

Review



Phytochemical Properties and Diverse Beneficial Roles of Eucalyptus globulus Labill.: A Review

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Abstract: Eucalyptus globulus Labill. is one of the most widely utilized medicinal plants throughout the world due to its wide spectrum of interesting biological activities that are mainly attributed to the diversity of phytochemical constituents in the plant parts. The emerging crisis of pathogen resistance for conventional antibiotics is considered a global concern for the diminishing effectiveness of antibiotics; hence, there is an urgent need to explore new antimicrobial ingredients from botanical sources, among which the most promising sources are medicinal plants. Moreover, the growing limitation toward synthetic antioxidants motivated the scientific community all over the world to identify plant-acquired antioxidants and antimicrobials. This is a huge global challenge, because of the increasing public health awareness and reliance on natural compounds, as these compounds are safer alternatives. Moreover, the undesirable impacts of synthetic pharmaceuticals can be avoided. Furthermore, plant extracts and their oil could be used as eco-friendly plant-based products for insects, weeds, and plant pathogen control, which will diminish the dependence on synthetic chemicals. Thus, this review is to highlight the richness of the E. globulus plant, with precious bioactive constituents, antioxidants, antimicrobials, and phytoremediation, and herbicidal activities, which will pave the way to the development of new pharmaceuticals and agrochemicals, as well as food preservatives. They may also provide potential commercial applications to counteract the limitations of synthetic antioxidants.

Keywords: antimicrobial activity; antioxidant activity; *E. globulus*; essential oil; herbicidal activity; 1,8-cineole; phytoremediation

1. Introduction

E. globulus belongs to the family of Myrtaceae; an evergreen broadleaf tree, with a straight trunk, indigenous to Australia, the genus *Eucalyptus* comprises of more than 700 species [1]. It is known as "the blue gum" or Tasmanian blue gum. Nowadays, *E. globulus* is extensively cultivated worldwide [2–16] because of its easy adaptability to environmental conditions, ease of cultivation, fast growth rate, and increase in the woody biomass. Furthermore, it can be planted in contaminated areas [17]. Obviously, *Eucalyptus* can adapt to biotic and abiotic stresses by selectively releasing defense compounds mainly of mono- and sesquiterpenes, as well as some hydrocarbons and quinones [18]. *E. globulus* has attracted the attention of researchers as well as environmentalists worldwide, due to it commonly being used in the pulp industry as a fast-growing source, and for the essential oil extracted from its leaves. Commercially, it is widely used for different purposes.

The essential oil of *Eucalyptus* spp. is among the 18 most frequently traded essential oils throughout the world. On account of this, there is an increasing amount of attention paid to their advantages as raw materials, which can be used in food, pharmaceuticals, and cosmetics, both in scientific and industrial research [1,19]. Among them *E. globulus* Labill. is the main source of the *Eucalyptus* leaf oil used globally [3]. Its leaves are alternate,



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Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). with yellowish petioles, precisely lanceolate, 10–30 cm long, 2.5–5 cm wide, shiny dark green on both surfaces, and are a rich source of essential oil [7,10,20–22]. The oil is typically extracted by hydrodistillation, as the greatest amount of extracted chemical compounds can be obtained by utilizing this method [4,15,21]. The essential oil yield ranges from 1–3% [1,3,9,19,20,23]. The chemical composition of the *Eucalyptus* leaf essential oil is a complex mixture of substances, commonly containing 20 to 54 components with varying concentrations [4,8,13,15,24]. The oil comprised particularly of oxygenated monoterpenes (80.65–87.32%) as well as monoterpene hydrocarbons (18.33–12.45%) [9,25].

The extracted leaf essential oil is more or less pale yellow and has a pleasant odor, having a camphor-like smell [5,20,26]. The physical properties of this oil include a refractive index from 1.4657 ± 0.0070 to 1.4693 ± 0.00057 , a specific gravity from 0.913 to 0.919 g/cm³ [5,20], an optical rotation of +1.5956, and a pH (22 °C) of 4.9 [5]. The chemical properties of the extracted leaf essential oil, which include acid value, saponification value, hydroxyl value, and iodine value, are 0.5945, 19.576, 31.61, and 41.52, respectively [5]. All of the previous physicochemical properties are considered significant for oil quality determination, especially for marketing strategies.

The major component of the essential oil of *Eucalyptus* leaves is monoterpene oxide 1,8-cineole (Figure 1), also known as Eucalyptol [3,9,13,20,21]. Eucalyptol is commonly utilized in flavoring, fragrance, and cosmetics. This is attributable to its pleasant spicy aroma and taste. It is also used in mouthwash applications and cough suppressants [22]. The commercial value of the essential oil depends chiefly on the existence of 1,8-cineole [9,26]. Consequently, the absence of 1,8-cineole and existence of α -phellandrene in the Nigerian-grown *E. globulus*, which has a high cytotoxic effect, make the oil suitable for insecticidal formulations and inappropriate for medicinal purposes [27].



Figure 1. Chemical structures of the main components of Eucalyptus leaf and fruit essential oils.

Eucalyptus leaf essential oil has drawn the attention of numerous researchers, as it represents a wide range of biological potentials, such as antibacterial efficacy toward both Gram-positive and Gram-negative bacteria [28,29] and considerable antibacterial potency against periodontal diseases [20,30]. Therefore, it can be incorporated into dental care products, as it is an anti-inflammatory agent [10,31]; has antifungal [16,28,32,33] and antidiabetic potential [34,35]; insecticidal [36–39], acaricidal, and repellent activities; is a biodegradable pesticide [40]; has bio-nematicide efficacy [7], phytopathogen control [8,23], and anthelmintic activity [41]; and it is a natural agent for food preservation [25]. Furthermore, this leaf essential oil has been previously applied in "folk medicine, in the treatment of respiratory problems, including, cold, cough, runny nose, sore throat, asthma, nasal congestion, bronchitis, and sinusitis" [42].

In a study conducted in Germany, the authors identified the main compound in the essential oil of hydro-distilled fruits to be; aromadendrene (Figure 1), which exerted antibacterial activity [3,43]. Nevertheless, Bey-Ould Si Said et al. [44], revealed the predominance of globulol (23.6%), which is the major component in the fruit oils extracted from

plants growing in the north-east of Algeria (Figure 1). The essential oil of fruits possesses antibacterial activity [43,44]; hence, fruit oil is a potential candidate for application in the pharmaceutical and food industries.

Leaves and root extracts possess antioxidant, anti-inflammatory, and antitumor activities [35,45–47], which correlate with the elevated amount of plant phytoconstituents. Additionally, leaf extracts possess fungicidal potency [48], allelopathic potential [49–51], anti-hyperglycemic potential [52], a potential anticancer activity [53], antibacterial activity [30,54,55], and neuroprotective activity [56]. In addition, leaf extracts are presently utilized in cosmetic formulations and food additives [35]. The *E. globulus* stump that is defined as "the basal part of the tree", including the near-the-ground stem portion, and the woody roots that remain after "stem felling", possesses antioxidant and antimicrobial activities [57].

