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Research Article

Phytochemical composition, radical scavenging activities and molecular docking of essential oils from *Bougainvillea formosa*

Oluwakayode Olubumi Odeja[1], Ovuokenye Omadoko[2], Sandra Ehigiator[3], Micheal Gabriel Ibok[4*], Israel Azogor Ekoro[1], Ejike Onwudiegwu Okpala[5], Afolabi-Owolabi Oluwafunke[6] and Nwafili Chinyere Ruth[1]

1. Department of Chemistry, College of Science, Federal University of Petroleum Resources, Effurun, Delta State. Nigeria.
2. Department of Chemistry, College of Natural Sciences, University of Maryland, College Park, Maryland, USA.
3. Crown Laboratories Inc., Johnson City, Tennessee, USA.
4. Department of Chemistry, Faculty of Science, University of Ibadan, Ibadan. Oyo State. Nigeria.
5. Department of Chemistry, Faculty of Science, Federal University, Lokoja, Kogi State, Nigeria.
6. Department of Mental health, Faculty of Sport, health and Engineering, Victoria University, Melbourne, Australia.

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Corresponding Author
Prof. Dr. Micheal Gabriel Ibok
E-mail: michaelibok08@gmail.com
Tel.: +2348166709831

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Abstract

Bougainvillea formosa N. Parks is traditionally an ornamental plant with numerous folklore applications, including antihyperlipidemic, antidiabetic, analgesic, cytotoxic, antioxidant anti-inflammatory, and antimicrobial properties, as well as the treatment of respiratory and gastrointestinal ailments. This study investigated the essential oils (EOs) composition of *Bougainvillea formosa* leaves and flowers, along with their antioxidant activity and molecular docking studies of the identified phytochemicals. Antioxidant activity was evaluated using the 2,2–diphenyl–1–picrylhydrazyl radical (DPPH*) radical scavenging assay, while molecular docking was performed against two oxidative stress-related proteins: heme oxygenase (1N3U) and NADPH oxidase (2CDU). Drug-likeness and toxicity predictions were assessed using SwissADME and ProTox-III. GC-MS analysis identified seven compounds in the leaves (72.81%) and fourteen compounds in the flowers (84.45%), which α-phellandrene and 1-octen-3-ol as the most predominant compounds, respectively. The flower EO exhibited stronger antioxidant activity (IC_{50} = 11.07 µg/mL) compared to the leaf EO (IC_{50} = 19.54 µg/mL), although both were less potent than ascorbic acid (IC_{50} = 2.05 µg/mL). Docking studies revealed strong binding affinities for 2(Z),6(Z)-farnesol (1N3U: -6.3 Kcal/mol; 2CDU: -5.9 Kcal/mol), α-phellandrene (1N3U: -6.0 Kcal/mol; 2CDU: -5.9 Kcal/mol) and aromadendrene (1N3U: -6.5 Kcal/mol; 2CDU: -6.8 Kcal/mol) compared to ascorbic acid (1N3U: -5.2 Kcal/mol; 2CDU: -6.1), with low inhibitory constants. These findings highlight the potential of *B. formosa* EOs as natural antioxidants and therapeutic agents, warranting further exploration for pharmaceutical and nutraceutical applications.

1. Introduction

There has been a significant increase in interest in medicinal plants and their naturally occurring bioactive constituents, especially due to their reported pharmacological activities [1,2]. Medicinal plants have been used in traditional treatments for various ailments and have provided the basis for active

exploration as potential sources for novel drug discovery and development [3]. Among the wide array of secondary metabolites found in plants, essential oils (EOs) (aromatic, volatile and lipophilic liquids) extracted from different plant parts [4] have recently gained attention due to their diverse biological activities. These include antidiabetic, antimicrobial, anti-inflammatory, anticancer, anticonvulsant, antispasmodic and cardioprotective activities.

As the chemistry of essential oils and their pharmacological mechanisms are elucidated [5], these plant-based volatiles are increasingly prioritized in drug discovery research. Additionally, the rising preference for natural therapeutics, due to their perceived safety and effectiveness compared to synthetic alternatives, has further boosted their acceptance in health-related applications. Beyond therapeutic use, essential oils are also valued in the cosmetic industry for their effectiveness as anti-acne, anti-aging and skin-lightening agents, making them key ingredients in a broad range of personal care products [6].

Bougainvillea Formosa N. Parks is a cultivar of *Bougainvillea glabra,* a widely distributed ornamental plant in the Nyctaginaceae family, known for its vibrant bracts and extended flowering season. Although it is commonly cultivated for aesthetic purposes, increasing scientific interest has arisen in its medicinal and nutraceutical properties [7]. Phytochemical analyses of the leaves and flowers have confirmed the presence of phenolics, flavonoids and betalains, which contribute to its antioxidant, anti-inflammatory and antimicrobial activities [7]. It is used in folklore in the treatment of respiratory and gastrointestinal ailments. Extracts from *Bougainvillea* species have demonstrated pharmacological activities, such as antihyperlipidemic, antidiabetic, analgesic and cytotoxic activities. In addition to their biological applications, floral pigments and polyphenols are used in the food industry as natural colourants [8, 9].

In silico methods, such as molecular docking studies, virtual screening and computational modelling, have greatly revolutionized the investigation of medicinal plants and their bioactive components. Using these methods, scientists can identify potential therapeutic targets, predict the biological activity of natural substances and optimize lead compounds for drug development. *In silico* research enables the identification of new medicinal compounds with high specificity and efficacy, requiring minimal time and expense for experimental validation. Computational studies have elucidated the relationships between key phytochemicals and molecular targets of essential oils, providing insights into their mechanisms of action in mitigating oxidative stress. In a recent study by Ibok et al. [10], the leaf and stem essential oils of *R. umbellulata* were characterized by GC–MS and evaluated for antioxidant and cytotoxic activities, complemented by molecular docking and ADMET analyses. Phytol and pentadecanal were identified as the dominant constituents, and the oils exhibited notable free radical scavenging activity. *In silico* studies have indicated the strong binding affinities of β-gurjunene and acorenone relative to doxorubicin, alongside lower predicted risks of mutagenicity, hepatotoxicity and carcinogenicity [10].

Owing to the preliminary phytochemical profile and ethnomedicinal applications of *B. formosa*, there is a dearth of information on the phytochemical composition of the leaf and flower essential oils. However, this study aimed to investigate the composition of essential oils (EOs) in *Bougainvillea formosa* leaves and flowers, their antioxidant activity and the molecular docking of identified phytochemicals.

2. Materials and methods

2.1. Plant collection and preparation

Fresh leaves and flowers of *Bougainvillea formosa* were harvested in July 2024 from the Botanical Garden of the University of Ibadan, Nigeria. The plant parts were identified and authenticated by Mr. Donatus at the Herbarium Unit, Department of Botany, University of Ibadan, Ibadan, Nigeria. A voucher specimen (FHI 114212) was deposited in the herbarium.

