and ME. However, the AE exhibited greater activity than ME against the CaCo2 cell line. Leaves ME was more powerful than AE against the HeLa cell line but AE was stronger than ME against the CaCo2 cell line [40]. Despite achieving relatively low SI values (0.86-1.57), leaves extracts demonstrated effectiveness against these cancer cell lines as well. SI values over 20 are generally regarded as having low cell toxicity attributing them an excellent candidates for the creation of pharmacological drugs [49].

8. Conclusion

In summary, S.*australe* has a wide range of bioactive chemicals that support its antimicrobial, anti-inflammatory, anticancer, and antioxidant properties, making it a potentially useful medicinal plant. Its fruit, which is rich in antioxidants like ascorbic acid, demonstrates its potential as a food that might improve health. Further studies are required to completely comprehend its pharmacological benefits and safety for humans. Clinical investigations and more research into its bioactive components could make *S. australe* a valuable resource for the pharmaceutical and nutraceutical industries.

9. Conflicts of interest

The authors declare no conflict of interest.

10. Abbreviations

Abbreviations	
ALA	Artemia lethality assay
A. niger	*Aspergillus niger*
AE	Aqueous extract
AS	Ankylosing spondylitis
CaCo2	Colon carcinoma cancer
C. albicans	*Candida albicans*
DPPH	2,2-Diphenyl-1-picrylhydrazyl
E. floccosum	*Epidermophyton floccosum*
equ. / g	Equivalent per gram
GAE /g DW	Gallic acid equivalent / gram of dry weight
GAE/g FW	Gallic acid equivalent / gram of fresh weight
HDF	Normal human primary dermal fibroblast
Hela	Cervical cancer
K. pneumoniae	*Klebsella pneumoniae*
ME	Methanolic extract
mg aa equivalent	Milligram ascorbic acid equivalent
mg TE/g	Milligram Trolox equivalent per gram
M. gypseum	*Microsporumgypseum*
MIC	The minimum inhibitory concentration
MTS	(3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay is used to assess cell proliferation, cell viability and cytotoxicity
PCL	Photochemiluminescence
S. australe	*Syzygiumaustrale*
S. leuhmannii	*Syzygiumleuhmannii*
S. pyogenes	*Streptococcus pyogenes*
S. cerevisiae	*Saccharomyces cerevisiae*
TEAC	Trolox equivalents antioxidant capacity
TE/g FW	Trolox equivalents per gram of fresh weight
T. mentagrophytes	*Trichophyton mentagrophytes*
TPC	Total phenolic compounds
T. rubrum	*Trichophyton rubrum*

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