The aim of the current review is to present recent information on the phytochemical, antioxidant, and antimicrobial aspects of the *E. globulus* plant parts, besides the factors influencing the essential oil composition of the plants, and also its eco-friendly applications. This may help gather fruitful information for the potential use of the plant, as a precious source of diverse ingredients, in multiple applications.

2. Bioactive Components

Miscellaneous investigations revealed the occurrence of considerable amounts of versatile bioactive components in the different plant parts, which are presented in Table 1. These phytochemicals are responsible for the therapeutic impacts of the plant [2,9,43,44,47]. In most of the studies, 1,8-cineole is the dominant component in the essential oils of leaves, with various percentages (Table 1), except for a few findings [26,27,58,59]. Furthermore, phytochemical analysis of the leaf extracts proved the presence of tannins, saponins, terpenoids, glycosides, alkaloids, phenolic compounds, steroids, cardiac glycosides, terpenes, reducing sugars, carbohydrates, resins, acidic compounds, and flavonoids [19,30,52,60]. In addition, the high phenolic content in the *Eucalyptus* plant parts (Table 1) that correlated with positive health influences against oxidative stress has also been formerly documented [2,46,56,57,61]. Additionally, triterpene compounds that possess significant pharmaceutical applications have been previously identified in *Eucalyptus* leaves, bark, and fruits [62–64].

Plant Parts	Major Constituents	References
Leaves	1,8-cineole (31.42%) and trans-3-carven-2-ol (10.10%), 2-Octen-1-ol, 3,7-dimethyl (9.37), and Cis-p-Menth-2,8-dienol (6.33)	[36]
Leaves	1,8-cineole (86.51%), α-pinene (4.74%), γ-terpinene (2.57%) and α-phellandrene (1.40%)	[3]
Leaves	1,8-cineole (95.61%) and alpha-pinene (1.5%)	[65]
Aerial parts	1,8-cineole (79.85%), Limonene (6.72%), <i>p</i> -cymene (5.14%), and γ -terpinene (3.93%)	[25]
Leaves	1,8-cineole (85.8%), α -pinene (7.2%), and β -myrcene (1.5%)	[9]
Leaves	γ-terpinene (94.48%) and 1,8-cineole (3.20%)	[58]
Leaves	1,8-cineole (33.6%), α-pinene (14.2%), and d-limonene (10.1%)	[38]
Leaves	Terpinen-4-ol (23.46%), γ-terpinene (17.01%), pathulenol (8.94%), ρ-ymene (8.10%) and ρ-cymen-7-ol (6.39 %), globulol (2.52%), and α-phellandrene (2.20%)	[27]
Leaves	1,8-cineole (22.35%), limonene (7.01%), solanol (6.05%), β-pinene (5.20%), trans-verbenol (4.02%), and terpinen-4-ol (3.10%)	[8]
Leaves	1,8 cineole (51.08%), α-pinene (24.60%), L-pinocarveol (9.98%), and globulol (2.81)	[5]
Leaves	1,8-Cineole (71.05%) and α-pinene (8.30%)	[1]
Leaves	Phenolics (quercetin and luteolin)	[2]
Leaves	1,8-cineole (76.65%), α -pinene (5.65%), α -terpineol acetate (4.85%), and alloaromadendrene (3.98%)	[11]

Table 1. Phytochemical compounds reported in the different parts of E. globulus Labill.

Plant Parts	Major Constituents	References
Leaves	1,8-cineole (62.38%), α-pinene (23.79%), α-terpinyl acetate (5.41%), globulol (1.68%), and β -pinene (1.1%)	[15]
Leaves	1,8-cineole (55.29%), spathulenol (7.44%), and α -terpineol (5.46%)	[20]
Leaves	1,8-cineole (36.68%), β-pinene (9.25%), aromedendrene (6.33%), and globulol (5.11%)	[6]
Leaves	Chlorogenic acid, rutin, and quercetin 3-glucuronide and ellagic acid derivatives	[45]
Leaves	1,8-cineole (54.79%), β-pinene (18.54%), α-pinene (11.46%), β-eudesmol (4.68%), α-phellandrene (2.06%), para cymene (1.60%), and gamma-eudesmol (1.20%)	[4]
Leaves	<i>p</i> -Cymene (18.18%), methyl eugenol (8.83%), 4-Terpinenol (8.45%), s-methyl 3-methylbutanethioate (7.26%), g-terpinene (5.12%), and 1,8-cineole (3.16%).	[59]
leaves and small branches	1,8-cineole (63.81%), α-pinene (16.06%), aromadendrene (3.68%), and o-cymene (2.35%)	[13]
Leaves	1,8-cineole (63.00%), α-pinene (16.10%), and camphor (3.42%)	[14]
Leaves	1,8-cineole (48.2%), α-pinene (16.1%), γ-terpinene (8.9%) and <i>p</i> -cymene (8.8%)	[35]
Leaves	1,8-cineole (75.8%), <i>p</i> -cymene (7.5%), α-pinene (7.4%), and limonene (6.4%)	[12]
Leaves	1,8-cineole (69.32%), camphene (9.41%), α-pinene (7.48%), and α-terpineol (5.08%)	[23]
Leaves	1,8-cineole (46.76%), D-limonene (9.61%), and o-cymene (6.49%)	[37]
Leaves	Phenolic compounds (quercetin, luteolin, kaempferol, iso-rhamnetin, phloretin, chlorogenic acid)	[56]
Leaves	1,8-cineole, phenolic acids (Gallic acid, ellagic acid, vanillic acid, <i>p</i> -hydroxybenzoic acid, <i>p</i> -coumaric acid, and quercetin), phenolics (catechin, rutin, and luteolin)	[46]
Leaves	1,8-cineole (70.94%), 3-cyclohexene-1-ol (3.13%), beta. fenchyl (5.38%), 1,2-benzenedicarboxylic acid (6.08%), dodecane (1.50%)	[66]
Leaves	Eucalyptol (59.63%), p-cymene (15.55%), and DL-limonene (14.90%)	[16]
Leaves	Eucalyptol (55.43%), α-pinene (25.55%), and D-limonene (5.687%)	[24]
Leaves	1,8-cineol (56.83%), L-pinocarveol (10.42%), α-pinene (9.47%), globulol (7.68%), and carvacrol (1.59%)	[33]
Leaves	<i>p</i> -cymene (20.24%), spathulenol (14.10%), and eucalyptol (11.30%)	[26]
Leaves	1,8-cineole (23.3%), citronellal (18.1%), geranial (17.6%), isopulegol (10.4%), myrcene (13.0%), cuminaldehyde (9.1%), and 2-pinene (8.5%)	[7]
Leaves	1,8-cineole (80.2%), <i>p</i> -cymene (6.6%), and limonene (5%)	[10]
Leaves	D-limonene (23.5%), m-cymene (24.8%), <i>o</i> -cymene (9.9 and 5.4%), 6-camphenol (7.2 and 10.7%), terpinen-4-ol (5.2 and 4.5%), and globulol (4.0 and 12.9%)	[34]
Leaves	Eucalyptol (51.62%), α-pinene (23.62%), <i>p</i> -cymene (10%), β-myrcene (8.74%), terpinen-4-ol (2.74%), and γ-terpinene (2.59%)	[22]
Leaves	1,8-cineol (67.4 and 67.6%) and α -pinene (12.8 and 13.1%)	[21]
Fruits	Aromadendrene (31.17%), 1,8-cineole (14.55%), globulol (10.69%), and ledene (7.13%)	[43]
Fruits	Globulol (23.6%), aromadendrene (19.7%), 1,8-cineole (19.8%), and α -pinene (3.8%)	[44]
Bark	Polyphenol and tannin	[61]
Deciduous bark	Fatty acids, aliphatic alcohols, sterols, and triterpenoids	[63]
Bark	Polygalloyl glucoses (gallotannins), catechin, epicatechin, ellagic acid, quercetin-3-o-rhamnoside, and isorhamnetin (phenolic compounds)	[67]
Stump	Phenolic compounds and flavonoids	[57]