2.2. Equipment and apparatus

An all-glass Clevenger apparatus was used for essential oil extraction, and absorbances were measured using a UV-Visible spectrophotometer (PerkinElmer Lambda 25). Phytochemicals

identification was performed using gas chromatography-mass spectrometry (GC-MS) with an Agilent 7809A system coupled to an Agilent mass spectrometric detector.

2.3. Extraction of essential oils

Freshly chopped *Bougainvillea formosa* leaves (500 g) and flowers (320 g) were subjected to hydrodistillation using an all-glass Clevenger-type apparatus, according to the method described by the British Pharmacopeia [11], Odeja et al. [12] and Ibok et al. [10, 13]. The essential oils were stored in a refrigerator at 4°C prior to analysis.

2.4. GC-MS analysis of the essential oil

Gas chromatography-mass spectrometry (GC-MS) was used to determine the chemical composition of the essential oils extracted from the leaves and flowers of *Bougainvillea formosa*. The analysis utilized an Agilent 7809A GC system coupled to a mass selective detector operating in electron ionization mode at 70 eV. The GC-MS consisted of a split/splitless injector and an HP-5MS capillary column (30 m × 0.25 mm internal diameter, 0.25 µm film thickness). The ion source temperature was maintained at 200 °C and spectral data were recorded over the m/z range of 50–700 at a scan rate of 1428 amu/s. The oven temperature was programmed as follows: initially held at 80°C for 2 min, then ramped at 10°C/min to 240°C and maintained for 6 min. Helium was used as the carrier gas at a constant flow rate of 1.0 mL/min. The injection volume was 1.0 µL, with a linear velocity of 362 cm/s and an inlet pressure of 56.2 kPa. Both the injector and detector temperatures were maintained at 250°C throughout the run. Compound identification was based on a comparison of their mass spectra with entries in the NIST library and the calculation of Kovart retention indices (KRIs) using a homologous series of *n*-alkanes (C_8–C_{30}) analyzed under identical chromatographic conditions (Equation 1) [14].

$$RI = n + \frac{(t_r(x) - t_r(n))}{t_r(n+1) - t_r(n)} \times 100 \quad (1)$$

Where:

t_r (x) = retention time of the unknown compound.

t_r (n) = retention time of the n-alkane eluting before the compound.

t_r (n+1) = retention time of the n-alkane eluting after the compound.

n = number of carbon atoms in the preceding alkane.

2.5. 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging method

DPPH radical scavenging activity was assessed using a modified method described by Odeja *et al*. [11] and Ibok et al. [12]. A stock solution was prepared by dissolving 0.004 g of DPPH in 100 mL methanol. Test samples were serially diluted to obtain concentrations ranging from 10 to 150 µg/mL. Next, 50 µL of each sample concentration was added to 150 µL of the DPPH solution. The plate was then incubated for 30 min at room temperature in a dark cupboard. After incubation, the absorbance was measured at 595 nm using a UV-Visible spectrophotometer (PerkinElmer Lambda 25). Ascorbic acid, prepared at the same concentration range (10–150 µg/mL), was used as a reference antioxidant. Methanol served as the negative control. The test samples, standards and controls were conducted in triplicate to ensure reliability. The percentage of DPPH radical inhibition was determined using Equation 2.

$$\text{Scavenging activity (\%)} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100 \quad (2)$$

Where:

$A_{control}$ is the absorbance of the control (DPPH + methanol)

A_{sample} is the absorbance of the test sample (DPPH + essential oil)

2.6. Molecular docking

Molecular docking, a key component of structure-based drug design (SBDD), was employed to predict the binding affinities of bioactive constituents to target proteins [15]. In this study, docking analyses were performed against heme oxygenase-1 (HO-1; PDB ID: 1N3U) and NADPH oxidase (PDB ID: 2CDU), both of which have been implicated in antioxidant-related pathways and previously reported in *in silico* studies [16, 17]. The three-dimensional crystal structures were retrieved from the Protein Data Bank. Protein preparation involved the removal of water molecules, heteroatoms, and co-crystallized ligands using BIOVIA Discovery Studio Visualizer [18, 19], followed by the addition of polar hydrogens and Gasteiger charges.

Ligand structures corresponding to the selected BF essential oil constituents identified by GC–MS were obtained from the PubChem database and energy-minimized using the Merck Molecular Force Field (MMFF94). Molecular docking was performed using AutoDock Vina, implemented in PyRx 0.8, with an exhaustiveness parameter of 8 [20-21]. Prior to docking the test ligands, re-docking validation was conducted by re-docking the native co-crystallized ligands into their respective binding sites using the same docking parameters. The resulting root-mean-square deviation (RMSD) values were ≤ 2.0 Å, confirming the reliability and reproducibility of the docking protocol.

The active sites were defined based on the coordinates of the co-crystallized ligands and supported by key residues reported in the literature. For 1N3U, the grid box was centered at X = −2.41, Y = 18.67, Z = 24.32 Å, whereas, for 2CDU, it was centered at X = 15.84, Y = −6.21, Z = 9.47 Å, with grid dimensions of 25 × 25 × 25 Å to ensure full coverage of the binding pockets and conformational flexibility. Docking poses were ranked based on binding affinity (kcal/mol), and the best pose was selected as the one with the lowest binding energy, occupying the validated active site and exhibiting favorable hydrophobic and hydrogen-bond interactions.

The inhibitory constant (Ki) was calculated from the binding free energy (ΔG) using Equation 3 [22, 23].

$$K_i = e^{\Delta G/(RT)} \quad 3$$

Where ΔG is the docking energy, R is the gas constant (1.987 cal·mol^{-1}·K^{-1}), and T is the temperature (298.15 K). Lower Ki values indicate a stronger binding affinity and higher inhibitory potential.

2.7. Drug-likeness and toxicity

The SwissADME online tool was used to test the drug-likeness properties of the constituents of the essential oils http://www.swissadme.ch/) [24]. The key physicochemical and pharmacokinetic parameters were analyzed according to Lipinski's Rule of Five [25]. The toxicity profiles of the compounds were performed using the ProTox-III web server (https://tox-new.charite.de/protox_III/) [26].

3. Results and discussion

3.1. Yield and GC-MS characterisation of essential oils

The hydrodistillation of *Bougainvillea formosa* leaves and flowers yielded relatively low quantities of essential oils, amounting to 0.22% and 0.23% (w/w) of the dry plant material, respectively. Such low yields are characteristic of many non-aromatic ornamental plants and may reflect inherent physiological factors, such as glandular density, plant part specificity, and environmental conditions. Despite the modest yields, both oils exhibited pleasant floral aromas, suggesting the presence of volatile compounds with potential applications in fragrance and pharmaceutical formulations.

