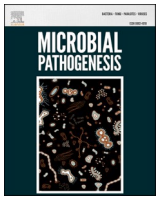
Microbial Pathogenesis 195 (2024) 106870

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath



Biological effects of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* extracts and their possible metabolomics therapeutics against the West Nile virus vector, *Culex pipiens* (Diptera: Culicidae)

Reham M. Mostafa [b], Mohamed M. Baz [a,**], Heba Talat Ebeed [c,d], Heba S. Essawy [b], Ghada E. Dawwam [b], Ahmed B. Darwish [e], Abdelfattah Selim [f,*], Nancy M. El-Shourbagy [a]

[a] Entomology Department, Faculty of Science, Benha University, Benha, 13518, Egypt
[b] Botany and Microbiology Department, Faculty of Science, Benha University, Benha, Qalyubiya, 13518, Egypt
[c] Botany and Microbiology Department, Faculty of Science, Damietta University, Damietta, 34517, Egypt
[d] National Biotechnology Network of Expertise (NBNE), Academy of Scientific Research and Technology (ASRT), Cairo, Egypt
[e] Zoology Department, Faculty of Science, Suez University, Suez, 43518, Egypt
[f] Department of Animal Medicine (Infectious Diseases), College of Veterinary Medicine, Benha University Toukh, 13736, Egypt

ARTICLE INFO

Keywords:
Culex pipiens
Larvicidal
Antimicrobial
GC-MS
HPLC
ADMET analysis
Phytochemicals
Ornamental plants

ABSTRACT

Plants are a treasure trove of biological materials containing a wide range of potential phytochemicals that are target-specific, rapidly biodegradable, and environmentally friendly, with multiple medicinal effects. Unfortunately, the development of resistance to synthetic pesticides and antibiotics led to the discovery of new antibiotics, antioxidants, and biopesticides. This has also led to the creation of new medications that work very well. The current study aimed to prove that ornamental plants contain specialized active substances that are used in several biological processes. Mosquitoes, one of the deadliest animals on the planet, cause millions of fatalities each year by transmitting several human illnesses. Phytochemicals are possible biological agents for controlling pests that are harmful. The potential of leaf extracts of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* against *Culex pipiens* and microbial agents was evaluated. Acetone extracts had more toxic effects against *Cx. pipiens* larvae (99.0–100 %, 72 h post-treatment), and the LC_{50} values were 142.8, 189.5, 95.4, and 71.1 ppm for *B. glabra, D. regia, L. camara,* and *P. orientalis*, respectively. Plant extracts tested in this study showed high insecticidal, antimicrobial, and antioxidant potential. GC-MS and HPLC analyses showed a higher number of terpenes, flavonoids, and phenolic compounds. The ADME analysis of element, caryophyllene oxide, caryophyllene, and copaene showed that they were similar to drugs and that they were better absorbed by the body and able to pass through the blood-brain barrier. Our results confirm the ability of ornamental plants to have promising larvicidal and antimicrobial activity and biotechnology.

1. Introduction

Mosquitos are vectors of many of the world's important human and veterinary diseases [1–5], including malaria, dengue, yellow fever, Japanese encephalitis, chikungunya, filariasis, and streptoderma of cattle [6,7]. Mosquito-borne diseases have an economic impact, including loss of commercial production and employment, the burden of disease and death, poverty, and social debilitation worldwide, particularly in countries with tropical and subtropical climates; however, no part of the world is free of vector-borne diseases [8–13].

Several methods are widely used to control the threats posed by mosquitoes. Synthetic insecticides have been introduced over the years, but despite their effectiveness, the insect is forced to adapt to such pesticides and, over time, acquire resistance to the pesticide products, coupled with environmental dangers from regular pesticide usage [14]. The most important alternatives to synthetic insecticides are phytochemicals (plant extracts or essential oils). Phytochemicals have a wide range of effects on mosquitos, including: ovidal, larvicidal, adulticidal, oviposition deterrent, developmental toxic, antifeedants, repellents, hatching blockers, and emergence blockers [15,16]. Many medicinal

* Corresponding author.
** Corresponding author.
E-mail addresses: mohamed.albaz@fsc.bu.edu.eg (M.M. Baz), Abdelfattah.selim@fvtm.bu.edu.eg (A. Selim).

https://doi.org/10.1016/j.micpath.2024.106870
Received 5 June 2024; Received in revised form 15 August 2024; Accepted 17 August 2024
Available online 18 August 2024

plant products have yet to be tested for their potency against mosquitoes.

Recently, great attention has been given to insecticides of plant origin and those that do not harm the ecosystem. Therefore, natural products are the most appropriate alternative to use because they cause less harm to the environment and non-target species, and they are eco-friendly, bio-sourced, and safe to use. Besides, many extracts and compounds from several plant groups have been investigated as potential new larvicides [17]. Studies have shown that saponin [18], steroids [19], isoflavonoids [20], essential oils [21], alkaloids [22], and tannins [23] can all be used to kill mosquito larvae. Many insect repellents are derived from plant compounds and essential oils. However, the botanicals have not been fully approved due to difficulties in formulation and marketing, which are attributed to a lack of chemical data and positive controls. Besides, many publications have included botanical pesticides with a skewed interest in insect pest management [24]. Furthermore, several studies failed to thoroughly investigate the effect of biopesticides generated from attractive plants on insects.

In addition to the beauty and splendour of ornamental plants and trees that grow in gardens, parks, houses, fields, and forests, they also carry deadly chemicals against insect pests within their tissues. We believed this since plants are known to possess a treasure mine of sustainable and renewable bioactive chemicals [25]. These plants contain compounds with larvicidal, ovicidal, and repellent activity, affecting the nervous respiratory, endocrine, and water balance systems of mosquitoes [26]. Researchers have extensively researched the ovicidal and larvicidal effects of these compounds on mosquitoes, effectively eliminating them during their immobile stages [27,28]. Researchers have used different plant-based chemicals, like essential oils, alkaloids, and aromatic compounds, as mosquito repellents. They have shown that these chemicals work to stop mosquitoes from looking for hosts when they are sprayed on the skin or inside homes [29].

One of these plants, *Lantana camara* Linn (Verbenaceae), is known as wide sage or lantana weed. It is a hefty, thorny, extensive evergreen shrub that can reach a height of 1–2 m, grows erect, and has a strong scent. The branches and stems have angular shapes and are organized along the margins with curving spines. Leaves are simple, opposite, oval, regularly dentate, and have an acute apex [30]. *L. camara* has also been used in traditional herbal medicines for the treatment of ailments, including cancer; skin itching, leprosy, rabies, chickenpox, measles, asthma, and ulcers [31].

All parts of this plant have been used conventionally for numerous diseases all over the world. This plant's leaves were used as an antibiotic and antihypertensive agent, while its roots were used to cure malaria, rheumatism, and skin rashes [32]. Extract from the leaves of *L. camara* displayed larvicidal action, while extract from the flowers of the plant shown repellent effect against adult mosquitoes [33].

Thuja, or *Platycladus orientalis*, is a bushy, thick, and conical to columnar evergreen and coniferous tree that belongs to the Cupressaceous family and is characterized by its resin and oil content in various forms. The leaves have triangular scales with a blunt point and are arranged in decussate pairs. Leaves emit an odor when bruised. In the winter, the foliage may turn bronze. cones, oval, up to 3/4″ long, rusty brown bark [34]. This tree thrives in both warm and temperate climates worldwide. *P. orientalis* is used in folk medicine to treat uterine cancer, psoriasis, amenorrhea, enuresis, rheumatism, cystitis, bronchial catarrh, and antibacterial action [35].

Bougainvillea glabra wild, also known as paper flower or Bougainvillea, is a woody vine belonging to the Nyctaginaceae family. It is native to South America, but it is spread all over the world for its wonderful ornamental properties. In fact, this plant blooms regularly, and the bracts are a stunning shade of purple, red, or white [36]. Plants have simple, alternate, ovate-acuminate leaves that are alternately 4–13 cm long, and their flowers are pink, magenta, purple, red, orange, white, or yellow [37]. There are 18 species in the genus Bougainvillea, some of which are used in traditional medicine to cure conditions like diarrhea, stomach acidity, sore throat, cough, leucorrhoea, and hepatitis. They also possess anti-inflammatory, antiviral, and antibacterial properties [38] and are larvicidal [39].

Delonix regia Rafin is a nearly evergreen, shallow-rooted legume tree found in temperate and tropical zones and widely grown throughout Africa and Southeast Asia. It is often referred to as the "flamboyant flame tree." It is a medium-sized decorative tree, and it is cultivated in gardens and avenues. The blooms with panicles, which are abundant in large, upright clusters along the branches and range in color from deep crimson to flaming orange to delicate salmon, make for a stunning appearance [40]. *D. regia* extract was reported to have a wide range of bioactivities. The plant has shown promising antioxidant [41], antimicrobial [42], antidiabetic [43], anti-inflammatory [44], and larvicidal [45] activities. The Mediterranean region's vegetation, particularly urban flora and vegetation is diverse in composition and distribution. The ecological and evolutionary trends of regional metropolitan regions are frequently disregarded. Researchers identified 338 plant species, including inferaspecific taxa, in Alexandria's urban areas. Therophytes constituted 50 % of the population, with approximately 19 % cultivated for ornamental or crop purposes. The study area recorded 91 alien plant species, accounting for 9.26 % of the total, including six invasive species [46].

Phytochemicals are regarded safe for human intake because of their remarkable ability to target specific damaged cells via many signalling pathways while sparing normal cells. Phytochemicals can function in a variety of ways, including activating enzymes, while others hinder cancer cells from proliferating by interfering with DNA replication. As a result, these phytochemicals can control cancer cell proliferation. Some may possess antibacterial characteristics, preventing pathogens from adhering to cell membranes. Numerous plant metabolites have antibacterial and insecticidal properties, giving plants natural protection against infections and pests. Citronella, eucalyptus, lavender, and peppermint are examples of ornamental plant essential oils that are useful against a variety of bacteria and pests [47,48]. Neem oil contains azadirachtin, which has antimicrobial activity and disrupts the feeding and reproductive processes of insects [49,50]. Pyrethrins are natural insecticides derived from the flowers of *Chrysanthemum cinerariaefolium* which affect the nervous system of insects but also possess some degree of antimicrobial properties [51]. Tannins, a wide collection of polyphenolic chemicals found in a variety of plant tissues, can have insecticidal properties by interfering with insect digestion and nutrient absorptionThey are known to have antibacterial properties against bacteria, fungus, and other microbes. Tannins' antimicrobial properties are due to their capacity to interact with microbial cell structures and enzymes [52]. Monoterpenoids are a type of chemical molecule composed of two isoprene units that are typically found in essential oils from various plants. These molecules have a variety of bioactivities, and their effects differ depending on the type of monoterpenoid and the context of consumption. Essential oils are liquid mixes of volatile and semi-volatile chemicals, primarily monoterpenes and sesquiterpenes, derived from plant secondary metabolism and have shown significant variability in terms of chemical composition [53].