Table 1. Cont.

The anthelmintic activity of the essential oil from extracted leaves has been previously reported by Taur et al. [41]. This has been ascribed to the occurrence of valuable phytoconstituents in the oil, such as borneol, linalool, cineol, geranyl acetate, anethol, and saffrol. Additionally, phytochemical and fingerprint analyses of the essential oil from leaves displayed a higher content of flavonoids, as compared to phenols, whereas the Fourier Transform Infrared Spectrophotometer proved the existence of polyphenolic compounds, such as rutin, tannic acid, vanillic acid, and ascorbic acid, which is vastly utilized in the food industry. Furthermore, the gas chromatography analysis characterized the major constituents of the essential oil as 1,8 cineole (29%), α -pinene (16.9%), and β -pinene (16%) [31].

Pyrolysis gas chromatography-mass spectrometry analysis of the Eucalyptus leaves' aqueous ethanol extract identified the presence of 21 compounds and the key characterized compounds were β -eudesmol (12.84%), γ -eudesmol (3.36%), globulol (2.87%), and alloaromadendrene (3.80%); in contrast, the presence of α -selinene and α -gurgujene was observed in low concentrations [54]. Furthermore, the detection of guaiacol, syringol, o-cymene, catechol, and phenol could be associated with the presence of small fragments of lignin and lignin-derived monomeric products in the leaf extracts [54]. The major triterpenic acids identified in the *E. globulus* leaf extracts were betulinic, betulonic, oleanolic, ursolic, 3-acetyloleanolic, and 3-acetylursolic acids, which were considered to be valuable pharmaceutical compounds [62]. Gas chromatography-mass spectrometry analysis (GC-MS) of the methanolic extract identified the existence of nine compounds, 9,10-secocholesta-5,7,10(19)triene 1, 3-diol,25 [(trimethylsily) oxy] (,3β, 5Z,7E)-, 1-Heptatriacotanol, Morphinan-4,5 epoxy3,6diol, 6 [7nitrobenzofurazan-4-yl] amino, 10-Heptadecen-8-ynoic acid, methyl ester, [E]-, Ethyl Iso-allocholate, 2-Myristynoyl pantetheine, Cholesta-8,24-dien-3-ol,4-methyl-, $[3\beta, 4\alpha]$ -, Cyclopropanedodecanoic acid, 2-octyl-, methyl ester, 9,12,15-Octadecatrienoic acid, and 2-phenyl-1,3-dioxan-5-yl ester [52]. Interestingly, hydrosol, obtained as a byproduct of leaf hydrodistillation, exhibited an effective insecticidal activity toward the mealybug, which nominated it as a potential biodegradable insecticidal compound, instead of a synthetic pesticide [68].

Regarding the chemical composition of the bark, Domingues et al. [64] reported the exploitation practicality of using the large quantities of bark generated by pulp industries as a by-product, instead of burning it for energy production, as it was rich in valuable triterpenoid compounds (betulonic, betulinic, 3-acetylbetulinic, ursolic, 3-acetylursolic, oleanolic, and 3-acetyloleanolic acids) in addition to β -amirine, β -sitosterol, palmitic acid, and aliphatic alcohols. Additionally, triterpenoid acids were chiefly concentrated in the surface layers of the trunk and the bark branches. The triterpenoid content was 1.2 g/kg in fruits and 121.1 g/kg in the surface layers of the bark branch residues.

Although the bark is an industrial waste product, its aqueous extract contains a natural source of antioxidant that is attributed to an abundant amount of gallotannins and some other phenolic components [67]. Similarly, the *E. globulus* bark has a plethora of polyphenolic compounds that exhibit anti-proliferative activity against carcinoma cells [69]. Moreover, De Melo et al. [63] stated that the deciduous bark of *E. globulus* contains ursolic and 3-acetylursolic acids, as the most abundant components, representing 52% of triterpenic acids, while hexacosan-1-ol and octacosan-1-ol from aliphatic alcohols represent approximately 7% of the total extract, even as the sterols fraction represents 4.24% of the total extract and β -sitosterol represents the most of this group (Sterols) (4.05% vs. 4.24%).

In recent times, Lourenço et al. [70], for the first time, identified using GC-MS, eight polyhydroxy triterpenoid acids from the milled wood of mature *E. globulus* mature trees (40 years), the dichloromethane extract, which included "hederagenin, (4 α)-23-hydroxybetulinic acid, maslinic acid, corosolic acid, arjunolic acid, asiatic acid, caulophyllogenin, and madecassic acid, with 2,3, and 4 hydroxyl substituents", which represented 10.4% of the wood extract. These characterized compounds are known to have interesting pharmaceutical and medical applications.

3. Factors Influencing the Essential Oil Composition of Plants

Several studies concentrated basically on the diversity of the essential oil composition extracted from the plant leaves, which is considered the main commercial source of 1,8-cineole, as depicted in Table 1. The fluctuation in essential oil components linked the phenological stage, environmental conditions, seasonal variations, occurrence of chemotypes, and extraction methods to geographical locations.