The chemical compositions of the leaf and flower essential oils were comprehensively characterized using gas chromatography–mass spectrometry (GC–MS). The identified constituents, along with their Kováts Retention Indices (KRIs) and relative abundances expressed as percentages of the total ion concentration (TIC), are summarized in Table 1 and illustrated in Figs 1 and 2. Seven compounds were identified in the leaf oil, accounting for 72.81% of the total composition, whereas fourteen compounds were identified in the flower oil, representing 84.45% of the total composition. The higher chemical diversity observed in the flower oil may be attributed to its ecological role in attracting pollinators and defending against predators, which often necessitates a broader spectrum of volatile metabolites.

Non-terpene compounds were dominant chemical class in both essential oils, contributing 33.57% to the leaves and 50.64% to the flowers. This predominance of non-terpenoid constituents distinguishes *B. formosa* from many aromatic plants, in which monoterpenes and sesquiterpenes typically prevail. Such compositional features may influence the biological activity and physicochemical properties of the oils.

α-Phellandrene was identified as the major constituent of the leaf essential oil, accounting for 19.13% of the total composition (Table 1). The occurrence of α-phellandrene as a dominant compound has been widely reported in several aromatic and medicinal plants, including *Curcuma zedoaria* (14.93%), *Eucalyptus dives* (17.3%), *Schinus terebinthifolius* (15.7%), *Schinus molle* (46.52%), and *Ligusticum marginatum* (50%), highlighting its broad distribution across diverse plant taxa. The presence of

Table 1. Essential oils constituents of *B. formosa* leaves and flowers.

PubChem ID	Identified compounds	*KRIs	*TIC (%)			Classes
			Reported KRIs	*B. formosa* leaves	*B. formosa* flower	
7460	α-Phellandrene	1006	1006 [41]	19.13	-	Monoterpene
18827	1-Octen-3-ol	976	976 [42]	-	19.52	Non-terpene
31289	Nonanal	1104	1104 [43]	-	6.18	Non-terpene
9895	β-Cyclocitral	1220	1220 [44]	-	2.32	Monoterpenoid
6432045	cis-Pulegone Oxide	1275	1275 [45]	-	1.87	Monoterpenoid
5364441	*cis*-4-Tetradecene	1378	1378 [46]	-	6.99	Non-terpene
90805	γ-Gurjunene	1439	1439 [47]	8.52	-	Sesquiterpene
91354	Aromandendrene	1440	1484 [48]	3.43	-	Sesquiterpene
638014	β-Ionone	1488.4	1488.4 [49]	-	1.84	Sesquiterpenoids
595137	2-Isopropyl-5-methyl-9-methylene-bicyclo-1-decene (4.4.0)	1503	1503 [50]	-	1.86	Sesquiterpene
5363741	*cis*-ψ-Ionone	1535	1535 [51]	-	6.33	Sesquiterpenoids
1549107	Farnesol	1695	1695 [52]	-	3.96	Sesquiterpenoids
984	Hexadecanal	1822	1822 [53]	3.3	-	Non-terpene
10408	Hexahydrofarnesyl acetone	1846.7	1846.7 [54]	-	2.24	Sesquiterpenoids
985	*n*-Hexadecanoic acid	1975	1975 [55]	16.46	-	Non-terpene
5280435	Phytol	2122	2122 [56]	8.16	3.09	Diterpene
5283387	Kemamide O	2375	2375 [57]	-	5.63	Non-terpene
85014	1-Heneicosanol	2380	2380 [58]	-	12.32	Non-terpene
638072	Squalene	2847.1	2847.1 [59]	-	10.3	Triterpene
5282761	*cis*-Vaccenic acid	2873.6	2873.6 [60]	13.81	-	Non-terpene
	Classes of identified compounds					
	Monoterpenes			*19.13*	-	
	Monoterpenoids			-	*4.19*	
	Sesquiterpene			*11.95*	*1.86*	
	Sesquiterpenoids			-	*14.37*	
	Diterpenes			*8.16*	*3.09*	
	Triterpenes			-	*10.30*	
	Non-terpene derivatives			*33.57*	*50.64*	
	Total			***72.81***	***84.45***	

*KRIs – Kovart Retention Indices, *TIC: Total ion concentration in percentage

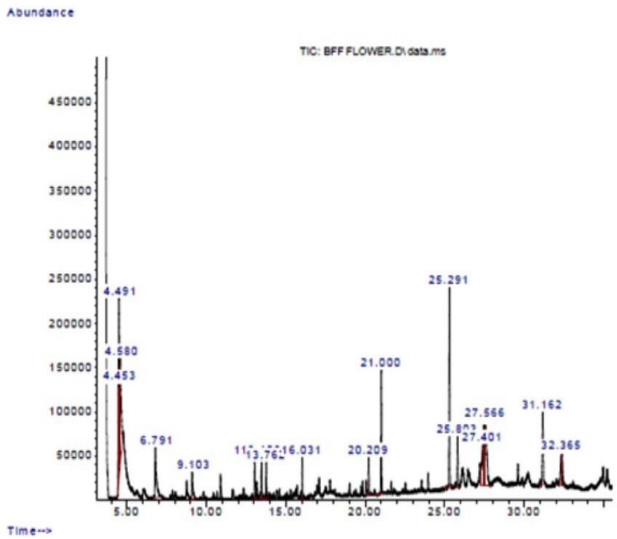

Figure 1. GC-MS chromatogram of *B. formosa* flower essential oil.

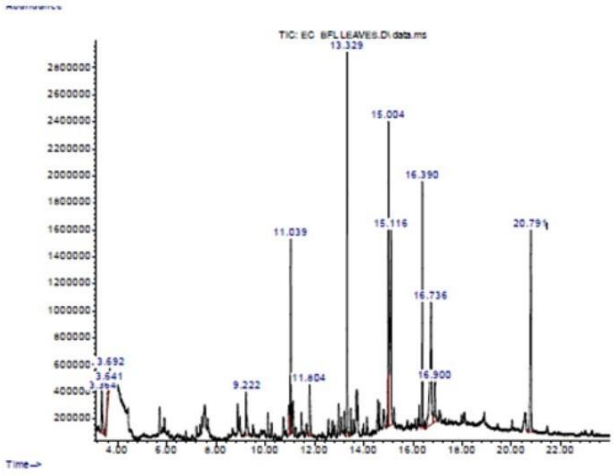

Figure 2. GC-MS chromatogram of *B. formosa* leaves essential oil.

this monoterpene suggests a potential contribution to the bioactivity of the leaf oil.