The screening of compounds with potential bioactivity is both expensive and time-consuming. However, computer-aided drug design (CADD) could save time and money on molecule synthesis, thereby lowering the cost of research. Such studies would culminate in the development of novel drug molecules at a faster pace against infectious pathogens. Additionally, the physicochemical properties of the molecule would provide vital information on the initial phase of drug development [54]. ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) analysis is a critical component of computational drug design, and ADMET research evaluates a drug's pharmacokinetics. Prediction of a drug's fate and effects inside the body, such as how much medication is absorbed if delivered orally and how much is absorbed in the gastrointestinal tract, is an essential element of drug discovery. Similarly, if absorption is poor, distribution and metabolism are

impaired, which can result in neurotoxicity and nephrotoxicity [55].

In this work, we hypothesize that ornamental plant extracts *B. glabra, D. regia, L. camara,* and *P. orientalis* have many biologically active phytochemical compounds with lethal effects against *Cx. pipiens* mosquito larvae and different multidrug resistant (MDR) pathogenic microbes (*Candida albicans, Listeria monocytogenes, Salmonella* sp., *and Pseudomonas aeruginosa*). Therefore, we aim to identify the phytochemical profile of these plants in acetone and aqueous extracts through GC-MS and HPLC analysis, then evaluate the larvicidal, antimicrobial, and antioxidant activities of these extracts, and assess the bioactivity and pharmacokinetic indices related to the ADMET aspects in light of the possible therapeutic powers of the selected plant metabolites. The flow chart of the article summarizes the steps for our study as shown in Fig. 1.

2. Materials and methods

2.1. Plant materials and analysis

2.1.1. Plant collection

Leaves of ornamental plants, *B. glabra* Choisy, *D. regia* Bojer, *L. camara* L., and *P. orientalis* Franco, were collected from farmlands at the Faculty of Agriculture, Qalyubiya Governorate, Egypt, during September–November 2021 (Table 1, Fig. 2). Plants were identified by Dr. Ahmed Moubarak at the Flora and Phytotaxonomy Section, Botany Department, Faculty of Science, Benha University, Egypt, according to reference books of Egyptian flora [56,57]. This comment has been mentioned in other articles because we rely on Dr. Ahmed Moubarak for the classification. The study plant specimens were deposited in an herbarium of the botany department, Faculty of Science, with respective voucher numbers for *Bougainvillea glabra* C. (B87), *Delonix regia* B. (B65), *Lantana camara* L. (B112), and *Platycladus orientalis* F. (B365). The plant materials were shade-air dried at room temperature until the plant was well-dried and the dry weight contracted. The dried tissues were ground in a stainless-steel electric mixer and transferred into airtight containers to protect them from humidity [58].

2.1.2. Plant extraction

The acetone extract was prepared by soaking 20 g of dry plant materials in 100–150 mL of acetone in a stoppered conical flask (capacity 250 mL) and allowed to stand at room temperature (27 ± 2 °C) for 3 days with frequent agitation until the soluble matter has dissolved. Another 20 g of plant materials were extracted using warm water (60 °C) at room temperature to prepare the aqueous extract. The extraction was done after 48 h, and then the solution was filtered using Whatman No. 1 filter paper through a Buchner funnel. The extracts were concentrated using a rotary evaporator and then stored in black bottles [16].

Table 1
List of plant species and plant parts tested against *Culex pipiens* larvae and selected microbial species.

No.	Common Name	Botanical Name	Family	Part used	Site of collection
1	Paperflower	Bougainvillea glabra	Nyctaginaceae	Leaf	Benha, Qalyubia[a]
2	Royal poinciana	*Delonix regia*	Fabaceae	Leaf	
3	Largeleaf lantana	*Lantana camara*	Verbenaceae	Leaf	
4	Thuja	*Platycladus orientalis*	Cupressaceae	Leaf	

[a] Coordinate 30°27′39″N 31°11′15″E.

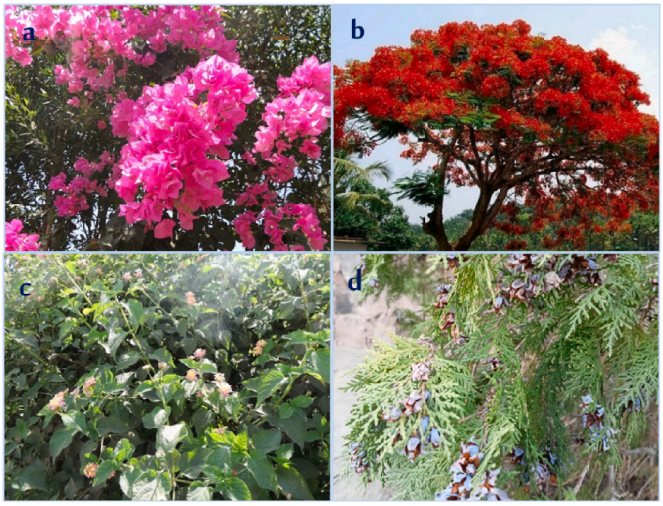


Fig. 2. Study plants: *Bougainvillea glabra* (a), *Delonix regia* (b), *Lantana camara* (c), and *Platycladus orientalis* (d).

2.2. Mosquito larvicidal assay

2.2.1. Rearing of Culex pipiens

Cx. pipiens larvae were reared in the insectary, and they were

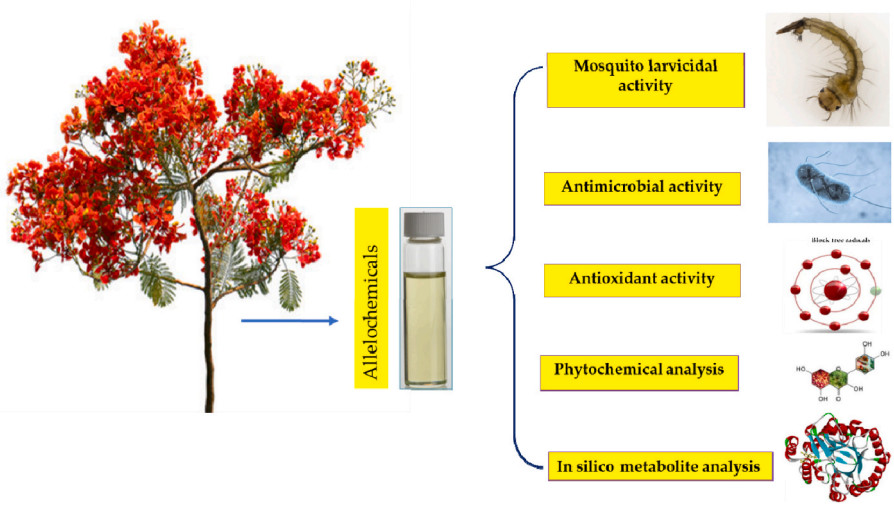


Fig. 1. Flowchart of research structure.

maintained at 27 ± 2 °C and 75 ± 5 % relative humidity for a photoperiod of 12:12 h (light/dark). The larvae were fed fish food (Tetramin) and ground bread in a 3:1 ratio. The pupae were then transferred from the enamel pans to a cup filled with dechlorinated water and placed in screened cages (35x35 × 40 cm in size), where the adults ultimately emerged. Female mosquitos were fed blood on a regular basis by a hamster rat, while the adult mosquito colony was given a 10 % sugar solution. Larvae and pupae, which are two phases of development, were always available for testing and stored in the same laboratory [59].

2.2.2. Larvicidal activity

The plant leaf acetone and aqueous extracts of *B. glabra, D. regia, L. camara,* and *P. orientalis* were evaluated against 4th larval instar of *Cx. pipiens* under laboratory conditions. The 4th larval instar was treated with the following concentrations: 62.5, 125, 250, 500, 1000, and 1500 ppm (1 g/1000 ml of distilled water). Twenty larvae per concentration were transferred to a glass beaker containing 250 mL of distilled water. Three replicates were used for each concentration. Mortalities were recorded 24, 48 h and 72 h after the initial exposure [9] and post-treatments (PT).

2.3. Antimicrobial assay

2.3.1. Collection of microbial pathogens

Multidrug-resistant bacteria such as *Listeria monocytogenes* (ATCC 19155), *Pseudomonas aeruginosa* (ATCC 9027), and *Salmonella* sp. (ATCC 14028), in addition to the pathogenic fungus *Candida albicans* (ATCC 10231) were utilized in the current study. The ATCC microbial strains tested in this study are obtained from Thermo Fisher Specialty Diagnostics Ltd, Hampshire, UK.

2.3.2. Antimicrobial activity

Antimicrobial activity of the acetone and aqueous extracts of *L. camara, D. regia, B. glabra,* and *P. orientalis* was tested against unicellular fungi (*C. albicans*), Gram-positive bacteria (*L. monocytogenes*), and Gram-negative bacteria (*Salmonella* sp. and *P. aeruginosa*) via the agar diffusion approach according to Aletayeb, Khosravi [60]. The bacteria were grown in a nutrient-liquid medium on a shaker bed at 200 rpm for 24 h at 37 °C. The bacteria (1.5 × 108 CFU) were swabbed on nutrient agar plates; subsequently, 200 μL of plant extract were deposited in wells (diameter of 7 mm) cut into agar plates. For 24 h, agar plates were incubated at 37 °C. All the studies were carried out in triplicate for all tested strains, and the inhibition zones surrounding the discs were quantified in millimeters.

2.3.3. Antioxidant DPPH assay

1,1-diphenyl-2-picryl hydrazyl (DPPH) was used to measure how well different extracts of plant leaves got rid of free radicals. In brief, a 0.1 mM solution of DPPH in ethanol was prepared. This solution (1 ml) was added to 3 ml of different extracts in ethanol at different concentrations (3.9, 7.8, 15.62, 31.25, 62.5, 125, 250, 500, and 1000 μg/ml). Here, only those extracts are used that are solubilized in ethanol, and their various concentrations were prepared by the dilution method. The mixture was shaken vigorously and allowed to stand at room temperature for 30 min. Then, absorbance was measured at 517 nm by using a spectrophotometer (UV–VIS, Milton Roy). The reference standard compound being used was ascorbic acid, and the experiment was done in triplicate. The IC50 value of the sample, which is the concentration of sample required to inhibit 50 % of the DPPH free radical, was calculated using the log dose inhibition curve. The DPPH scavenging effect (%) is calculated according to the following equation: DPPH scavenging effect (%) or Percent inhibition = A0 - A1/A0 × 100, where A0 was the absorbance of the control reaction and A1 was the absorbance in the presence of a test or standard sample [61].