One of the major ingredients of the *Eucalyptus* leaf oil is 1,8-cineole (Eucalyptol). It is a cyclic ether with an empirical formula C_{10} H₁₈O. Eucalyptol determines the commercial

value of Eucalyptus essential oil for various industries [71]. Recent studies have demonstrated the tremendous potential of Eucalyptol and its antimicrobial properties (reviewed in [71]). It's percent and antibacterial activity depends on the specific species [1,19]. The predominance of Eucalyptol is overwhelming, as seen in the previous studies (Table 1). It has been formerly mentioned that oil from cultivated plants, from diverse regions of the world, denote the following various percentages: 86.51% in Germany [3], 85.8% in Montenegro [9], 80.2% in Turkey [10], 76.65% in Iran [11], 75.8% in Brazil [12], 71.05% in Brazil [1], 69.32% in Brazil [23], 63.81% in Spain [13], 63.00% in Ethiopia [14], 62.38% in Ethiopia [15], 59.63% in Serbia [16], 56.83% in Algeria [33], 55.43% in Ethiopia [24], 55.29% in Algeria [20], 54.79% in India [4], 51.62% in Tanzania [22], 51.08% in Algeria [5], 48.2% in Tunisia [35], 46.76% in Egypt [37], 36.68% in Portugal [6], 23.3% in Nigeria [7], and 22.35% in Morocco [8]. It is observed from the above cited studies that the patterns of leaf essential oil compositions differ notably in the plants cultivated in different locations, which consequently reflect on their biological activities.

On the other hand, some previous findings also characterize the various main components from plants growing in other regions, where the major component of leaf essential oil from plants grown in Algeria is identified by GC as γ -terpinene (94.48%) and 1,8-cineole (3.20%) [58]. Additionally, Benabdesslem et al. [26], reported that p-cymene (20.24\%) is the major constituent in the Algerian-grown *E. globulus* plants (southwest Algeria) and the authors concluded that *Eucalyptus* leaves originating from the same region, as well as their essential oils, can be utilized for the influenza virus, as inhalants and as a substitute for imported materials. Both the aforementioned studies were in contrast with the results obtained by Harkat-Madouri et al. [20], for the plants grown in north east Algeria, where the authors identified 1,8-cineole (55.29%), spathulenol (7.44%), and α -terpineol (5.46%) as the predominant components. The oil from the plants grown in Nigeria had terpinen-4-ol (23.46%) as the most abundant component, but 1,8-cineole was not detected in the leaf essential oil [27]. Additionally, p-cymene was a predominant component in Tunisian-grown Eucalyptus and accounted for 18.18%, while 1,8-cineole represented 3.16% [59]. In contrast, Pino et al. [21] found that the chemical composition of the leaf essential oil was not significantly influenced by the growth region in Ecuador.

The phenological stage led to marked influences on the essential oil yield and composition. Salem et al. [72] found, on Tunisian-grown *Eucalyptus*, that the plants harvested at the late fructification stage produced the highest oil yield (0.32% w/w) as compared to the essential oil yield of plants harvested at the vegetative and full flowering stages (0.11 and 0.14% w/w, respectively), which was ascribed to the development of secretory structures of essential oil, that are often associated with plant ontogeny. Furthermore, plant growth development and essential oil accumulation were greatly influenced by environmental conditions. Additionally, the essential oil ingredients were also altered by the growth stage; thus, at the vegetative and full flowering stages, the major components were 1,8-cineole and *p*-cymene (13.23 and 32.19%, respectively); although, in the fructification stage, the main compound was 1,8-cineole (37.82%).

Abdossi et al. [11] stated that the *E. globulus* essential oil composition was greatly influenced by environmental circumstances. According to Luís et al. [13], the variation in the main components of essential oil could be ascribed to the "genetic variation, plant organ, and different environmental factors".

With regard to seasonal variations, Usman et al. [34], found that the essential oil of *E. globulus* grown in north-central Nigeria had D-limonene and m-cymene chemotypes as the predominant compounds (23.5 and 24.8%, respectively) detected in the leaf oil procured in the dry and rainy seasons, respectively. For efficient oil extraction from *E. globulus* leaves, hydrodistillation was used to produce a higher amount of oil yield, such as 1.1 and 1.21% of essential oil (w/w, based on the fresh weight of the mature leaves) [4,15] rather than the oil obtained (0.2% w/w) from steam distillation [5]. Although steam distillation was more favorable than traditional hydrodistillation, the aromatic oil obtained from steam distillation was appropriate for food processing as a plant-derived flavoring agent.

4. Antioxidant Activity of E. globulus Labill.

The increasing awareness of synthetic antioxidants motivated a number of scholars, on a global scale, to identify alternative antioxidants of plant origin, to avoid the unfavorable effects of synthetic antioxidants [13,34,45]. In this regard, the antioxidant potential of different *Eucalyptus* plant parts (leaves, fruits, roots, and stump wood) as well as their essential oils were formerly reported as being able to be utilized to diminish oxidative stress-associated diseases, and also as food preservatives [13,31,47,57]

The leaf essential oil of Nigerian-grown *E. globulus* exhibited a low antioxidant capacity via its potential to scavenge DPPH radicals, with elevated IC₅₀ values (136.87 μ L/mL) as compared to the standard antioxidant ascorbic acid. This may be attributed to the absence of some components such as 1,8-cineole in the leaf oil as well as the potential antagonistic impact between other components in *Eucalyptus* oil [27]. Conversely, Luis et al. [13] reported that the essential oil of *E. globulus* exerted a remarkable antioxidant efficacy through its ability to scavenge DPPH radicals with an IC₅₀ value (2.90 ± 0.35 v/v), with respect to the IC₅₀ value (4.56 ± 0.70 v/v) for *Eucalyptus radiata*. This may be related to the existence of 1,8-cineole as the main constituent only in *E. globulus* essential oil of *E. globulus* showed great activity to inhibit the lipid peroxidation with an IC₅₀ value (2.72 ± 0.01 v/v) inferior to the activity of the synthetic antioxidant BHT, with an IC₅₀ value of 3.58 ± 0.02 w/v, in the β -carotene bleaching test. This was considered a promising result that supported the *E. globulus* essential oil as a potential natural substitute, to overcome the adverse side effects of synthetic antioxidants, especially for food preservation.

Salem et al. [72] stated that the elevated antioxidant activity was detected at the full flowering and fructification stage; thus, a positive relationship existed between the essential oil content and its antioxidant potential. Furthermore, the essential oil of the aerial parts showed a potent DPPH scavenging capacity as well as moderate reducing power efficacy as compared with butylated hydroxyanisole (BHA) and ascorbic acid, respectively [11,34]. Additionally, the chelating ability of the ferrous ions of the essential oil extracted at the vegetative and full flowering stages was more prominent than that of the oil extracted at the fructification stage, which was attributed to the metal chelating impacts of 1,8-cineole, α -terpineol, and methyleugenol. Interestingly, Usman et al. [34] studied the effect of the seasonal variation on the antioxidant activity of Eucalyptus essential oil and demonstrated the richness of the leaf essential oil harvested in the rainy season with oxygenated monoand sesquiterpenoids, which was reflected in its higher scavenging activity for the DPPH radical as well as significant ferric-reducing power, as compared to the leaf essential oil gathered in the dry season. Of late, Sharma et al. [68] stated that Eucalyptus essential oil evidenced a powerful antioxidant potential that was clearly observed via IC₅₀ values of 70.12, 48.26, 17.94, and 15.45, for DPPH, Nitric oxide, Hydroxyl radical, and ABTS radical scavenging activities, respectively, as compared to 9.62, 57.19, 119.38, and 127.16, being the IC₅₀ values for ascorbic acid, while the IC₅₀ value of 18.37 was for the iron-reducing power, with respect to the IC_{50} value of ascorbic acid (59.33). The marked reducing power was an important factor for pharmacological drugs that were responsible for the alleviation of free radicals and oxidative stress-associated diseases. The authors attributed the elevated antioxidant activity of essential oil to its richness with flavonoids and phenolic compounds.