α-Phellandrene is a cyclic monoterpene originally isolated from *Eucalyptus phellandra* and is widely utilized in the pharmaceutical, cosmetic, food, and fragrance industries due to its distinctive aroma and bioactive properties. It is commonly found in aromatic plants, such as eucalyptus, angelica, mint, and black pepper. Beyond its industrial relevance, α-phellandrene has been implicated in the formation of atmospheric particles through monoterpene oxidation processes [27–28]. Importantly, several pharmacological activities have been attributed to phellandrene-type compounds, including antifungal [29–30], anti-inflammatory [31], analgesic, antidepressant [32], and anticancer [33–34] effects, highlighting their therapeutic relevance in natural product research [35].

In addition to α-phellandrene, cis-vaccenic acid constituted a significant proportion (13.81%) of the leaf essential oil. This omega-7 monounsaturated fatty acid has been previously isolated from *Quercus leucotrichophora* leaves and is well recognized for its antibacterial activity and hypolipidemic effects, particularly in experimental rat models [36–37]. presence The presence of this compound in the oil may contribute to membrane modulation and metabolic effects, thereby enhancing the overall bioactivity profile of the leaf extract. Similarly, *n*-hexadecanoic acid (palmitic acid), present at 16.46%, has been reported to exhibit notable anti-inflammatory activity [38], further supporting the potential therapeutic relevance of the leaf oil.

Aromadendrene, although detected at a relatively low concentration (3.43%), represents a biologically significant constituent of the leaf oil. This tricyclic sesquiterpene is known to possess a wide range of pharmacological activities, including antioxidant, anti-inflammatory, analgesic, antibacterial, insecticidal, and cytotoxic effects. Structurally, aromadendrene contains a reactive exocyclic methylene group and a cyclopropane ring, which enable it to interact with protein residues and alter protein conformation. Its pronounced lipophilicity also facilitates membrane disruption, a mechanism previously reported in the literature [7], which may underlie its diverse biological activities, despite its low abundance.

In contrast to the leaf oil, the flower essential oil was dominated by 1-octen-3-ol, which accounted for 19.52% of the total composition. Commonly referred to as mushroom alcohol, 1-octen-3-ol is widely distributed in fungi and higher plants and is recognized for its strong odor and antimicrobial properties. Xiong et al. [39] reported that this compound exhibits potent antibacterial activity against a broad spectrum of pathogenic microorganisms, including *Staphylococcus aureus*, *Bacillus subtilis*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Fusarium tricinctum*, and *Fusarium oxysporum*. The abundance of this compound in flower oil suggests a potential defensive role against microbial invasion.

The flower oil also contained a considerable amount of 1-hexacosanol (12.32%), a long-chain fatty alcohol previously isolated from *Prosopis africana*. This compound has been reported to possess antibacterial activity and inhibitory effects against *Mycobacterium tuberculosis* [40], highlighting its relevance in infectious disease management. Furthermore, squalene was identified at a significant level (10.3%). Squalene, a triterpene and key intermediate in cholesterol biosynthesis is widely distributed in natural sources, including olive oil, palm oil, wheat germ oil, amaranth oil, and rice bran oil [40]. Beyond its metabolic role, squalene is valued for its antioxidant, skin-protective, and chemopreventive properties, which may enhance the functional value of the flower essential oil.

In addition to the major constituents, several other minor compounds were identified in the essential oils, including β-cyclocitral (2.32%), cis-pulegone oxide (1.87%), γ-gurjunene (8.52%), 2-isopropyl-5-methyl-9-methylene-bicyclo[4.4.0]dec-1-ene (1.86%), β-ionone (1.84%), cis-ψ-ionone (6.33%) and farnesol (3.96%). Although present at lower concentrations, these constituents are known for their pharmacological relevance and likely exert synergistic effects, enhancing the overall biological activities of the essential oil. Overall, the distinct chemical profiles of the leaf and flower essential oils of *B. formosa* reflect plant part–specific biosynthetic pathways and ecological functions. The presence of bioactive

Table 2. Antioxidant activity of the essential oils of leaves and flowers *B. formosa.*

Concentration (µg/mL)	Scavenging activity (%)		
	BF leaves	BF flower	Vitamin C
10.0	26.11714	26.11714	58.39124
20.0	27.95428	29.39421	89.72194
50.0	28.50046	30.43691	89.8709
100.0	29.94038	33.51536	90.21847
150.0	31.52926	35.79937	91.80734
IC₅₀ (µg/mL)	***19.5433***	***11.0674***	***2.0501***

BF: *B. Formosa*

monoterpenes, fatty acids, fatty alcohols, and triterpenes provides a plausible chemical basis for the antioxidant and antimicrobial potential reported for related species. These findings underscore the importance of *B. formosa* as a promising source of biologically relevant natural products and warrant further pharmacological and mechanistic investigations.

3.2. Antioxidant activity

The antioxidant potential of the essential oils obtained from the leaves and flowers of *B. formosa* was assessed using the DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical scavenging assay, a widely accepted method for evaluating the hydrogen- or electron-donating capacity of the bioactive compounds. The essential oils exhibited marked DPPH* radical scavenging activity, indicating a strong ability to neutralize reactive oxygen species, also known as free radicals. As presented in Table 2 and illustrated in Fig. 3, the observed inhibition of DPPH* radicals increased in a concentration-dependent manner, suggesting that the antioxidant effect is directly related to the abundance and reactivity of the phytochemical constituents present in the oils.

The essential oils extracted from the leaves and flowers of *B. formosa* exhibited moderate antioxidant activity, demonstrating their capacity to scavenge free radicals. The maximum percentage inhibition (%I) recorded was 35.80%, which, while substantially lower than that of the standard antioxidant ascorbic acid (%I = 91.81%), still indicates an appreciable radical neutralization potential. Interestingly, the flower-derived essential oil showed superior antioxidant activity compared to the leaf oil, as reflected by its higher percentage inhibition (I%) value. This enhanced activity may be attributed to

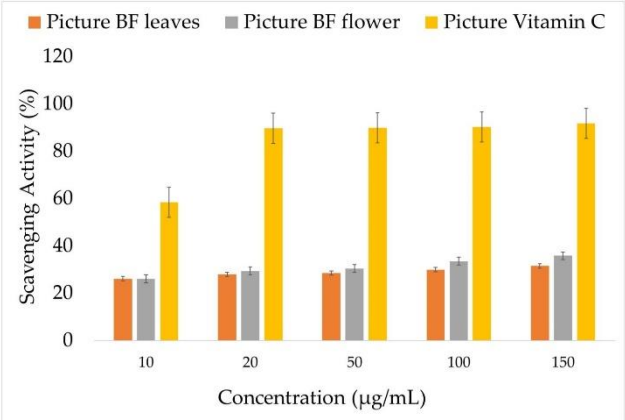

Figure 3. Scavenging activity of *B. formosa* flowers and leaves essential oils.

differences in chemical composition, particularly the concentration and synergistic effects of the bioactive constituents in the floral extract [13].