2.4. Phytochemical identification and in silico analysis

2.4.1. GC/MS analysis

For the biochemical analyses of the plant leaf acetone and aqueous extracts, Thermo Scientific Trace GC Ultra/ISQ Single Quadrupole MS and TG-5MS fused silica capillary columns, 0.1 mm, 0.251 mm, and 30 m thick, were used. It was done using an electronic ionizer with 70 eV ionization energy. As a carrier gas, helium gas was used (flow rate: 1 ml/min). The MS transmission line and injector were both set to 280 °C. The oven was preheated to 35 °C, then increased to 150 °C at a rate of 7 °C per min, 270 °C at a rate of 5 °C per minute (pause for 2 min), and lastly, 310 °C at a rate of 3.5 °C per minute (continued for 10 min). A relative peak area was employed to explore the quantification of all components discovered. It was possible to figure out what chemicals they were by comparing their retention times and mass spectra to data from the NIST and Willy libraries on the GC/MS instrument. Identification was done using the aggregate spectrum of user-generated reference libraries. To evaluate peak homogeneity, single-ion chromatographic reconstructions were performed. To verify GC retention times, co-chromatographic analysis of reference substances was used whenever possible [62].

2.4.2. HPLC measurement of the concentration of polyphenol contents

Using an Agilent 1260 series, high-performance liquid chromatography was carried out for polyphenol detection analysis in the *L. camara* and *P. orientalis* acetone extracts (the most efficient plant leaf extracts in sections "2.3 & 2.4"). An Eclipse C18 column (4.6 mm × 250 mm i.d., 5 m) was used for the separation procedure. A mixture of water (solution A) and 0.05 % trifluoroacetic acid in acetonitrile (solution B), injected at a flow rate of 0.9 mL/min, made up the mobile phase. The linear gradient of the following time intervals was programmed for the mobile phase in order: 0 min (82 % A), 0–5 min (80 % A), 5–8 min (60 % A), 8–12 min (60 % A), 12–15 min (82 % A), 15–16 min (82 % A), and 16–20 min (82 % A). A 280 nm wavelength was selected for the multi-wavelength detector. Five liters of each sample solution were injected. To keep the column temperature at 40 °C, an adjustment was made [63].

2.4.3. In silico absorption, distribution, metabolism, excretion, and toxicity (ADMET) analysis

The identified phytochemicals in *L. camara* acetone extract (the most efficient plant in antimicrobial analysis) were analyzed for their ADMET analysis using the Swiss ADME server (http://www.swissadme.ch/index.php). This server evaluates the compounds for their physicochemical properties, lipophilicity, water solubility, pharmacokinetics, drug likeness, and medicinal chemistry. Further, the toxicity properties of the identified phytochemicals were analyzed using online servers, Protox-II (https://tox-new.charite.de/protox_II/) [64] and StopTox (https://stoptox.mml.unc.edu/) [65]. Protox-II predicted the LD50 (mg/kg) of the identified ligands and toxicity class, whereas StopTox identified cardiotoxicity (hERG liability prediction).

2.4.4. Statistical analysis

The data were analyzed by the software, SPSS V23 (IBM, USA), for doing the Probit analyses to calculate the lethal concentration (LC) values and the Two-way analysis of variance (ANOVA) (Post Hoc/Turkey's HSD test). The significant levels were set at $P < 0.05$.

3. Results

3.1. Mosquito larvicidal activity

In this study, plant extracts from *Bougainvillaea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* were evaluated on 4th instar larvae of *Cx. pipiens*. All the tested plant extracts in this study showed high insecticidal activity against mosquito larvae, *Culex pipiens,* after different intervals of exposure. The results showed that acetone extracts of plant materials in this study had more toxic effects against mosquito

larvae, *Cx. pipiens* than aqueous extracts.

The mortality percent (MO%) at 24 h post-treatment (PT) of *Cx. pipiens* with 1500 ppm acetone extracts of *B. glabra, D. regia, L. camara, and P. orientalis* was 99, 94, 100, and 100 % (MO%) (Table 2) with LC_{50} (50 %, median lethal concentration) = 270.1, 357.0, 183.2, and 148.1 ppm, respectively (Table 3); whereas those of aqueous extracts were 93, 90, 96, and 87 (MO%) with LC_{50} values = 382.0, 444.3, 335.7, and 502.8 ppm.

The highest larval mortality was recorded after 48 h of PT, where the mortality reached 100 % in acetone extracts for *B. glabra, D. regia, L. camara,* and *P. orientalis* and 100, 99, 100, and 93 % in aqueous extracts, respectively, at 1500 ppm. In terms of lethal concentrations, LC_{50} (50 %, median lethal concentration) for *P. orientalis* acetone extracts appeared to be most effective against *Cx. pipiens* larvae (LC_{50} = 98.5 ppm), followed by *L. camara* (LC_{50} = 127.4 ppm) and *B. glabra* (LC_{50} = 194.2 ppm) (Table 3, Fig. 3a), while *D. regia* was the least effective on *Cx. pipiens* (LC_{50} = 254.1 ppm). Among those aqueous extracts, *L. camara* appeared to be most effective against *Cx. pipiens* (LC_{50} = 268.0 ppm), followed by *B. glabra* (LC_{50} = 292.7 ppm) and *D. regia* (LC_{50} = 319.6 ppm), while *P. orientalis* was the least effective on *Cx. pipiens* larvae (LC_{50} = 376.1 ppm) (Table 4, Fig. 3b).

It is obvious from Tables 3 and 4 and Fig. 3 that the LC_{50} values of acetone of *B. glabra* (142.8 ppm), *D. regia* (189.5 ppm), *L. camara* (95.4 ppm), and *Platycladus orientalis* (71.1 ppm) were more effective than aqueous extracts (LC_{50} = 177.7, 228.5, 164.8, and 263.5 ppm, respectively, against the 4th larval instar of *Cx. pipiens*, 72 h PT).

3.2. Biological characteristics of the plant extracts

3.2.1. Antimicrobial activity

To investigate the antimicrobial activity of the aqueous and acetone extracts of the four plants, four different pathogenic microbes were used in the antimicrobial activity analysis. The diameters of the inhibition zones served to express the results of antimicrobial activity. Data in Table 5 demonstrated that *L. camara* acetone extract inhibited all the tested microbial isolates giving inhibition zones ranging between 13 mm for *C. albicans* to 20 mm for *L. monocytogenes*. In addition, acetone extracts of *D. regia* and *P. orientalis* inhibited the growth of *L. monocytogenes* and *P. aeruginosa*, giving inhibition zones of 18 and 14 mm, respectively. No antibacterial activity was recorded for *B. glabra* (Fig. 4). The results also showed that the antimicrobial activity was not effective in the aqueous extracts.

3.2.2. Antioxidant Activity—DPPH assay

To investigate the antioxidant capacity of acetone extracts as most efficient than aqueous extracts in the antimicrobial activity, DPPH scavenging was used. The DPPH radical scavenging activity values of the acetone extracts of *D. regia, B. glabra, L. camara,* and *P. orientalis*, along with standard Ascorbic acid, are shown in Table 6 and Fig. 5. The highest DPPH free radical scavenging activity was obtained from the extract of *D. regia*, followed by *P. orientalis* and *B. glabra*, while the lowest DPPH free radical scavenging activity was recorded from *L. camara*. As shown in Fig. 5, the DPPH scavenging assay of the extract increases in a concentration-dependent manner, as exhibited by the standard, ascorbic acid. The IC50 values of *D. regia, B. glabra, L. camara,* and *P. orientalis* extract were found to be 5.95, 22.65, 29.80, and 15.25 μg/ml, respectively, whereas the IC50 value of Ascorbic acid was 2.52 μg/ml. The free radical activity of DPPH ranged from 5.95 μg/ml to 29.80 μg/ml. The *D. regia* extract (IC50 = 5.95 μg/ml) was found to be more effective than the other plant extracts. The extracts of *D. regia* and *P. orientalis* were moderately good compared to ascorbic acid.

Table 2
Efficacy of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* extracts on *Culex pipiens* larval mortality, 24, 48, and 72 h post-treatment (mean ± SE).

Plant species	Conc. (ppm)	Acetone			Aqueous		
		24	48	72	24	48	72
Bougainvillea glabra	0	0 ± 0^{gA}	0 ± 0^{gA}	0 ± 0^{fA}	0 ± 0^{gA}	0 ± 0^{gA}	0 ± 0^{fA}
	62.5	11 ± 1.87^{fC}	17 ± 1.22^{fB}	22 ± 1.22^{eA}	8 ± 2.55^{fC}	11 ± 1.87^{fB}	19 ± 1.87^{eA}
	125	24 ± 1.87^{eC}	33 ± 2.55^{eB}	42 ± 3.39^{dA}	16 ± 2.92^{eC}	25 ± 2.24^{eB}	34 ± 2.92^{dA}
	250	42 ± 4.36^{dC}	57 ± 2.55^{dB}	66 ± 3.67^{cA}	32 ± 2.55^{dC}	41 ± 1.87^{dB}	59 ± 4.30^{cA}
	500	66 ± 1.87^{cC}	80 ± 3.54^{cB}	94 ± 3.67^{bA}	57 ± 4.64^{cC}	66 ± 3.32^{cB}	82 ± 2.55^{bA}
	1000	92 ± 1.22^{bC}	98 ± 1.22^{bB}	100 ± 0.00^{aA}	78 ± 4.36^{bC}	88 ± 3.39^{bB}	98 ± 1.22^{aA}
	1500	99 ± 1.00^{aA}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	93 ± 3.00^{aC}	100 ± 0.00^{aA}	100 ± 0.00^{aA}
Delonix regia	0	0 ± 0^{gA}	0 ± 0^{gA}	0 ± 0^{fA}	0 ± 0^{gA}	0 ± 0^{gA}	0 ± 0^{gA}
	62.5	11 ± 1.87^{fC}	18 ± 1.22^{fB}	21 ± 1.00^{eA}	7 ± 1.22^{fC}	8 ± 1.22^{fB}	14 ± 1.00^{fA}
	125	22 ± 2.55^{eC}	29 ± 1.87^{eB}	34 ± 2.92^{dA}	14 ± 1.87^{eC}	21 ± 2.45^{eB}	26 ± 1.87^{eA}
	250	36 ± 4.85^{dC}	41 ± 3.67^{dB}	54 ± 4.85^{cA}	28 ± 1.22^{dC}	34 ± 1.87^{dB}	49 ± 1.87^{dA}
	500	55 ± 5.00^{cC}	66 ± 3.67^{cB}	82 ± 2.55^{bA}	50 ± 2.24^{cC}	64 ± 4.30^{cB}	78 ± 2.00^{cA}
	1000	75 ± 4.74^{bC}	90 ± 3.54^{bB}	99 ± 1.00^{aA}	74 ± 3.67^{bC}	84 ± 2.45^{bB}	90 ± 2.24^{bA}
	1500	94 ± 2.45^{aB}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	90 ± 1.58^{aB}	99 ± 1.00^{aA}	100 ± 0.00^{aA}
Lantana camara	0	0 ± 0^{gA}	0 ± 0^{fA}	0 ± 0^{eA}	0 ± 0^{gA}	0 ± 0^{gA}	0 ± 0^{fA}
	62.5	16 ± 1.87^{fC}	23 ± 1.22^{eB}	30 ± 2.24^{dA}	9 ± 1.87^{fB}	14 ± 1.87^{fB}	20 ± 1.58^{eA}
	125	34 ± 2.92^{eC}	48 ± 2.55^{dB}	61 ± 2.92^{cA}	18 ± 1.22^{eB}	26 ± 2.92^{eB}	37 ± 3.39^{dA}
	250	59 ± 4.85^{dC}	75 ± 2.24^{cB}	91 ± 4.00^{bA}	37 ± 2.00^{dB}	44 ± 4.30^{dB}	62 ± 7.18^{cA}
	500	82 ± 2.55^{cC}	95 ± 2.74^{bB}	100 ± 0.00^{aA}	60 ± 2.24^{cB}	69 ± 6.60^{cB}	84 ± 4.85^{bA}
	1000	98 ± 2.00^{bB}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	82 ± 3.39^{bB}	91 ± 3.32^{bB}	100 ± 0.00^{aA}
	1500	100 ± 0.00^{aA}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	96 ± 1.87^{aB}	100 ± 0.00^{aA}	100 ± 0.00^{aA}
Platycladus orientalis	0	0 ± 0^{fA}	0 ± 0^{eA}	0 ± 0^{dA}	0 ± 0^{gA}	0 ± 0^{gA}	0 ± 0^{gA}
	62.5	18 ± 1.22^{eC}	27 ± 3.74^{dB}	43 ± 3.39^{cA}	7 ± 2.00^{fC}	13 ± 1.22^{fB}	16 ± 1.00^{fA}
	125	39 ± 2.92^{dC}	61 ± 3.32^{cB}	80 ± 2.74^{bA}	15 ± 4.18^{eC}	21 ± 2.92^{eB}	27 ± 3.00^{eA}
	250	71 ± 3.67^{cC}	91 ± 2.92^{bB}	100 ± 0.00^{aA}	28 ± 4.36^{dC}	35 ± 4.18^{dB}	43 ± 6.82^{dA}
	500	93 ± 3.39^{bB}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	46 ± 6.40^{cC}	52 ± 5.39^{cB}	64 ± 2.92^{cA}
	1000	100 ± 0.00^{aA}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	65 ± 5.70^{bC}	72 ± 2.55^{bB}	84 ± 4.30^{bA}
	1500	100 ± 0.00^{aA}	100 ± 0.00^{aA}	100 ± 0.00^{aA}	87 ± 5.83^{aC}	93 ± 2.55^{aB}	100 ± 0.00^{aA}