The highest phenolic content was provided by methanol and methanol:water extracts of dried *Eucalyptus* leaves, as compared to other utilized solvents. Additionally, the greatest antioxidant activity was achieved from the dry leaf methanol:water extract and its antioxidant efficacy strongly correlated with the phenolic content [45]. The greatest DPPH radical scavenging potential was achieved from the leaf methanol extract, with an IC₅₀ value of 23 µg/mL, followed by the leaf ethyl acetate extract and hexane extract, with IC₅₀ values of 29 and 65 µg/mL, respectively. With respect to BHT (IC₅₀ = 17 µg/mL) and vitamin E (IC₅₀ = 26 µg/mL), the authors correlated the strongest activity of the methanol extract to its high content of phenolic compounds [35]. Similar findings were also achieved by Nile and Keum [46], wherein the leaves of the methanol extract displayed considerable

 $18.9 \pm 1.5 \,(\mu g/mL)$ lower than BHT (5.7 $\pm 1.2 \,\mu g/mL$). The fruit extract displayed a high reducing power capacity with an IC_{50} value of 39.52 μ g/mL, as compared to α -tocopherol (117.76 μ g/mL). Moreover, the extract represented a moderate lipid peroxidation inhibition activity. Furthermore, the authors depicted the antioxidant activity due to the abundance of phenolic compounds, especially hydrolyzable tannins, in the fruit extract [73]. The results obtained by Bey-Ould Si Said et al. [44] suggested that the essential oil extracted from the fruits of Nigerian-grown E. globulus showed lower antioxidant activities, through the higher IC₅₀ values of the DPPH radical, reducing the power and lipid peroxidation activities (27.0 \pm 0.2, 32.8 \pm 1.8, and 4.9 ± 0.2 mg mL⁻¹, respectively) with respect to the IC₅₀ values of the tested BHA standard (0.05 \pm 0.0, 0.03 \pm 0.0, and 0.5 \pm 0.2 mg mL⁻¹, respectively). However, the three antioxidant activities were more effective when compared with the results of the antioxidant activities of the essential oil from the leaves, observed by Harkat-Madouri et al. [20], in the same growth region where the essential oil of the hydro-distilled leaves showed a DPPH radical scavenging capacity ranging from 11.72 to 60.63% inhibition percentage, with an $IC_{50} = 33.33 \pm 0.55 \text{ mg/mL}$, with respect to the standard BHA ($IC_{50} = 0.033 \pm 0.002 \text{ mg/mL}$), while the reducing power efficacy, with an IC₅₀ value of 115.39 \pm 1.45 mg/mL, was lower than the activity of the standard BHA (IC₅₀ = 0.048 ± 0.015 mg/mL). Additionally, the oil exerted a high lipid peroxidation inhibition activity that had an IC_{50} value of 6.75 \pm 0.39 mg/mL, as compared to an IC₅₀ value of 0.455 \pm 0.19 mg/mL of the standard BHA. The abundance of ineffective compounds in the tested oil may be responsible for its low efficacy.

the *E. globulus* leaves exerted the DPPH radical scavenging activity with an IC_{50} value of

By using the DPPH and β -carotene bleaching test methods, the polar extracts (ethanol, methanol, and 75% aqueous ethanol) of the *E. globulus* stumps showed a significant antioxidant capacity, with a lower IC_{50} value than the non-polar extract (n-hexane). This was because the phenolic structures were easily extracted by the polar extracts, which explained the economic importance of the stumps as the oldest part of the tree. Furthermore, the ability of stump extracts to inhibit lipid peroxidation indicated the possibility of using these extracts as food preservatives, particularly with a high fat content [57]. Moreover, Ita (2020) found that the ethanol root extract of E. globulus, which considered limited outcomes, showed a potent antioxidant activity through the DPPH radical scavenging potential, promising a reducing power that correlated with the relationship between the antioxidant activity and root content of phenolics and flavonoids, which suggested that the roots were a promising source of natural antioxidants for diminishing the reactive oxygen species in biological systems. Additionally, the crude bark extracts as well as fruit extracts had an antioxidant activity that could be used as an alternative for pure compounds, such as plant-derived antioxidants [61,73], to overcome the deleterious effects of synthetic antioxidants.

5. Antimicrobial Activity

5.1. Antibacterial Activity

The emerging concern of the ineffectiveness of conventional antimicrobial agents, as well as the growing multidrug resistant strains, as a global threat, generated a true need for the exploration of natural alternatives, with a potent antibacterial potential to cure infectious diseases that were an increasing threat to human health [21,55]. Thus, the antibacterial impact of different parts of the plant, as well as their essential oils, have been greatly investigated for tremendous Gram-positive and Gram-negative bacterial strains, as summarized in Table 2, demonstrating that *E. globulus* is a promising antibacterial agent

with enormous therapeutic applications. The efficiency of *Eucalyptus* essential oil, as well as plant part extracts, against bacterial species are attributed to the following:

Table 2. Antibacterial activities reported in different parts of *E. globulus* Labill.

Plant Parts	Solvent Used	Method Used	Target Species	References
Leaves	Essential oil	Agar diffusion technique	Staphylococcus aureus CECT 4459 Escherichia coli O157:H7 CECT 4267	[58]
Aerial parts	Essential oil	Disc diffusion assay	Salmonella enteritidis (CECT 4155) Escherichia coli (CECT 4267) Pseudomonas aeruginosa (CECT 110) Staphylococcus aureus (CECT 239) Enterococcus faecium (CECT 239) Listeria monocytogenes (CECT 935) Listeria monocytogenes EGD-e	[25]
Leaves	Essential oil	Agar disc diffusion method	Staphylococcus aureus ATCC 25923 Escherichia coli ATCC 25922 Pseudomonas aeruginosa ATCC 27853 Phylococcus aureus Escherichia coli Pseudomonas aeruginosa klebsiella pneumoniae Proteus mirabilis Streptococcus pyogenes Morganella morganii Providencia stuartii Enterobacter cloacae Acinetobacter baumannii Citrobacter freundii Salmonella infantis	[9]
Leaves	Essential oil	Agar disc diffusion and dilution broth methods	Escherichia coli Staphylococcus aureus	[74]
Leaves	Essential oil	Agar dilution method	Helicobacter pylori ATCC 700392	[75]
Leaves	Methanol extract	Cup-plate method	Staphylococcus aureus Bacillus subtilis	[60]
Leaves	Ethyl acetate	Agar well diffusion method	Lactobacillus acidophilus (MTCC-*447) Lactobacillus casei (MTCC-1423) Staphylococcus aureus (MTCC-890) Streptococcus mutans (MTCC-96)	[19]
Fruits	Aqueous methanol (80%)	Disc diffusion method	Staphylococcus aureus ATCC 6538 Bacillus subtilis ATCC 6633 Klebsiella pneumoniae E 47	[73]
Leaves	Oil encapsulated silica nanoparticle	Agar well diffusion method	Escherichia coli (ATCC 25922)	[29]
Leaves	Essential oil	Cylinder plate method	Bacillus subtilis Escherichia coli Staphylococcus aureus Pseudomonas aeruginosa	[28]
Stump	n-hexane, ethanol, methanol and 75% aqueous ethanol	Disc diffusion assay	Staphylococcus aureus ATCC 25923 Bacillus cereus ATCC 11778 Listeria monocytogenes LMG 16779 Enterococcus faecalis ATCC 29212 Escherichia coli ATCC 25922 Pseudomonas aeruginosa ATCC 27853 Klebsiella pneumoniae ATCC 13883 S. aureus: SA 01/10, SA 02/10, SA 03/10 and SA 08 S. aureus: MRSA 10/08 and MRSA 12/08	[57]