A detailed GC–MS analysis revealed that the flower essential oil was dominated by α-Phellandrene, 1-Octen-3-ol, and phytol, along with other notable compounds such as cis-pulegone oxide (1.87%), γ-gurjunene (8.52%), 2-isopropyl-5-methyl-9-methylene -bicyclo[4.4.0]decene (1.86%), β-ionone (1.84%), cis-ψ-ionone (6.33%), and farnesol (3.96%). Phytol is well-documented for its potent antioxidant properties, primarily due to its ability to donate electrons or hydrogen atoms to neutralize DPPH* radicals, thereby reducing oxidative stress [12–13]. The presence of these additional compounds may also contribute additively or synergistically to the observed activity, emphasizing the importance of chemical diversity in determining the antioxidant potential of plant-derived essential oils.

Quantitative evaluation using IC_{50} values further supported these observations, revealing the following rank order of activity: ascorbic acid (2.0501 µg/mL) >>

Table 3. Binding affinity score and inhibitory constant for selected BF leave essential oil compounds.

PubChem ID	Binding affinity score		Inhibitory constant (μM)	
	PDB: 1N3U	PDB: 2CDU	PDB: 1N3U	PDB: 2CDU
7460	-6.0	-5.9	39.9	47.3
90805	-6.3	-7.4	24.1	3.7
91354	-6.5	-6.8	17.2	10.35
985	-5.1	-5.3	182.4	130.2
5280435	-5.0	-5.8	216.0	56.0
5282761	-5.5	-5.7	92.8	66.3
984	-4.9	-5.4	255.8	110.0
#54670067	-5.2	-6.1	154.1	33.7

#Ascorbic acid

Table 4. Binding affinity score and inhibitory constant for selected BF flower essential oil compounds.

PubChem ID	Binding affinity score (Kcal/mol)		Inhibitory constant (*μM*)	
	PDB: 1N3U	PDB: 2CDU	PDB: 1N3U	PDB: 2CDU
5280435	-5.0	-5.8	216.0	56.0
18827	-5.0	-4.5	216.0	502.4
31289	-5.2	-4.2	154.2	834.2
9895	-5.1	-5.3	182.4	130.2
6432045	-5.6	-6.2	78.4	28.5
638014	-5.7	-6.0	66.3	39.9
595137	-6.3	-7.1	24.1	6.2
10408	-6.1	-5.8	33.7	56.0
5364441	-5.9	-4.9	47.3	255.8
85014	-5.2	-5.1	154.1	182.4
1549107	-6.3	-5.9	24.1	47.3
5363741	-6.1	-6.1	33.7	33.7
638072	-6.9	-7.5	8.7	3.1
5283387	-5.5	-5.6	92.8	78.4
#54670067	-5.2	-6.1	154.1	33.7

#Ascorbic acid

leaf essential oil (19.5433 μg/mL) > flower essential oil (11.0674 μg/mL) (Table 2). Although the essential oils are less potent than ascorbic acid, the lower IC_{50} value of the flower oil compared to the leaf oil underscores its relatively stronger free radical scavenging ability. This suggests that the higher antioxidant capacity of the flower oil could be exploited in complementary therapeutic applications or as a natural antioxidant in food, cosmetics, and pharmaceutical formulations. Overall, these findings highlight that the chemical composition and relative abundance of key phytoconstituents, such as phytol and *α*-phellandrene, are critical determinants of the antioxidant activity in *B. formosa* essential oils, underscoring the potential for targeted extraction strategies to maximize bioactivity.

3.3. Molecular docking interactions

The docking results of the identified constituents found in BF plant essential oils are shown in Tables 3-4 and visualized in Figs 4-9, illustrating the mode of interaction with two major target proteins, 1N3U and 2CDU. The influence of the inhibitors on the active-site conformation of heme oxygenase (1N3U) and NADPH oxidase (2CDU) was examined through a detailed analysis of docking poses and protein–ligand interaction patterns. For heme oxygenase (1N3U), the active site is characterized by a predominantly hydrophobic pocket that accommodates planar and nonpolar ligands around residues, such as Ala28, Met34, and Phe207. Upon binding of high-affinity inhibitors (e.g., γ-gurjunene and aromadendrene), the ligands adopt orientations that maximize hydrophobic and π–

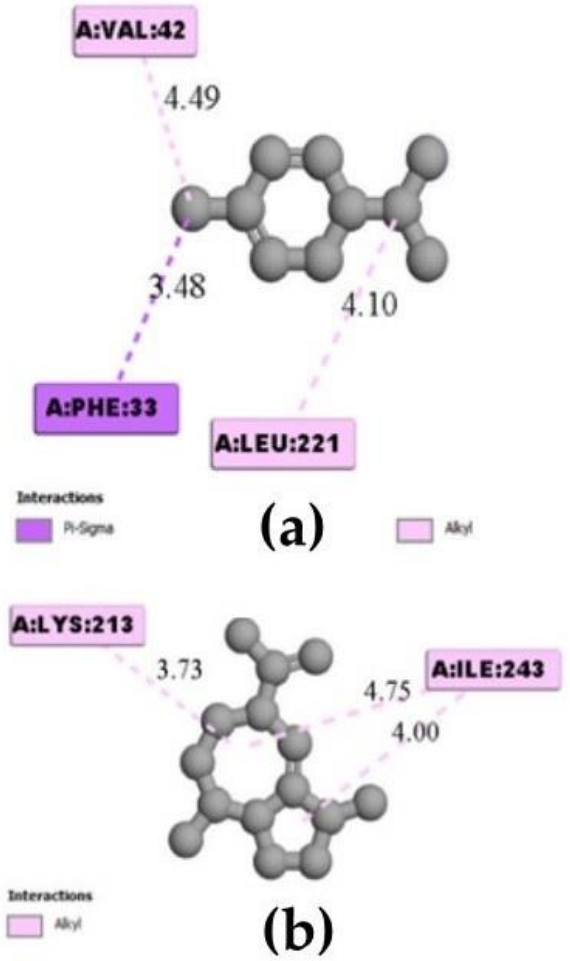

Figure 4. Docking interactions α-phellandrene and proteins (a) PDB: 1N3U (b) PDB: 2CDU.

alkyl interactions in this cavity. These interactions promote a stable ligand-bound conformation by effectively occupying the heme-binding region, thereby restricting substrate access and potentially limiting the conformational flexibility of nearby residues. Although rigid-receptor docking does not explicitly capture large-scale protein rearrangements, the consistent positioning of the ligands within the catalytic pocket suggests local stabilization of the active-site architecture.