a, b & c …. etc: There is no significant difference ($p > 0.05$) between any two means within the same column have the same superscript letter, and A, B & C … etc: There is no significant difference ($p > 0.05$) between any two means for the same solvent within the same row have the same superscript letter. Five replicates were used for each concentration (20 larvae/replicate were used).

Table 3
Lethal concentrations (ppm) of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* acetone extracts against *Culex pipiens*, 24, 48 and 72 h post-treatment.

Time (h)	Plant species	LC_{50} (Low. - Up.)	LC_{90} (Low. - Up.)	LC_{95} (Low. - Up.)	Equation**	X^2 (Sig.)
24	*B. glabra*	270.1 (237.9–305.2)	1022.6 (860.9–1258.6)	1491.4 (1216.0–1917.3)	2.216 ± 0.138	6.106 (0.191)
	D. regia	357.0 (308.0–413.8)	1841.6 (1436.1–2533.4)	2932.1 (2173.6–4328.3)	1.798 ± 0.132	7.794 (0.099)
	L. camara	183.2 (160.6–207.3)	623.2 (526.0–767.7)	881.8 (720.8–1136.5)	2.410 ± 0.168	4.429 (0.351)
	P. orientalis	148.1 (130.8–166.3)	429.2 (367.0–521.5)	580.2 (481.8–735.5)	2.774 ± 0.206	2.448 (0.654)
48	*B. glabra*	194.2 (168.3–221.8)	767.5 (636.0–969.1)	1133.2 (904.5–1508.6)	2.147 ± 0.152	4.268 (0.370)
	D. regia	254.1 (217.5–295.0)	1285.8 (1012.8–1747.8)	2036.0 (1524.7–2973.2)	1.820 ± 0.139	8.114 (0.087)
	L. camara	127.4 (111.1–144.0)	397.9 (344.1–473.7)	549.5 (462.6–680.2)	2.591 ± 0.179	1.939 (0.918)
	P. orientalis	98.5 (87.1–109.9)	237.0 (205.1–286.5)	303.9 (255.6–384.4)	3.363 ± 0.308	1.285 (0.863)
72	*B. glabra*	142.8 (125.1–161.3)	444.8 (378.0–544.6)	613.7 (505.6–786.3)	2.598 ± 0.194	6.497 (0.165)
	D. regia	189.5 (128.3–263.1)	848.4 (630.7–1637.9)	1297.6 (948.9–2870.8)	1.968 ± 0.154	10.375 (0.034)
	L. camara	95.4 (83.6–107.0)	240.6 (207.4–292.4)	312.8 (261.6–398.7)	3.190 ± 0.295	3.065 (0.546)
	P. orientalis	71.1 (62.0–79.4)	149.2 (130.7–179.5)	184.0 (156.7–233.1)	3.987 ± 0.464	2.491 (0.646)

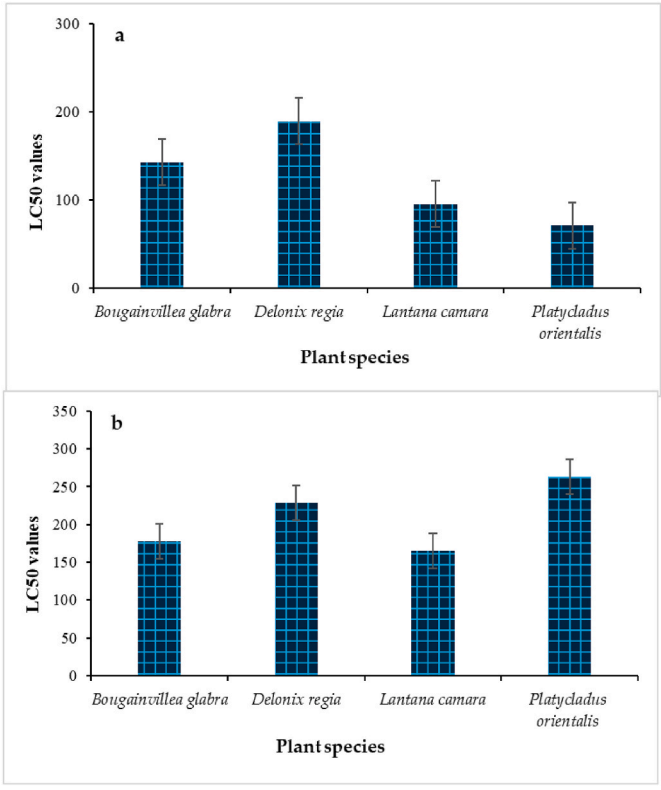


Fig. 3. The mean number of larval mortalities induced by the effects of *Lantana camara, Delonix regia, Bougainvillea glabra,* and *Platycladus orientalis* acetone (a) and aqueous (b) extracts against 4th larval instars of *Culex pipiens*, 72 h post-exposure.

3.3. Metabolomic analysis of four plant extracts

3.3.1. GC-MS data analysis

Metabolomic analysis of the eight extracts and comparison between aqueous and acetone extracts were done by the help of GC-MS analysis. Results of GC-MS analysis in our study led to the identification of various compounds such as terpenes, fatty acids, esters, ketone, alkane, steroids, aliphatic amine, and phenols in the leaves of *B. glabra, D. regia, L. camara,* and *P. orientalis* by using two different solvents (acetone and aqueous) (Tables 7–10 and Fig. 6).

B. glabra acetone leaf extract contained 19 compounds (Table 7), while the aqueous leaf extract contained 12 compounds, in which *B. glabra* showed abundance of Pimaric acid (24.65 %), 2-Pentanone, 4-hydroxy-4-methyl (16.49 %), and Caryophyllene (14.61 %) in the acetone extract, while in the aqueous extract it was Cis-13-Eicosenoic acid (36.78 %), 9-Hexadecenoic acid, 9-octadecenyl ester,(Z,Z)- (15.74 %), and Oleyl oleate (12.61 %).

D. regia acetone leaf extract had 22 compounds, as shown in Table (8), while aqueous leaf extract had 12 compounds. The highest concentrations of the detected compounds in acetone were Dl-à-tocopherol (28.39 %) and squalene (20.83 %), while in aqueous extract they were Erucic acid (30.92 %) and (E)-13-Docosenoic acid

Table 5
Antimicrobial activities of acetone extracts of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* against several pathogenic microorganisms.

Microorganism	Inhibition zone (mm)			
	B. glabra	D. regia	L. camara	P. orientalis
L. monocytogenes ATCC 19155	0 ± 0.0	18 ± 0.0	20 ± 0.28	0 ± 0.0
P. aeruginosa ATCC 9027	0 ± 0.0	0 ± 0.0	15 ± 0.30	14 ± 0.52
Salmonella sp. ATCC 14028	0 ± 0.0	0 ± 0.0	14 ± 0.27	0 ± 0.0
C. albicans ATCC 10231	0 ± 0.0	0 ± 0.0	13 ± 0.39	0 ± 0.0

Table 4
Lethal concentrations (ppm) of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* aqueous extracts against *Culex pipiens*, 24, 48 and 72 h post-treatment.