Plant Parts Solvent Used Method Used References **Target Species** Methanolic extracts Disk diffusion method Pseudomonas aeruginosa Leaves [2] Essential oil Agar diffusion method Streptococcus mutans (ATCC 700610) Leaves [1] Staphylococcus aureus (MTCC 3160), Staphylococcus epidermidis (MTCC 435) Leaves Essential oil Agar well diffusion method [15] Pseudomonas aeruginosa (MTCC 7453) Klebsiella pneumonia (MTCC 4030) Fusobacterium nucleatum ATCC 25586 Aggregatibacter actinomycetemcomitans ATCC 29522 Porphyromonas gingivalis ATCC 33277, ATCC 49417, Leaves Essential oil Broth microdilution method HW24D1, and W83) [20] Streptococcus mutans ATCC 35668 ATCC 33535, ATCC 25175 S. sobrinus ATCC 33478, ATCC 27607 ATCC 27352 Staphylococcus aureus Essential oil Escherichia coli incorporated into [59] Agar diffusion assay Leaves Pseudomonas aeruginosa chitosan films Klebsiella pneumonia Salmonella typhi Salmonella paratyphi Salmonella typhimurium [14] Essential oil Agar diffusion method Shigella species Leaves Pseudomonas aeruginosa Staphylococcus aureus Escherichia coli Pseudomonas aeruginosa ATCC 27853 E. coli ATCC 25922 K. pneumoniae ATCC 13883 Salmonella Typhimurium ATCC 13311 Leaves and Acinetobacter baumannii LMG 1025 Acinetobacter Essential oil Disc diffusion assay [13] small branches baumannii LMG 1041 P. aeruginosa PA 08 P. aeruginosa PA 12/08 E. coli EC 08 K. pneumoniae KP 08 Staphylococcus aureus ATCC 43300 Bacillus subtilis ATCC 6633 Fruits Essential oil Agar diffusion test Listeria innocua CLIP 74915 [44] Escherichia coli ATCC 25922 Pseudomonas aeruginosa ATCC 27853 Escherichia coli ATCC 25922 Pseudomonas aeruginosa Essential oil Disk infusion [76] Leaves ATCC 27853 Staphylococcus aureus ATCC 25923 Staphylococcus aureus (MTCC 3160) Aqueous, ethanol, Agar disc diffusion method Escherichia coli (MTCC 1655) Streptococcus mutans Leaves [30] and methanol (MTCC 890) Listeria innocua (NCTC 10528) Staphylococcus aureus (ATCC 6538) Escherichia coli Leaves Aqueous ethanol Serial dilution technique (ATCC 25922) Bacillus cereus (DSM 4313) [54] Pseudomonas aeruginosa (10145) Salmonella enteritidis (ATCC 3076) Nanoemulsions [12] Broth microdilution technique Pseudomonas aeruginosa PA01 Leaves containing oil Staphylococcus aureus ATCC 6816 Staphylococcus aureus (MRSA) Bacillus cereus ATCC 14579 Listeria monocytogenes Aerial parts Essential oil Disk diffusion method [72] ATCC 19115 Enterococcus faecalis ATCC 29212 Escherichia coli ATCC 25922 Klebsiella pneumoniae

CIP 104727 Salmonella enteridis DMB 560

Table 2. Cont.

Plant Parts	Solvent Used	Method Used	Target Species	References
Leaves	Essential oil	Double-dilution micro-plate assay	E. coli 1 E. coli 2 S. aureus 1 S. aureus 2 P. aeruginosa P. mirabilis	[16]
Leaves	Essential oil	In vitro microdilution method	Propionibacterium acnes ATCC 6919 P. acnes ATCC 11827 Staphylococcus aureus ATCC 6538 S. epidermidis ATCC 12228	[10]
Leaves	Essential oil	Agar diffusion test	Enterococcus hiare (ATCC 10,541) Baccilus licheniformis (ATCC 8480) Staphyllococcus aureus (ATCC 6538) Pseudomonas aeruginosa (ATCC 9027) Serratia marcescens (ATCC 13,880) Escherchia coli (ATCC 8739)	[77]
Leaves	Zinc oxide nanoparticles from essential oil of	Agar well diffusion method	Staphylococcus aureus ATCC 43300 Staphylococcus aureus ATCC 25923 Enterococcus faecalis ATCC 29212 Escherichia coli ATCC 25922 Klebsiella pneumoniae Salmonella enteritidis ATCC 13076 Salmonella typhimurium Pseudomonas aeruginosa ATCC 27853 Acinetobacter baumannii	[33]
Leaves	Aqueous extract	Agar disk diffusion method	Staphylococcus aureus ATCC 6536 Bacillus subtilis ATCC 6633 Escherichia coli ATCC 8739	[55]
Leaves	Essential oil	Broth microdilution method	Staphylococus aureus ATCC 25923 Streptococus pyogenes ATCC 28422 Eschericha coli	[21]
Leaves	Essential oil	Agar disc diffusion method	Acetobacter aceti Pseudomonas aeruginosa MTCC 427 Escherichia coli MTCC 40 Bacillus subtilis MTCC 121 Staphylococcus aureus MTCC 3160 Saccharomyces cerevisiae	[31]

Table 2. Cont.