In the case of NADPH oxidase (2CDU), the active site is more extended and involves residues critical for electron transfer and substrate binding, including Lys213, Ile243, Tyr159, and Tyr188. Binding of potent inhibitors, such as γ-gurjunene and squalene, resulted in favorable hydrophobic contacts that anchored the ligands within the catalytic region. These interactions likely induce subtle local conformational adjustments, particularly in flexible side chains, thereby disrupting the spatial arrangement required for efficient electron transfer and reactive oxygen species (ROS) generation. The observed binding modes suggest that inhibitor occupancy stabilizes an inactive or less catalytically competent conformation of the enzyme.

Overall, although the docking protocol employed assumes a rigid protein backbone, the interaction profiles indicate that inhibitor binding predominantly influences the local active-site environment rather than inducing global conformational changes. The stabilization of hydrophobic pockets and key catalytic residues by these inhibitors is consistent with a mechanism of competitive or pseudo-competitive inhibition, in agreement with previous reports on the small-molecule modulation of heme oxygenase and NADPH oxidase activities.

3.4. In silico drug-likeness and toxicity predictions

The characteristics of drug-likeness and toxicity of the compounds which having favourable binding affinity scores were assessed using molecular descriptive alignment with the Lipinski Rule of Five and toxicity prediction conditions (Table 5).

A clear negative correlation was observed between the binding affinity (kcal/mol) and the inhibitory constant, Ki (μM), confirming that compounds with more negative binding energies exhibit higher inhibitory potential. Among the BF leaf essential oil (BF-LEO) constituents, γ-gurjunene (PubChem ID 90805) was the most potent inhibitor, with binding affinities of -6.3 kcal/mol (1N3U) and -7.4 kcal/mol (2CDU), corresponding to Ki values of 24.1 μM and 3.7 μM, respectively. Interaction mapping revealed that γ-gurjunene stabilized the ligand-protein complex primarily through hydrophobic interactions with residues Ala28, Met34, and Phe207 in 1N3U, and Lys213 and Ile243 in 2CDU (Fig. 5). The dominance of hydrophobic contacts, including π-alkyl and alkyl interactions, underscores their crucial role in ligand stabilization, consistent with previous studies that emphasize hydrophobic effects as central determinants of protein-ligand affinity [26]. PubChem ID 91354 (aromadendrene) exhibited a

Table 5. Drug-likeness and toxicity potential of BF essential oil constituents.

Source	PubChem ID	Drug-Likeness					Toxicity	
		MW (g/mol)	Log Po/w	HBD	HBA	Lipinski violation	Carcinogenicity	Cardiotoxicity
BF-LEO	90805	204.35	4.58	0	0	0	Inactive	Inactive
	91354	204.35	4.27	0	0	0	Inactive	Inactive
BF-FEO	5364441	196.38	5.48	0	0	1	Inactive	Inactive
	1549107	222.37	4.39	1	1	0	Inactive	Inactive
	638072	410.73	10.61	0	0	1	Inactive	Inactive

*flower essential oil (BF-FEO); leaf essential oil (LEO); *Bougainvillea formosa* (BF).

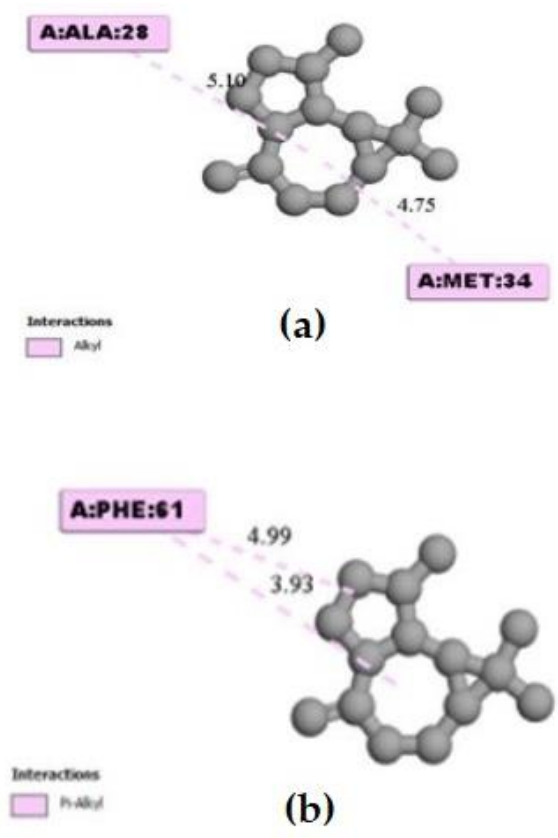

Figure 5. Docking interactions aromadendrene and proteins (a) PDB: 1N3U (b) PDB: 2CDU.

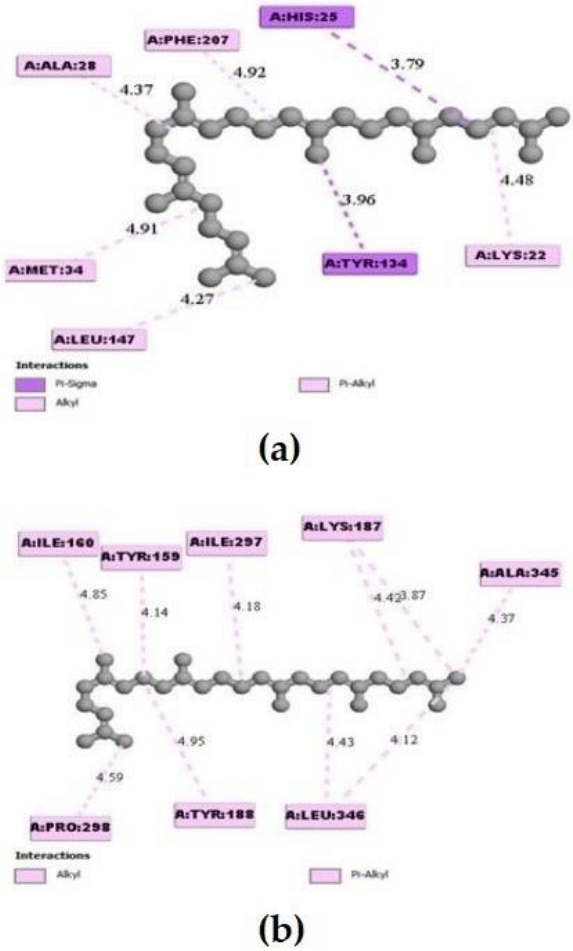

Figure 6. Docking interactions of squalene and proteins (a) PDB: 1N3U (b) PDB: 2CDU.

similar trend, with docking scores of -6.5 kcal/mol (1N3U) and -6.8 kcal/mol (2CDU), and Ki values of 17.2 μM and 10.35 μM, respectively, reinforcing the importance of hydrophobic interactions in maintaining high-affinity binding (Fig. 6). In contrast, compounds such as PubChem IDs 5280435 and 984 displayed lower docking scores (-4.9 to -5.4 kcal/mol) and higher Ki values (110–255.8 μM), reflecting weaker binding and reduced inhibitory potential.