Time (h)	Plant species	LC_{50} (Low. - Up.)	LC_{90} (Low. - Up.)	LC_{95} (Low. - Up.)	Equation**	X^2 (Sig.)
24	*B. glabra*	382.0 (333.8–437.3)	1635.8 (1315.8–2151.5)	2470.6 (1905.6–3442.6)	2.028 ± 0.141	4.147 (0.386)
	D. regia	444.3 (387.4–511.3)	1981.6 (1567.9–2670.4)	3027.6 (2289.9–4341.7)	1.973 ± 0.141	4.383 (0.356)
	L. camara	335.7 (293.9–382.9)	1376.5 (1122.1–1776.0)	2053.5 (1609.6–2796.3)	2.091 ± 0.143	5.274 (0.260)
	P. orientalis	502.8 (433.3–588.8)	2657.8 (2010.0–3828.8)	4260.6 (2050.4–6626.6)	1.772 ± 0.136	5.581 (0.232)
48	*B. glabra*	292.7 (252.3–338.9)	1380.5 (1087.2–1878.2)	2142.6 (1607.2–3123.4)	1.903 ± 0.145	1.884 (0.756)
	D. regia	319.6 (280.8–363.0)	1218.3 (1004.7–1547.2)	1780.3 (1415.9–2376.60	2.205 ± 0.149	7.815 (0.098)
	L. camara	268.0 (229.6–311.3)	1333.5 (1044.8–1828.5)	2101.5 (1564.9–3099.0)	1.839 ± 0.143	5.140 (0.273)
	P. orientalis	376.1 (261.3–546.0)	2150.9 (1542.6–4769.9)	3526.2 (2453.8–9169.7)	1.692 ± 0.129	10.195 (0.037)
72	*B. glabra*	177.7 (155.0–201.8)	631.9 (531.0–782.9)	905.4 (735.7–1176.4)	2.326 ± 0.164	6.027 (0.197)
	D. regia	228.5 (199.9–259.5)	858.1 (715.4–1073.3)	2523.0 (1889.5–3653.2)	2.230 ± 0.151	6.512 (0.163)
	L. camara	164.8 (143.9–186.9)	563.7 (475.5–695.5)	798.8 (652.1–1032.7)	2.400 ± 0.171	7.667 (0.104)
	P. orientalis	263.5 (174.2–380.9)	1225.0 (915.0–2496.5)	1893.7 (1411.7–4411.7)	1.920 ± 0.137	13.403 (0.0.009)

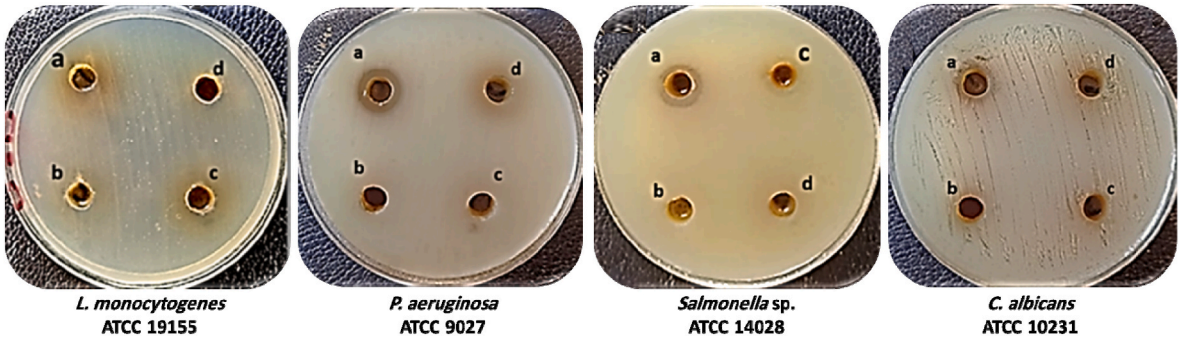


Fig. 4. Antimicrobial activities of acetone extract of (a) *Lantana camara*, (b) *Delonix regia*, (c) *Bougainvillea glabra*, and (d) *Platycladus orientalis*, against *L. monocytogenes* ATCC 19155, *P. aeruginosa* ATCC 9027, *Salmonella* sp. ATCC 14028, and *C. albicans* ATCC 10231 microorganisms.

Table 6
The DPPH scavenging for *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis* acetone extracts.

Concentrate (ug/ml)	DPPH scavenging %				
	Ascorbic acid St.	*B. glabra*	*D. regia*	*L. camara*	*P. orientalis*
1000	99.3	92.6	97.1	90.5	96.3
500	96.3	85.4	94.4	82.5	91.3
250	94.8	77.6	91.6	74.3	83.0
125	91.9	69.5	83.5	66.6	74.8
62.5	84.2	61.6	75.4	58.9	67.2
31.25	76.1	53.4	67.7	50.9	58.7
15.63	67.6	45.8	60.1	42.6	50.7
7.813	60.4	38.0	52.4	34.4	42.2
3.9	52.1	30.0	45.0	26.3	33.8
1.95	43.7	22.2	36.8	18.8	25.5
0.0	0.0	0.0	0.0	0.0	0.0
IC	**2.52**	**22.65**	**5.95**	**29.80**	**15.25**

(20.26 %).

L. camara acetone leaf extract had 17 compounds, as shown in Table (9), while aqueous leaf extract had 13 compounds. The highest concentrations of the detected compounds in acetone were: 1-Dodecanamine, N,N-dimethyl- (29.24 %), and Caryophyllene (26.71 %), while in aqueous extract were 9-Hexadecenoic acid, 9-octadecenyl ester, (Z,Z)- (20.53 %), and 2-Hydroxy-3-[(9e)-9-octadecenoyloxy]propyl (9e)-9-octadecenoate (16.28 %).

P. orientalis acetone leaf extract had 14 compounds, as shown in Table (10), while aqueous leaf extract had 11 compounds. The highest concentrations of the detected compounds in acetone were: Cedrol (41.58 %), 1,4,8-cycloundecatriene, 2,6,6,9-tetramethyl-, (e,e,e)- (31.88 %), while in aqueous extract, they were: Epicedrol- (38.25 %) and Caryophyllene (24.62 %). There is a variety in percentage and number of secondary metabolites in the acetone and water extracts of four plants, where the highest yield (52.6 %), (40.70 %), (38.70 %), and (35.60 %) with *P. orientalis, L. camara, D. regia,* and *B. glabra*, respectively.

The Venn diagram in Fig. 6 summarizes the conservation and occurrence of chemical compounds extracted from different plants in acetone and aqueous extracts. It was observed that there was an increase in the number of compounds extracted from each plant using acetone compared to water extraction (Fig. 6a and b). In acetone and aqueous extracts, there was a different signature in each plant while there were

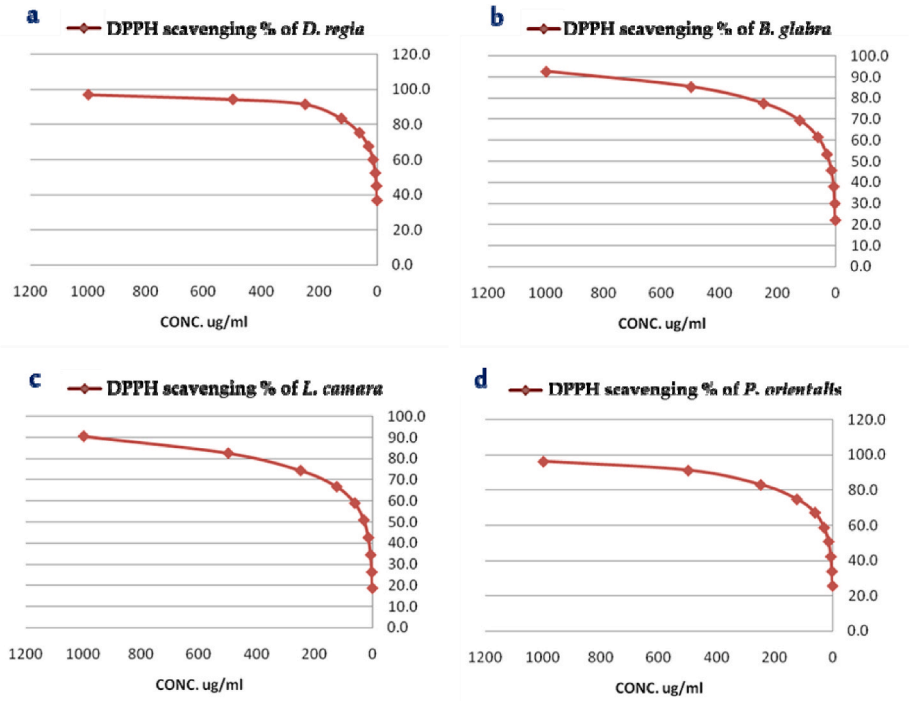


Fig. 5. Antioxidant activities of acetone extract of *D. regia* (a), *B. glabra* (b), *L. camara* (c), and *P. orientalis* (d), using DPPH Assay.

Table 7
The major chemical constituents of *B. glabra* leave acetone and aqueous extracts.

No	RT	Compound Name	M. F.	Area %	
				acetone	aqueous
Antimalrial activity					
1	4.03	Halofantrine	$C_{26}H_{30}C_{l2}F_3NO$	1.11	–
Aliphatic amine					
2	4.55	N,1-Dimethylhexylamine	$C_8H_{19}N$	0.57	–
3	4.62	2-Methyl-2-propanamine	$C_4H_{11}N$	0.65	–
4	5.26	Urea, N,N′-dimethyl-	$C_3H_8N_2O$	0.26	–
5	5.67	Benzeneethanamine, à,à-dimethyl-	$C_{10}H_{15}N$	2.92	–
Phenol					
6	6.74	à-Pinene, 10-(dimethylaminomethyl)-	$C_{13}H_{23}N$	1.68	–
7	8.64	Benzene, 1,2-dimethyl-	C_8H_{10}	0.38	–
Terpene (Monoterpene and Sesquiterpene)					
8	9.34	à-Pinene	$C_{10}H_{16}$	2.0	–
9	13.84	Eucalyptol	$C_{10}H_{18}O$	0.86	–
10	20.52	Nerolidol-epoxyacetate	$C_{17}H_{28}O_4$	0.95	–
11	27.49	Caryophyllene	$C_{15}H_{24}$	14.61	1.14
12	35.61	1-Heptatriacotanol	$C_{37}H_{76}O$	6.08	–
Fatty acid and Esters					
13	8.97	2-Pentanone, 4-hydroxy-4-methyl-	$C_6H_{12}O_2$	16.49	–
14	13.22	Cyclohexene, 4-isopropenyl-1-methoxymethoxymethyl-	$C_{12}H_{20}O_2$	0.36	–
15	23.34	Methyl 10,12-pentacosadiynoate	$C_{26}H_{44}O_2$	2.33	–
16	24.73	10,12-Tricosadiynoic acid, methyl ester	$C_{24}H_{40}O_2$	6.51	–
17	27.18	10-12-Pentacosadiynoic acid	$C_{25}H_{42}O_2$	7.74	–
18	28.71	Linoleic Acid methyl ester	$C_{19}H_{34}O_2$	–	3.55
19	37.73	Pimaric acid	$C_{20}H_{30}O_2$	24.65	–
20	39.93	E,E,Z-1,3,12-Nonadecatriene-5,14-diol	$C_{19}H_{34}O_2$	–	4.81
21	40.37	Cis-13-Eicosenoic acid	$C_{20}H_{38}O_2$	–	36.78
22	40.97	9-Hexadecenoic acid, 9-octadecenyl ester, (Z,Z)-	$C_{34}H_{64}O_2$	–	15.74
23	43.33	Oleyl oleate	$C_{36}H_{68}O_2$		23.86
24	45.50	(Z)-Icos-11-en-1-yl oleate	$C_{38}H_{72}O_2$	–	11.51
Ketone					
25	36.15	2-Butyne-1,4-dione, 1-(2,3-dihydro-3,3-dimethyl-1h-inden-5-yl)-4-phenyl-	$C_{21}H_{18}O_2$	9.85	–

some conserved compounds in two or three plants in the case of acetone and aqueous extracts, respectively. Four common fatty acids and esters (erucic acid, linoleic acid methyl ester, 9-octadecenoic acid methyl ester, and 9-hexadecenoic acid, 9-octadecenyl ester) have been identified in aqueous extracts of *B. glabra, D. regia,* and *L. camara*, whereas there was no shared compound in these three plants in the case of acetone extract. Two terpenes (1-heptatriacotanol and caryophyllene) were identified in *B. glabra* and *D. regia* acetone extracts (Fig. 6a), while three different compounds (cis-11-enhicosenoic acid, cis-13-eicosenoic acid, and E,E,Z-1,3,12-nonadecatriene-5,14-diol) are shared in the aqueous extracts of *B. glabra* and *D. regia* (Fig. 6b). Interestingly, data showed that the chemical parts of the *P. orientalis* plant do not overlap with those of *B. glabra, D. regia,* or *L. camara*, either in acetone or water extracts (Fig. 6a and b). In addition, the Venn diagram showed that *B. glabra* was overlapped with *L. camara* in Eucalyptol, and *D. regia* was overlapped with *L. camara* in two organic constituents (Squalene and Ethyl iso-allocholate). The differential and conserved occurrence of chemical constituents in acetone and aqueous extracts of four plants.