The extracted essential oil from fruits exerted pronounced antibacterial potency against tested multidrug-resistant bacteria. Furthermore, the combination of 1,8-cineole and aromadendrene from fruit oils produced a higher inhibition through an additive and synergistic effect against methicillin-resistant *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Bacillus subtilis*, as compared to using a single compound [43]. The antibacterial efficacy was ascribed to the highest percentage of oxygenated monoterpenes (87.32%) in *Eucalyptus* leaf oil, and the synergism also resulted from other minor components [9]. The antimicrobial effects of the methanolic extract from leaves, against *S. aureus* and *B. subtilis*, could be attributed to the existence of tannins and saponins [60]. Similarly, leaf extracts proved the anticariogenic activity, due to the existence of sesquiterpene alpha-farnesene that would lead to an advancement of effective drugs for the treatment of dental caries [19].

The greatest antibacterial activity was obtained from the synergism between *E. globulus* essential oil or leaf extracts and antibiotics toward *P. aeruginosa* [2]. Additionally, Goldbeck et al. [1] observed a synergism effect as a result of the combination between *E. globulus* and *E. urograndis* essential oils against *Streptococcus mutans*. Furthermore, the highest antibacterial activity was correlated with the elevated concentration of 1,8-cineole (71%) in *E. globulus*, as compared to *E. urograndis* (36%), which supported the potential usage of *E. globulus* essential oil, through its incorporation into biodegradable films, as an environmentally benign strategy to control *S. mutans*, as an important oral pathogen.

As outlined by Luís et al. [13], the synergistic action of essential oil with the presence of chloramphenicol, ciprofloxacin, and tetracycline toward *Acinetobacter baumannii* strains was observed. On the other hand, there was no synergistic activity between the combination

of essential oil with cefoperazone and piperacillin against the aforementioned strains. The powerful antibacterial efficacy was correlated with the high content of α -pinene and 1,8-cineole in the essential oil extracted from the leaves [14]. Notwithstanding, Quatrin et al. [12] reported that nano-emulsions contained a low amount of *Eucalyptus* essential oil (5%) and were ineffective against the Gram-negative bacterium, which was generally found in immunocompromised patients. Interestingly, synergism was detected in the combination of ampicillin and *Eucalyptus* essential oil against Methicillin-resistant *Staphylococcus aureus*, which accordingly brought down the MIC value of the antibiotic by 32-fold and the MIC of the essential oil to half against *S. aureus*. This combination also reduced the essential oil toxicity of the healthy cells [72].

The methanol extract of leaves displayed a promising antibacterial activity against *S. mutans, S. aureus,* and *E. coli,* as compared to the aqueous and ethanol leaf extracts, which was attributable to the extraction of highly diverse components by methanol, with respect to other extracts [30]. The *Eucalyptus* aqueous ethanol leaf extract showed a similar trend and exhibited antibacterial activity against the tested species. The authors attributed the additive or synergistic effect as being related to the existence of various bioactive molecules [54]. The aqueous extract of *E. globulus* leaves showed the same mode of action as Ampicillin against *S. aureurs*. Furthermore, the extract showed a significant inhibitory action against *S. aureus* and *B. subtilis* as compared to Gentamicin, which could explain the profound amount of polyphenols and flavonoids in the extract [55].

Eucalyptus essential oil and its main component (1,8-cineole) exerted a potent antibacterial activity against the development of the biofilm produced by methicillin-resistant *S. aureus* strains [78]. Interestingly, Obeizi et al. [33] proved that the ZnO nanoparticles biosynthesized from the leaf essential oil displayed effective anti-biofilm activity against *S. aureus* ATCC 25923 and *P. aeruginosa* ATCC 27853, which are known for their elevated biofilm formation potential that will help to overcome antibiotic resistance resulting from a bacterial biofilm, which is considered the major reason for nosocomial infection transition. The antimicrobial potential of the *Eucalyptus* leaf essential oil may be due to the synergistic effects of the polyphenolics [31].

Generally, Gram-negative bacterial cells were more resistant to the presence of *Eucalyptus* extracts as well as its essential oil than the Gram-positive ones [20,25,58,72]. In addition, the fruit extract showed antibacterial activity only against the Gram-positive bacteria, which was due to its richness in phenolic compounds, even as no activity was detected against the Gram-negative bacteria, which could be ascribed to their outer lipopolysaccharide membrane [73].

5.2. Antifungal Activity

Few studies have been conducted on the impact of *E. globulus* leaves and stumps as antifungal agents (Table 3) to eradicate fungal infections that are antibiotic-resistant, as a major challenge worldwide, for example, in the case of *Candida* spp. and other fungal species. Furthermore, due to the growing number of cases infected by the *Candida* spp. and the increased risk of drug resistance, finding a new therapeutic strategy is considered to be of fundamental importance. The induced antifungal efficacy has been attributed to the richness of the plant parts with diverse phytochemical constituents (Table 1) that represent a cost-effective approach to combat fungal infections.

E. globulus essential oil showed a potent anti-candidal efficacy, indicating that the oil is a potential candidate for mouth wash applications [32]. Similarly, *Eucalyptus* essential oil surpassed the antifungal nystatin (a drug utilized to control fungal infections on the skin, mouth, vagina, and intestinal tract) twice over, in the antifungal efficacy against *C. albicans*, which could likely be ascribed to the high content of 1,8-cineole (85.8%) in the leaf essential oil [9]. Nanoemulsions containing *E. globulus* essential oil that was commercially acquired possessed antifungal and antibiofilm activities against *C. albicans*, which were the main microorganisms responsible for initiating fungal infections globally [12]. These findings were due to the nanoencapsulation-enhanced functionality of the essential oil via the

protection of essential oil components, as well as the reduced size of the nanoemulsions that resulted in rapid penetration.

Plant Parts	Solvent Used	Method Used	Target Species	References
Leaves	Essential oil	Micro dilution method	Candida albicans ATCC 90028 Candida albicans 15B	[32]
leaves	Essential oil	Agar-well diffusion method	Candida spp.	[65]
Leaves	Essential oil	Broth microdilution assay	Candida albicans ATCC 10231	[9]
Leaves	Methanol extract	Cup-plate method	Trichophytor rubrum	[60]
Leaves	Essential oil	Cylinder plate method	Aspergillus niger Candida albicans	[28]
Stump	n-hexane, ethanol, methanol, and 75% aqueous ethanol	Disc diffusion assay	Candida albicans ATCC 90028 Candida tropicalis ATCC 750	[57]
Leaves	Essential oil incorporated into chitosan films	Agar diffusion assay	Candida albicans Candida parapsilosis	[59]
Leaves	Essential oil	Agar diffusion method	<i>Trichophyton</i> spp. <i>Aspergillus</i> spp.	[14]
Leaves	Nanoemulsions containing oil	Broth microdilution technique	C. albicans (ATCC 14053) C. tropicalis (ATCC 66029) C. glabrata (ATCC 66032)	[12]
Aerial parts	Essential oil	Disk diffusion assay	Candida albicans ATCC 10231	[72]
Leaves	Essential oil	Double-dilution micro-plate assay	C. albicans1 C. albicans2	[16]
Leaves	Zinc oxide nanoparticles from essential oil	Agar well diffusion method	Candida albicans	[33]

Table 3. Antifungal activities reported in different parts of *E. globulus* Labill.