Among the BF flower essential oil (BF-FEO) constituents, PubChem ID 638072 (squalene) emerged as the most favourable inhibitor, with docking scores of -6.9 kcal/mol (1N3U) and -7.5 kcal/mol (2CDU) and Ki values of 8.7 μM and 3.1 μM, respectively. This compound formed multiple stabilizing hydrophobic interactions with residues Lys22, Ala28, Met34, Tyr134, Leu147, and Phe207 in 1N3U, and Tyr159, Tyr160, Lys187, Tyr188,

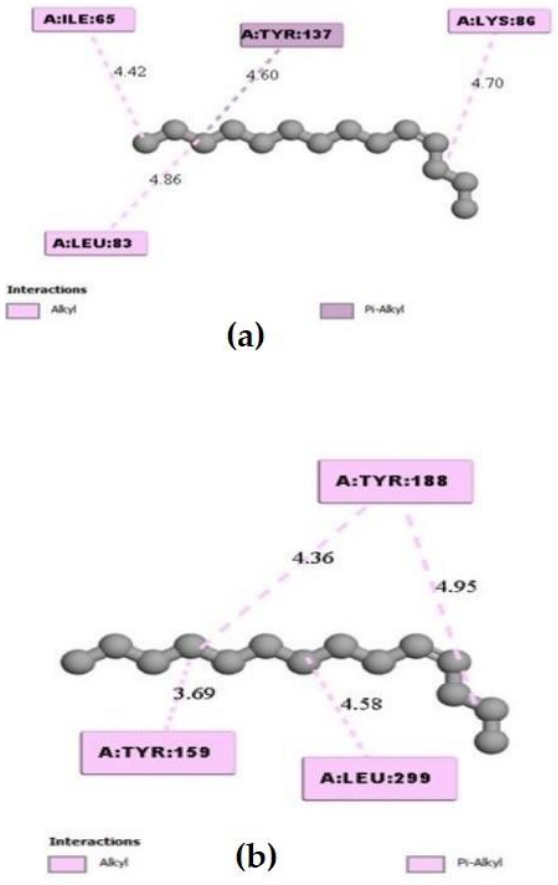

Figure 7. Docking interactions of tetradecene and protein (a) PDB: 1N3U (b) PDB: 2CDU.

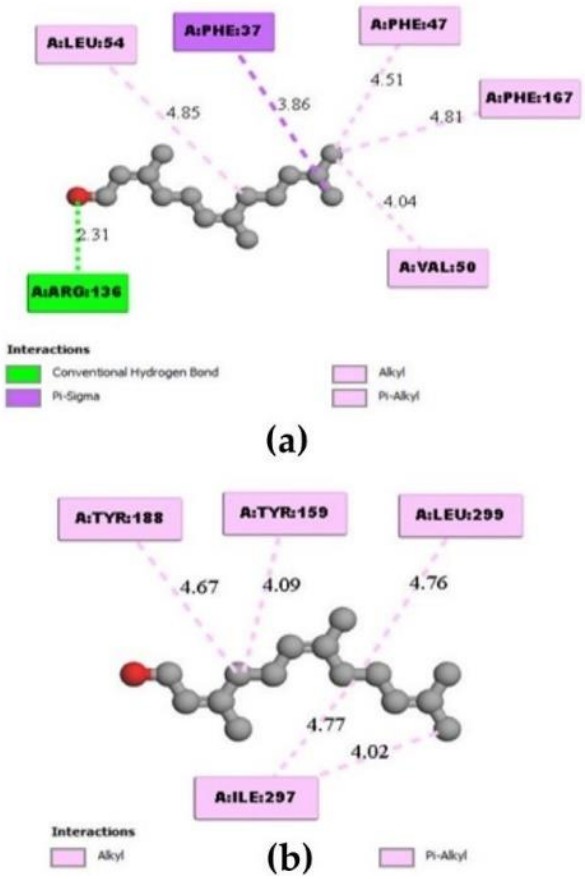

Figure 8. Docking interactions of farnesol and protein (a) PDB: 1N3U (b) PDB: 2CDU.

Ile297, Pro298, Ala345, and Leu346 in 2CDU (Fig. 7). Other BF-FEO constituents, including PubChem IDs 595137 (tetradecene) and 15491072 (farnesol), also demonstrated significant binding potential, with docking scores ranging from -5.9 to -7.1 kcal/mol and Ki values of 6.2–47.3 μM (Figs. 8–9, Table 4). PubChem ID 5363741 exhibited moderate binding (-6.1 kcal/mol) with a similar Ki value (33.7 μM). Collectively, the top-performing BF-LEO and BF-FEO compounds demonstrated superior inhibitory potential relative to ascorbic acid, highlighting their relevance as bioactive natural products (Fig. 3, Table 2).

Evaluation of drug-likeness using Lipinski's Rule of Five revealed that PubChem IDs 90805 and 91354 (BF-LEO) are highly favourable for oral bioavailability, with molecular weights of 204.35 g/mol, log P0/w values of 4.58 and 4.27, and zero hydrogen bond donors or acceptors, resulting in no Lipinski violations [25]. They were also predicted to be non-carcinogenic and non-cardiotoxic, further supporting their therapeutic potentials. Among the BF-FEO constituents, PubChem ID 15491072 also complied with Lipinski's criteria, whereas PubChem IDs 5364441 and 638072 exceeded the log P0/w threshold (5.48 and 10.61, respectively), suggesting potential limitations in oral bioavailability. Nonetheless, these compounds were predicted to be inactive for cardiotoxicity and carcinogenicity, indicating an acceptable safety profile.

The *in silico* pharmacokinetic and toxicity profiling further substantiated the therapeutic relevance of the top-ranked compounds. γ-gurjunene, aromadendrene, and squalene demonstrated favourable Human Intestinal Absorption (HIA) predictions and met Veber and Egan oral bioavailability criteria, indicating a high likelihood of adequate gastrointestinal absorption and systemic exposure. These compounds also exhibited acceptable molecular flexibility and polar surface areas, supporting their predicted oral