Fig. 7 shows the heatmap obtained for the analysis of organic compounds in the acetone and aqueous extracts of *B. glabra, D. regia, L. camara,* and *P. orientalis*. The scale shows the percentage of chemical classes resembled in each extract; a low percentage is indicated by a pale red color, while a darker red indicates a higher percentage. In general, the acetone extract showed a higher number of chemical classes, with a higher chemical abundance of the terpene compounds, while fatty acid compounds were most common in the aqueous extract, followed by terpenes (Fig. 7).

3.3.2. HPLC analysis

The phenolic acids and flavonoids in the acetone extracts of *L. camara* and *P. orientalis* were determined by HPLC analysis, and the results showed the presence of flavonoid compounds such as Sylimarine, Rutin, and Ellagic in both extracts. Six acids were identified in *L. camara*; Sylimarine acid (0.55141 mg/g), Rutin (0.12310 mg/g), and Thymol (0.10825 mg/g) were the major constituents found in the *L. camara* extract, while phenolic acids Ferulic (0.00035 mg/g) and Ellagic (0.00035 mg/g) were less abundant (Table 11). Similarly, Sylimarine (0.045114 mg/g), Rutin (0.18680 mg/g), and Myricetin (60.10311 mg/g) were the major constituents found in the *P. orientalis* extract, while Ellagic (0.00045 mg/g) and Amentoflavone (0.00024 mg/g) were the minor constituents (Table 11).

3.3.3. ADMET analysis

L. camara acetone extract showed the most effective antimicrobial activity against all the tested pathogenic organisms. So, four phytochemicals of identified metabolites in *L. camara* acetone extract (elemene, caryophyllene, and copaene) were evaluated for ADME aspects (physicochemical characteristics, water solubility, lipophilicity, pharmacokinetics, drug resemblance, and medicinal chemistry) using Swiss ADME software (Table 12). These phytochemicals have been selected based on their potential activity as antimicrobial or insecticidal compounds. All four phytochemicals studied exhibited drug-like properties without breaking Lipinski's rule of five. Furthermore, all of the phytochemical compounds had a bioavailability score of 0.55, indicating that they had drug-like characteristics. Furthermore, while all of the phytochemicals studied were found to be absorbed in the gastrointestinal system, caryophyllene oxide and copaene could only penetrate the blood-brain barrier. The topological polar surface area ranged from 0 to 12.532, while the consensus log Po/w (an indication of lipophilicity) ranged from 3.15 to 3.37. Furthermore, none of the substances examined showed permeability to glycoprotein substrate (P-gp). Furthermore, all the phytochemicals evaluated interacted with two isoenzymes of the cytochrome P family, CYP2C19 and CYP2C9, and only copaene interacted with CYP1A2, implying that they are efficacious while being low in toxicity (Table 13). The bioavailability radar plots of the studied phytochemicals (Fig. 8) showed that the phytochemicals were mostly inside the pink area, indicating a better drug-likelihood profile. Furthermore, a red point on the boiled egg graph of elemene,

Table 8
The major chemical constituents of *D. regia* leave acetone and aqueous extracts.

No	RT	Compound Name	M. F.	Area %	
				acetone	aqueous
Terpene (Monoterpene and Sesquiterpene)					
1	38.94	Isochiapin b	$C_{19}H_{22}O_6$	1.88	–
2	39.93	1-Heptatriacotanol	$C_{37}H_{76}O$	1.38	–
3	14.97	Caryophyllene	$C_{15}H_{24}$	2.16	–
4	24.42	Neophytadiene	$C_{20}H_{38}$	2.00	–
5	24.92	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	$C_{20}H_{40}O$	1.14	–
6	27.69	Ethylene brassylate	$C_{15}H_{26}O_4$	0.70	–
7	29.66	Phytol	$C_{20}H_{40}O$	8.13	–
8	30.66	Octadecanoic acid	$C_{18}H_{36}O_2$	1.95	–
9	35.06	Ethanol, 2-(9-octadecenyloxy)-, (z)-	$C_{20}H_{40}O_2$	2.55	–
10	39.82	Squalene	$C_{30}H_{50}$	20.83	–
Phenol					
11	11.69	Cyclohexanol, 2-(1,1-dimethylethyl)-	$C_{10}H_{20}O$	0.27	–
12	11.86	Phenol, 2-methyl-5-(1-methylethyl)-	$C_{10}H_{14}O$	0.68	–
Fatty acid and Esters					
13	13.10	Triacetin	$C_9H_{14}O_6$	0.64	–
14	26.20	Hexadecanoic acid, methyl ester	$C_{17}H_{34}O_2$	1.57	–
15	26.97	Hexadecanoic acid	$C_{16}H_{32}O_2$	3.76	–
16	28.69	Linoleic Acid methyl ester	$C_{19}H_{34}O_2$	–	10.49
17	28.87	9-Octadecenoic acid, methyl ester, (E)-	$C_{19}H_{36}O_2$	–	14.02
18	29.33	Methyl 10-trans,12-cis-octadecadienoate	$C_{19}H_{34}O_2$	10.14	–
19	30.19	9,12,15-octadecatrienoic acid, (z,z,z)-	$C_{18}H_{30}O_2$	3.13	–
20	40.25	Cis-13-Eicosenoic acid	$C_{20}H_{38}O_2$	–	6.90
21	40.76	ethyl iso-allocholate	$C_{26}H_{44}O_5$	2.67	–
22	42.34	9-Hexadecenoic acid, 9-octadecenyl ester, (z,z)-	$C_{34}H_{64}O_2$	0.42	9.38
23	42.74	Ethanol, 2-(9-octadecenyloxy)-, (Z)-	$C_{20}H_{40}O_2$	–	2.69
24	43.04	Dl-à-tocopherol	$C_{29}H_{50}O_2$	28.39	–
25	44.56	Erucic acid	$C_{22}H_{42}O_2$	–	30.92
26	45.08	(E)-13-Docosenoic acid	$C_{22}H_{42}O_2$	–	20.26
Alkane					
27	40.61	Tetratetracontane	$C_{44}H_{90}$	3.16	–
28	42.81	17-pentatriacontene	$C_{35}H_{70}$	2.45	–

Table 9
The major chemical constituents of *L. camara* leave acetone extracts.

No	RT	Compound Name	M. F.	Area %	
				acetone	aqueous
Terpene (Monoterpene and Sesquiterpene)					
1	3.15	Eucalyptol	$C_{10}H_{18}O$	7.59	–
2	10.24	Caryophyllene	$C_{15}H_{24}$	26.71	–
3	10.92	Humulene	$C_{15}H_{24}$	7.48	–
4	12.94	ç-Elemene	$C_{15}H_{24}$	1.24	–
5	13.95	Caryophyllene oxide	$C_{15}H_{24}O$	8.22	–
6	14.55	á-copaene	$C_{15}H_{24}$	1.56	–
7	31.98	Squalene	$C_{30}H_{50}$	1.88	–
8	36.77	Tricyclo[20.8.0.0(7,16)] triacontane, 1(22),7(16)-diepoxy-	$C_{30}H_{52}O_2$	–	7.91
9	38.55	1-Heptatriacotanol	$C_{37}H_{76}O$	–	2.21
Fatty acid and Esters					
10	28.70	Linoleic acid methyl ester	$C_{19}H_{34}O_2$	–	10.25
11	11.90	1-Dodecanamine, N,N-dimethyl-	$C_{14}H_{31}N$	29.24	–
12	18.06	17-Octadecynoic acid	$C_{18}H_{32}O_2$	1.32	–
13	22.31	9-Octadecenoic acid (Z)-, methylester	$C_{19}H_{36}O_2$	0.54	15.62
14	22.98	Oleic Acid	$C_{18}H_{34}O_2$	1.18	–
15	33.92	Ethyl iso-allocholate	$C_{26}H_{44}O_5$	1.57	–
16	35.95	Oleic acid, 3-(octadecyloxy) propylester	$C_{39}H_{76}O_3$	0.75	–
17	42.27	9-octadecenoic acid (z)-, 9-hexadecenyl ester, (z)-	$C_{34}H_{64}O_2$	–	24.30
18	44.72	Oleyl oleate	$C_{36}H_{68}O_2$	–	14.15
Phenol					
19	3.96	Benzene, (chloromethyl)-	$C_7H_7C_l$	0.81	–
20	22.48	2-Methylenebrexane	$C_{10}H_{14}$	4.44	–
21	43.45	Ethanol, 2-(9-octadecenyloxy)-, (Z)-	$C_{20}H_{40}O_2$	–	312
22	41.68	Z-(13,14-Epoxy)tetradec-11-en-1-ol acetate	$C_{16}H_{28}O_3$	–	268
Alkane					
23	14.34	Cyclooctenone, dimer	$C_{16}H_{24}O_2$	2.79	–
24	32.79	Dotriacontane	$C_{32}H_{66}$	2.68	–
Glycerides					
25	41.05	2-Hydroxy-3-(palmitoyloxy) propyl (9E)-9-octadecenoate	$C_{39}H_{72}O_5$	–	620

caryophyllene oxide, caryophyllene, and copaene predicts their brain penetrability as a non-substrate of P-gp.

4. Discussion

The management of mosquito resistance to chemical insecticides and the behavior of mosquitoes towards stimulating their resistance to the synthetic pesticides used stimulate the search for complementary and/or alternative control methods. We identified the molecules found in ornamental plants and determined their biological effects to determine the extent to which these plant extracts can be used to combat insects, inhibit microbes, and provide antioxidants. We also used in-silico prediction for further biotechnology research.