The essential oil from the Tunisian *Eucalyptus* aerial parts proved to have a potent antifungal efficacy against *C. albicans* that was greater than the antifungal (Amphotericin B), especially the essential oil obtained in the fruiting stage, rather than the essential oil obtained in the vegetative and full flowering stages. This was probably because of the defense mechanisms of the plant during fruit formation or the variation in oil components during the different growth stages, as the oil contains considerable amounts of α -pinene and *p*-cymene with a high essential oil yield during the final developmental stage. Furthermore, the combined application of *Eucalyptus* essential oil alone against *C. albicans*, from 1000 to 31.25 µg/mL in the case of a combination [72]. Similarly, Bogavac et al. [16] showed the potent antifungal efficacy of essential oil as a promising alternative against vaginal *C. albicans* strains that were multidrug-resistant to conventional antifungals.

6. Eco-Friendly Approaches for Application of E. globulus

The efficiency of *E. globulus* for protecting plants from undesirable impacts of heavy metals and invasive plants as well as insects have been recognized as an efficient alternative for controlling weed growth, insects, and extracting pollutants from contaminated soil. This could be considered as an environmentally benign method.

For enhancing the ability of plants for phytoextraction, Luo et al. [79] recommended the replanting of *E. globulus* as an appropriate method for removing cadmium from the contaminated soil via root removal during every harvest, rather than following the coppicing system, regardless of the elevated cost of replanting. This also reduced the phytoremedia-

tion time, considering that the greatest amount of heavy metals will be absorbed by the *Eucalyptus* roots as a non-metabolically active component. Additionally, in the observations outlined by Luo et al. [79–81], *E. globulus* had potent heavy metal phytoremediation due to its fast growth and high above-ground biomass, as well as its ability to decline the physiological damage through aggregation of toxic materials in the less sensitive parts, as compared to the metabolically active parts. Likewise, the *E. globulus* trees could accumulate cadmium (Cd) and lead (Pb), which made them potential candidates for the efficient capture of heavy metals from contaminated areas [82]. In recent times, Reboredo et al. [17] stated that *E. globulus* was able to remove arsenic from plantations close to mining activities and its root system was considered to be the greatest organ for accumulation, although translocation to the above-ground organs is poor. This promoted the phytoremediation efficacy of *Eucalyptus* plants as cost effective and provided an efficient process for removing heavy metals from contaminated lands; thus, it could help to counteract the limitations of conventional methods in the heavy metal elimination process.

For the phototoxic effect of *E. globulus*, the leaf methanolic extract had greater allelopathic activity, and accordingly, it diminished the percentage of germination, the germination rate, root and shoot growth, and the fresh and dry weights of eggplant, than the other extracts used [49]. In addition, Morsi and Abdelmigid [51] proved the allelopathic activity of the *Eucalyptus* aqueous leaf extract via the inhibition of seed germination, and the seedling growth of the *Hordeum vulgare* plants was ascribed to the presence of phytotoxic phenolics in the leaf extract.

Implementation of the Eucalyptus allelopathic properties in weed management will ameliorate the herbicide resistance resulting from the excessive application of synthetic herbicides; additionally, this strategy will maximize crop production by suppressing weeds that compete with crops for the same resources. With regard to this concern, Puig et al. [83,84] stated that the incorporation of *E. globulus* residues into the soil as green manure will diminish synthetic herbicide usage, especially in organic farming, to control weeds, as an environmental friendly practice. A leaf extract with an allelopathic potential can be used as a natural promising bioherbicide to inhibit both broad and narrow leaf weeds associated with the pea plant [50]. Furthermore, the leaf aqueous extract adversely influences the germination and seedling growth of teff and barley plants, as compared to the juvenile stem and root extracts [85]. Therefore, the allelopathic compatibility between crops and *Eucalyptus* trees must be essentially checked to avoid the potential adverse effects of trees on the associated crops. Additionally, the aqueous extract of the oven-dried leaves has a herbicidal potential as a biocide against the widespread weed of Portulaca oleracea L., which is attributable to the existence of a significant amount of allelochemicals [86]. The above-mentioned results recommend that the bioactive compounds present in *Eucalyptus* plants must be further investigated in weed control, as bioherbicides, with possible commercial applications.

The essential oil of *Eucalyptus* is considered to be a good ecological choice for maintaining the vase-life quality of "Carola" roses. This will help to overcome the use of toxic pesticides, as a routine procedure after harvest, of rose growers, which causes an undesirable impact on the environment and humans as well, as it can increase pathogen resistance [87]. In addition, the insecticidal activity of *Eucalyptus* essential oil has been previously assessed against the housefly [36], *Musca domestica* L. [38,88], *Culexpipiens* [37], and *Myzuspersicae* [66]. Furthermore, *Eucalyptus* essential oil and Co₂ extract showed chronic toxicity and antifeedant efficiency against *Leptinotarsa decemlineata* [6]. Additionally, the nanocapsule formulation of hydroalcoholic leaf extracts exhibited repellent and biocidal activities against *Aphis fabae* [89]. Therefore, essential oil and plant extracts could be used as botanical insecticides, repellents, as well as fumigants, instead of chemical insecticides due to their non-phytotoxic activity. Seemingly, the use of these natural insecticides is a promising approach for dealing with the emerging problem of insect resistance, potential toxicity to non-target insects as well as the environmental pollution caused due to excessive insecticide applications. On account of the increasing advocacy of organic agriculture in many countries, including Egypt, additional investigations on the possibility of using *Eucalyptus* plant parts, as well as their essential oils, in organic farming should be undertaken to enrich the quality of agricultural products, which will be reflected in the environment and human health.

7. Future Perspectives

The above-mentioned encouraging results support the use of different *E. globulus* plant part extracts, as well as their essential oils, as antioxidant and antimicrobial agents that stimulate further clinical trials, which should be implemented to confirm the aforementioned findings for further medical purposes. For a deep understanding of all the bioactive compound mechanisms involved in all the studied bioactivities, further trials should be implemented to explore the synergistic or antagonistic interactions among the complex mixtures of essential oils. In addition, the mechanism of action after the combination of oils and conventional antibiotics, which may influence multiple targets at the same time, should be investigated more thoroughly.

Additional studies are warranted to counteract the poor penetration of natural antimicrobial agents into the microorganism biofilm matrix, which can be achieved through nanocarriers. However, in the case of using biosynthesized nanoparticles, further investigation will be needed to demonstrate the impact of their cytotoxicity, with emphasis on optimizing the separation processes of the phenolic compounds, with detailed chemical characterization for possible extract quality improvement. Taking into consideration implementation of the available information on the effect of *Eucalyptus* essential oil and its extracts on the antimicrobial potency, it will be considered a great alternative to combat the resistance problem. Furthermore, the potent antimicrobial, herbicidal, and insecticidal activities of essential oil and plant parts should be transformed into commercial products.

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