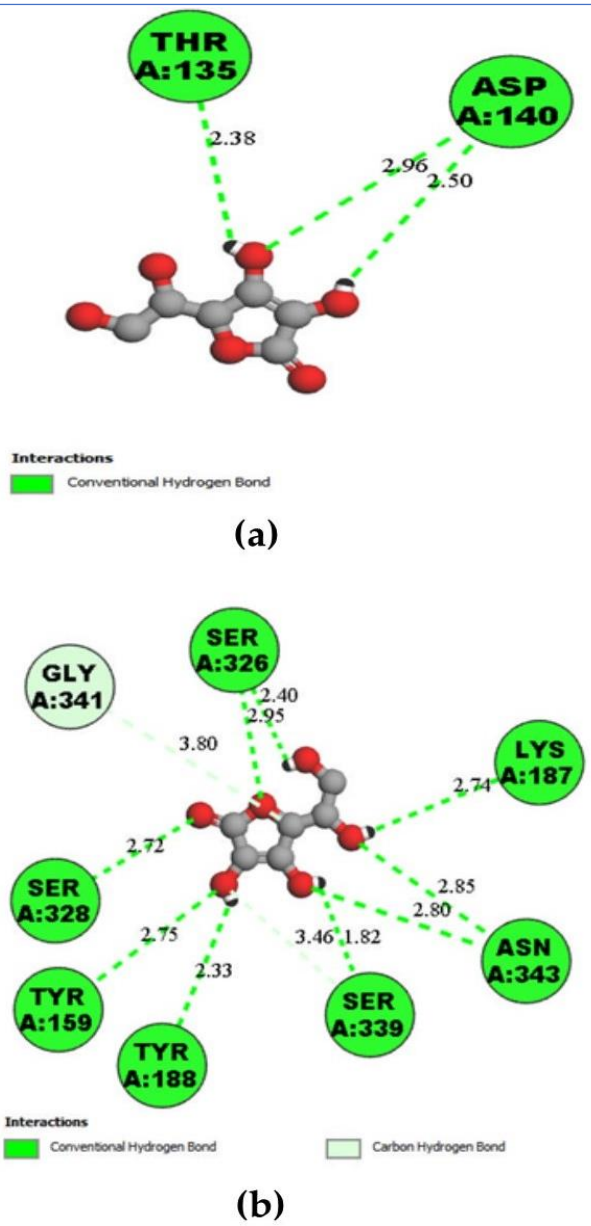

Figure 9. Docking interactions of ascorbic acid and protein (a) PDB: 1N3U (b) PDB: 2CDU.

bioavailability. Toxicity assessment revealed that the selected phytoconstituents were predominantly non-mutagenic (AMES), non-cytotoxic, non-carcinogenic, and non-hepatotoxic, suggesting a favourable safety profile at the preliminary screening level. Importantly, P-glycoprotein (P-gp) interaction analysis indicated that these compounds are weak substrates and non-inhibitors of P-gp, implying a reduced risk of efflux-mediated bioavailability limitations and transporter-driven drug–drug or herb–drug interactions. Collectively, these pharmacokinetic and toxicity predictions complement the molecular docking results, underscoring the significance of hydrophobic interactions in stabilizing ligand–protein complexes and mediating inhibitory potential. The convergence of strong binding affinities, favourable ADME characteristics, and acceptable safety profiles positions γ-gurjunene, aromadendrene, and squalene as promising candidates for further pharmacological investigation. These findings are consistent with previous reports highlighting the bioactivity of sesquiterpenes and triterpenes in plant-derived essential oils [27, 28] and reinforce the utility of integrated *in silico* approaches as reliable tools for natural product-based drug discovery.

Overall, this integrated experimental and computational analysis provides a mechanistic understanding of the bioactivity of BF leaf and flower essential oils. The combination of high-affinity binding, favourable ADMET profiles and safe pharmacological predictions supports the potential development of these essential oil constituents as therapeutic agents. Furthermore, the findings validate the traditional use of *B. formosa* and highlight its constituents as promising leads for the development of antioxidant and anticancer drugs.

4. Conclusions

This study provides a comprehensive experimental and computational evaluation of the essential oils derived from the leaves and flowers of *B. formosa*. GC–MS analysis identified 7 and 14 constituents in the leaves and flowers essential oils, accounting for 72.8% and 84.45% of the total composition, respectively, with α-phellandrene (19.13%) and gurjunene (8.52%) in the leaf EO and 1-octen-3-ol, accounting for 19.52% in the flower EO, as the dominant compounds. The essential oils exhibited moderate antioxidant activity, achieving a DPPH radical scavenging inhibition of 35.80%, indicating a substantial free radical–quenching capacity. Molecular docking studies revealed a clear inverse relationship between binding affinity and the inhibitory constant (Ki), confirming that more negative binding energies correspond to a stronger inhibitory potential. Among the bioactive constituents, γ-gurjunene (PubChem ID 90805) demonstrated the highest inhibitory activity, with

binding affinities of –6.3 kcal/mol (Ki = 24.1 μM) for 1N3U and –7.4 kcal/mol (Ki = 3.7 μM) for 2CDU. Aromadendrene (PubChem ID 91354) and squalene (PubChem ID 638072) also exhibited strong binding interactions, with docking scores ranging from –6.5 to –7.5 kcal/mol and Ki values as low as 3.1 μM, outperforming the reference compound ascorbic acid. Protein–ligand interactions were predominantly stabilized by hydrophobic contacts, including alkyl and π-alkyl interactions, highlighting their critical roles in binding stability and inhibitory efficacy. *In silico* pharmacokinetic analysis further demonstrated that γ-gurjunene and aromadendrene satisfied Lipinski, Veber and Egan oral bioavailability criteria, with favorable Human Intestinal Absorption predictions and no violations of drug-likeness rules. Toxicity assessments indicated that these compounds were non-mutagenic (AMES), non-carcinogenic, non-hepatotoxic, and non-cytotoxic, while P-glycoprotein interaction profiling suggested minimal risk of efflux-mediated bioavailability limitations or transporter-related drug–drug interactions. Overall, the integration of chemical profiling, biological assays, molecular docking and ADME–toxicity predictions provide strong mechanistic support for the antioxidant and cytotoxic potential of *B. formosa* essential oils. These findings validate the ethnomedicinal relevance of the plant and highlight γ-gurjunene, aromadendrene, and squalene as promising lead compounds for further pharmacological and drug development studies.

Abbreviations

SBDD: Structure-based drug design
DPPH: 2,2–Diphenyl–1–picrylhydrazyl radical
EO: Essential oil
1N3U: Oxidative stress-related proteins—heme oxygenase 1N3U
GC-MS: Gas Chromatography-Mass Spectrometry
LEO: Leaf essential oil
FEO: Flower essential oil
BF: *Bougainvillea formosa*

Disclaimer (artificial intelligence)

Author(s) hereby state that no generative AI tools such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators were utilized in the preparation or editing of this manuscript.

Authors' contributions

Laboratory work, conceptualization, result interpretation, and edited final manuscript, O.O.O., S.E.; drafted manuscript, M.G.I., A.O.O.; *in silico* molecular docking and toxicity studies, I.A.E., O.O.T., O.O.; essential oil extraction, laboratory works, and result interpretation, E.O.O., N.C.R.

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Availability of data and materials

All data obtained in this research have been included in the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

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