Several important natural components are found in plant extracts and essential oils (EOs) and can be safely used in pest and disease control due to their ability to achieve the purpose of killing harmful pests and then their ability to degrade in nature in a smooth manner [66]. Despite their insecticide benefits, only 5 % of the world's pesticides are biopesticides [67,68]. However, biopesticides are expanding rapidly and are expected to overtake chemical pesticides in the near future at an average annual growth rate of 9–20 % [69], due to the unique characteristics of biopesticides that encourage their application, including their non-toxicity to the environment.

In this study, all ornamental plant extracts tested showed strong insecticidal effectiveness against mosquito larvae (moderate to high larvicidal activities). The plant acetone extracts of *B. glabra, D. regia, L. camara, and P. orientalis* killed mosquito larvae with 94–100 % mortality and 87–96 % mortality for aqueous extracts 24 h post-treatment.

Our data showed the most effective plant extracts against mosquito larvae were *P. orientalis* and *L. camara,* followed by *B. glabra* and *D. regia*. Our data agreed with Bosly's findings [70], who studied the effectiveness of *Thuja orientalis* leaf and fruit extracts against *Cx. pipiens* larvae and found that all plant extracts killed all the larvae (100 % mortality), except for the plant hexane extract, which killed only 98 % of the larvae.

Similarly, 3rd larval instar of *Anopheles stephensi* and *Culex pipiens* died when the essential oil from the leaves of *T. orientalis* was used to test it [71]. The author indicated the toxicity of the Thuja plant because it contains several main components, mainly the compounds carene and cedrol.

Evaluation of the larvicidal effects of *Chamaecyparis obtusa* and *Thuja orientalis* oils on *Aedes aegypti* and *Culex pipiens* 4th instar larvae compared to stem, fruit, and seed oils found that, the larvicidal effects of leaf oils from *C. obtusa* and *T. orientalis* were much higher. These findings demonstrate that *C. obtusa* and *T. orientalis* have strong larvicidal action against *Ae. aegypti* and *Cx. pipiens* in both the leaf part and age class II as natural larvicides [72].

In this study, one of the most effective plant extracts against mosquito larvae was *Lantana camara*, either in acetone or aqueous extract. In a similar study, *L. camara* leaf extracts with concentrations of 0.3, 0.6, 0.9, and 1.2 g/l were shown to kill *Aedes aegypti* larvae in the lab for 24 h. The mortality reached 91.66–96.66 % with ethanolic leaf extract, while less than 35 % of larvae died in aqueous extract. The outcome

Table 10
The major chemical constituents of *P. orientalis* leave acetone extracts.

No	RT	Compound Name	M. F.	Area %	
				acetone	aqueous
Terpene (Monoterpene and Sesquiterpene)					
1	9.74	Cyclohexene, 1,5,5-trimethyl-6-methylene-	$C_{10}H_{16}$	0.36	–
2	10.88	Cedrene	$C_{15}H_{24}$	4.13	–
3	11.76	Caryophyllene	$C_{15}H_{24}$	31.88	24.62
4	12.99	ç-Muurolene	$C_{15}H_{24}$	7.86	–
5	13.19	Naphthalene, 1,2,3,5,6,8a-hexahydro-4,7-dimethyl-1-(1-methylethyl)-, (1S-cis)-	$C_{15}H_{24}$	2.65	–
6	13.79	Aromandendrene	$C_{15}H_{24}$	3.51	–
7	14.32	Caryophyllene oxide	$C_{15}H_{24}O$	–	3.20
8	14.83	Cedrol	$C_{15}H_{26}O$	41.58	38.25
Fatty acid and Esters					
9	8.34	Acetic acid, 1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl ester	$C_{12}H_{20}O_2$	0.44	–
10	15.22	Doconexent	$C_{22}H_{32}O_2$	0.29	7.80
11	24.92	Methyl 4,7,10,13,16,19-docosahexaenoate	$C_{23}H_{34}O_2$	0.80	–
12	25.40	Podocarp-7-en-3á-ol, 13á-methyl-13-vinyl-	$C_{20}H_{32}O$	2.67	–
13	26.33	5,8,11-Heptadecatriynoic acid, methyl ester	$C_{18}H_{24}O_2$	0.73	–
14	28.23	Androstan-17-one, 3-ethyl-3-hydroxy-, (5à)-	$C_{25}H_{40}O_2Si$	1.85	–
Phenol					
15	26.22	1-Phenanthrenemethanol, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1S-(1à,4aà,10aá)]-	$C_{20}H_{30}O$	286	–
16	32.07	Retinol	$C_{20}H_{30}O$	1.25	3.36
Steroids					
17	25.39	Androst-4-en-3-one, 17-hydroxy-, (17á)-	$C_{19}H_{28}O_2$	288	–
Ketone					
18	12.42	Naphthalene, decahydro-4a-methyl-1-methylene-7-(1-methylethenyl)-, [4ar-(4aà,7à,8aá)]-	$C_{15}H_{24}$	5.59	–
19	28.25	Cholan-24-oic acid, 3,7,12-trihydroxy-, (3à,5á,7à,12à)-	$C_{24}H_{40}O_5$	408	–

demonstrated that *A. aegypti* larvae were more fatally affected by the ethanolic extract than the aqueous extract [73]. The previous findings may be attributed to the fact that most of the active compounds are lipophilic in character and are therefore more readily extracted into an organic medium to be more efficient [74].

In a similar study, the effectiveness of *L. camara aculeata* leaf extracts was tested against 4th instar larvae of *Aedes aegypti, Anopheles stephensi,* and *Culex quinquefasciatus*. The mortality rate of different types of mosquitoes was evaluated in aqueous (LC_{50} = 98.10), ethanol (LC_{50} = 60.93), methanol (LC_{50} = 39.54), acetone (LC_{50} = 60.64), and chloroform (LC_{50} = 86.91 ppm) extract 24 h post-treatment. The extracts of this plant showed strong efficacy in killing larvae, especially at methanol and acetone [8]. Another study conducted by Alghamdi and Basher [75] showed the high toxicity of leaf extracts of *L. camara* than flowers on *Anopheles arabiensis* and *Culex quinquefasciatus*.

When we look at these ornamental plants, we find that they have been mentioned in the past in many treatments for human diseases, and due to the lack of technology, most treatments in the ancient system were derived from plants, and their effectiveness as medicines has also been proven. Which indicates its effectiveness in eliminating microbes and thus killing pests harmful to human health. Among these plants is the aromatic ornamental plant *Lantana camara*, which contains a wide variety of healing ingredients [76,77]. This herb has long been used to treat a variety of ailments, including malaria, fever, colds, and coughs [78–80].

Thuja or *P. orientalis* also referred to as the "tree of life" or "white cedar," is a well-known ornamental tree. In traditional medicine, it is frequently used to treat conditions like rheumatism, bacterial skin infections, cold sores, enuresis, amenorrhea, psoriasis, bullous bronchitis, and enuresis. It is also used as an insect repellent [81]. Among the aromatic ornamental plants, *Bougainvillea*, whose leaves, flowers, and stem bark have long been used as medicinal plants in the form of infusions, decoctions, and tinctures, Also used as a tea, *Bougainvillea* extracts are used to treat a variety of ailments, including cough, sore throat, fever, diarrhea, diabetes, hepatitis and liver problems, asthma, and bronchitis, as well as to regulate menstruation, stop leucorrhea, reduce stomach acidity, dissolve blood clots, and treat anemia linked to gastrointestinal bleeding and epigastric pain. Drinking a floral infusion can help decrease blood pressure [82].

D. regia is known as flame of the forest or royal Poinciana and has been widely used traditionally or in Ayurveda, an alternative medicine system, to treat various ailments, including jaundice, ulcers, wounds, arthritis, malaria, vomiting, infection, inflammation, pain, and diarrhea [30–32,34), due to the many bioactive compounds it contains, such as alkaloids, flavonoids, triterpenoids, sterols, tannins, saponins, steroids, and carotene hydrocarbons [83,84]. However, the effectiveness of this plant against insects, microbes, or biological aspects is scant, according to literary articles. This shows the ability of the current ornamental plant

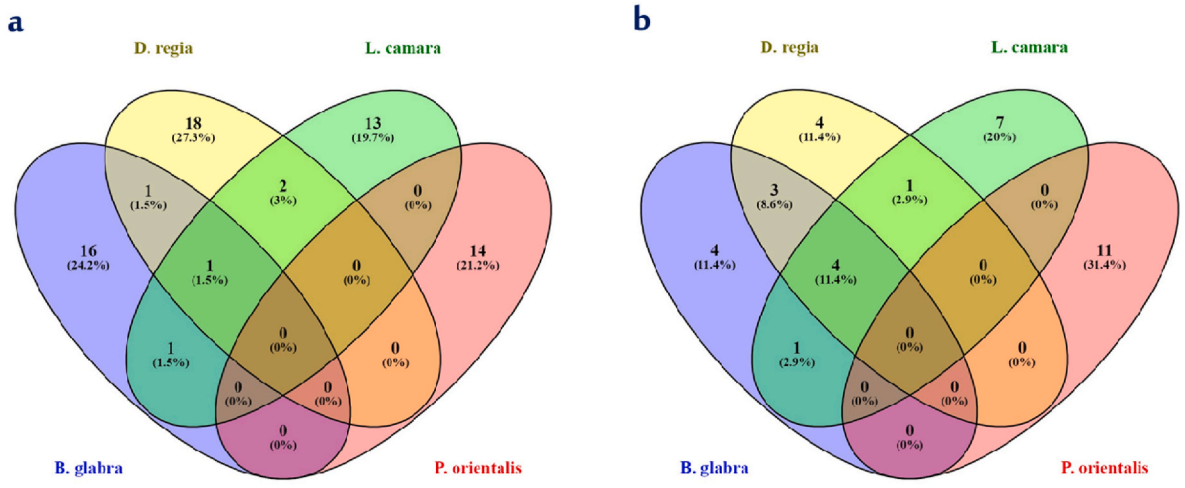


Fig. 6. A Venn diagram showed the relationships among chemical constituents in acetone (a), and aqueous (b) extracts of *B. glabra, D. regia, L. camara,* and *P. orientalis.*

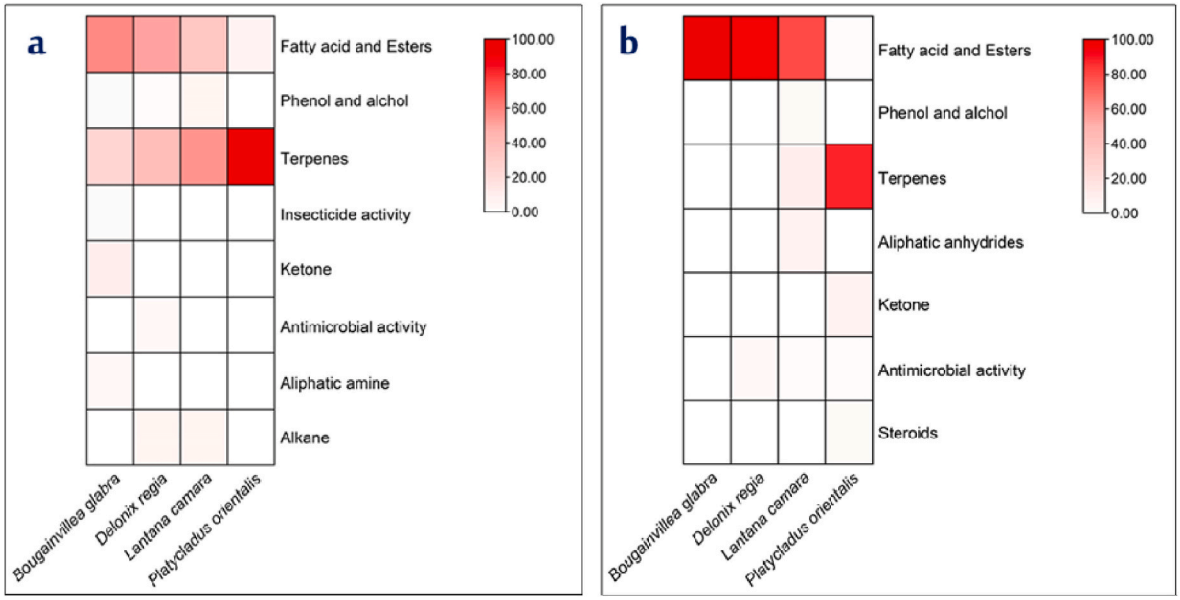


Fig. 7. Heatmap showing the percentage of chemical constituents of acetone (a) and aqueous (b) leaves extracts of *Bougainvillea glabra, Delonix regia, Lantana camara,* and *Platycladus orientalis*. In the heat map, red and pale pink colors indicate higher and lower chemical abundance, respectively.

Table 11
HPLC analysis for Total polyphenolic compounds from *L. camara* and *P. orientalis* acetone extracts.

	No.	Reten. Time (min)	Amount (mg/ml)	Compound Name
L. camara	1	1.793	0.00053	Gallic Acid
	2	10.025	0.10825	Thymol
	3	15.258	0.00035	Ferulic
	4	23.917	0.55141	Sylimarine
	5	26.188	0.00035	Ellagic
	6	28.132	0.12310	Rutin
P. orientalis	1	4.812	0.00403	Para Amino Benzoic Acid
	2	10.305	0.00457	Syringic Acid
	3	15.968	0.18680	Rutin
	4	20.387	0.01963	Apeinine
	5	22.243	0.45114	Sylimarine
	6	24.252	0.10311	Myricetin
	7	26.515	0.00024	Amentoflavone
	8	35.828	0.00045	Ellagic

extracts to control mosquitoes, which is in line with the results of several studies on mosquitoes [85,86].

Some plant compounds, including certain terpenes as elemene, caryophyllene, and copaene may interfere with different processes or pathways as: interfering with the nervous system of insects, potentially causing neurotoxic effects. This could lead to disruptions in nerve function, affecting the insects' ability to move, feed, or reproduce [87], interfering with feeding deterrence [88], interfering with chitin synthesis in insects which is a key component of the insect exoskeleton, and disruption of its formation can lead to developmental abnormalities [89], inhibition of cholinesterase activity [90], disruption of cell membranes, leading to cell leakage and eventual cell death [91], and may act as a repellent, influencing the behavior of insects and deterring them from certain areas [92].

According to our results, *L. camara* possessed high antibacterial activity; this could be due to the presence of phenolics, anthocyanins, and proanthocyanins in *L. camara* leaves [92,93]. The active principle of the extracts disrupts the permeability barrier of cell membrane structures and thus inhibits bacterial growth [94]. Also, EOs may interact with and affect the plasma membrane, interfering with respiratory chain activity and energy production [95].

Sukul and Chaudhuri [96] tested petroleum ether, benzene, chloroform, and methanol from *L. camara* leaves on *Escherichia coli* (ATCC 10536), *Salmonella typhi* (ATCC 686), *S. aureus* (ATCC 6538), and *Pseudomonas aeruginosa* (ATCC 25619). Chloroform and methanol extracts showed activity against all the bacteria tested, while the petroleum ether fraction only showed activity against *P. aeruginosa* and the benzene fraction only against *S. typhi*. Also, Basu, Ghosh [97] found that chloroform and methanolic extracts of *L. camara* were more specific toward the Gram-positive strains, although Gram-negative *P. aeruginosa* was also inhibited by the methanol extract, while the aqueous extract was found to be inactive. Furthermore, Amutha [98] investigated the antimicrobial activities of methanol, chloroform, acetone, petroleum ether, and hexane extracts of *L. camara* seed against *S. aureus, P. aeruginosa, P. vulgaris,* and *E. coli*. Methanolic extract showed maximum inhibition against *S. aureus, P. aeruginosa,* and *E. coli* and no inhibition against *P. vulgaris*. The compound Dotriacontane in the alkan group is associated with the antimicrobial effect, as reported by Gallo and Sarachine [99], who showed that dotriaconane is known to possess diverse biological activities such as antioxidant and antimicrobial.

Thuja orientalis has good antimicrobial activity against gram-positive bacteria, while all the tested gram-negative bacteria recorded weak or no susceptibility [100]. Due to the presence of *Thuja* essential oils, coumarins, flavonoids, tannins, and proanthocyanidins, the chemical components of *T. occidentalis* have attracted study attention for many years. Its pharmacology includes antibacterial, antifungal, anticancer, antiviral, antioxidant, gastrointestinal protective, anti-inflammatory, radioprotective, antipyretic, and lipid-metabolizing activities [81, 101]. The discovery that *Bougainvillea* leaf extracts had antiviral activities resulted in the extraction and characterization of bouganin, a protein with traits common to type 1 ribosome-inactivating proteins (RIPs) [36]. Caryophyllene oxide compounds overlap with all study plants that possess anticarcinogenic, anti-inflammatory, and antibacterial properties [102]. Amalia, Syafitri [103] showed that the bark of *D. regia* harbored antimalarial activity against *Plasmodium berghei* in mice. The antimicrobial activity of leaves extracts of *D. regia* against the tested microbes might be linked to the presence of phenolic acids such as gallic, protocatechuic, 3-hydroxybenzoic, chlorogenic acids and flavonoids [104].

These phytochemicals could kill bacteria on their own, inhibit their

Table 12
In silico ADME analysis of phytochemicals tested.

Descriptors	Elemene	Caryophyllene oxide	Copaene	Caryophyllene
SMILE	CC(=C)C$_1$CCC(C(C1)C(=C)C)(C)C=C	CC$_{12}$CCC$_3$C(CC$_3$(C)C)C(=C)CCC$_1$O$_2$	CC(C)[C@@H]$_1$CC[C@@]$_3$(C)[C@@H]$_2$C(/C)=C\C[C@H]$_3$[C@H]$_{12}$	C$_1$(=C)\CC/C=C(/CC[C@@H]$_2$[C@@H]$_1$CC$_2$(C)C)C
Physicochemical properties				
Number of heavy atoms	15	16	15	15
Number of aromatic heavy atoms	0	0	0	0
Fraction Csp3	0.6	0.87	0.87	0.73
Number of rotatable bonds	3	0	1	0
Number of H-bond acceptors	0	1	0	0
Number of H-bond donors	0	0	0	0
Molar refractivity	70.42	68.27	67.14	68.78
Topological polar surface area (Å^2)	0	12.53	0	0
Lipophilicity				
Log Po/w (iLOGP)	3.37	3.15	3.4	3.25
Log Po/w (XLOGP3)	6.11	3.56	4.47	4.38
Log Po/w (WLOGP)	4.75	3.94	4.27	4.73
Log Po/w (MLOGP)	4.53	3.67	5.65	4.63
Log Po/w (SILICOS-IT)	4.5	4.07	3.73	4.19
Consensus log Po/w	4.65	3.68	4.3	4.24
Water solubility				
Log S (ESOL)	−4.76	−3.45	−3.86	−3.87
Solubility (mg/ml)	3.57E-03	7.84E-02	2.84E-02	2.78E-02
Class	Moderately soluble	Soluble	Soluble	Soluble
Log S (Ali)	−5.89	−3.51	−4.19	−4.1
Ali Solubility (mg/ml)	2.62E-04	6.83E-02	1.32E-02	1.64E-02
Class	Moderately soluble	Soluble	Moderately soluble	Moderately soluble
Log S (SILICOS-IT)	−3.58	−3.51	−3.07	−3.77
Solubility	5.36E-02	6.81E-02	1.74E-01	3.49E-02
Class	Soluble	Soluble	Soluble	Soluble
Pharmacokinetics				
GI absorption	Low	High	Low	Low
BBB permeant	No	Yes	Yes	No
P-gp substrate	No	No	No	No
CYP1A2 inhibitor	No	No	Yes	No
CYP2C19 inhibitor	Yes	Yes	Yes	Yes
CYP2C9 inhibitor	Yes	Yes	Yes	Yes
CYP2D6 inhibitor	No	No	No	No
CYP3A4 inhibitor	No	No	No	No
Log Kp (skin permeation) (cm/s)	−3.21	−5.12	−4.37	−4.44
Drug-likeness				
Lipinski	1	0	1	1
Ghose	0	0	0	0
Veber	0	0	0	0
Egan	0	0	0	0
Muegge	2	1	1	1
Bioavailability score	0.55	0.55	0.55	0.55
Medicinal chemistry				
PAINS	0	0	0	0
Brenk	1	2	1	1
Lead likeness	2	2	2	2
Synthetic accessibility	3.63	4.35	4.62	4.51

Table 13
In silico toxicity analysis of phytochemicals tested.

no.	Phytochemicals	Oral toxicity of phytochemicals (PROTOX II)		Acute Inhalation Toxicity	Acute Oral Toxicity	Acute Dermal Toxicity
		Predicted LD50 (mg/kg)	Predicted toxicity class			
1	Elemene	5000	5	Non-cardiotoxic (66 %)	Non-cardiotoxic (96 %)	Non-cardiotoxic (74 %)
2	Caryophyllene oxide	5000	5	Toxic (52 %)	Non-toxic (93 %)	Non-toxic (78 %)
3	Copaene	3700	5	Non-toxic (56 %)	Non-toxic (95 %)	Non-toxic (75 %)
4	Caryophyllene	5300	5	Non-toxic (61 %)	Non-toxic (94 %)	Non-toxic (79 %)

molecular targets within the cell, reduce bacterial virulence factors that are essential for cell growth and division, or work synergistically with existing antibiotics by inhibiting resistance factors in antibiotic-resistant bacteria [105,106]. Just as plant extracts interfere with insect physiology, they also interfere with microbe physiology, hindering its activity and reproduction.

Reactive oxygen species (ROS) are involved in the pathogenesis of various diseases. Free radicals are the root cause of uncontrolled oxidation. Free radicals oxidize all major classes of biomolecules. The products of these oxidation reactions diffuse from the original site of

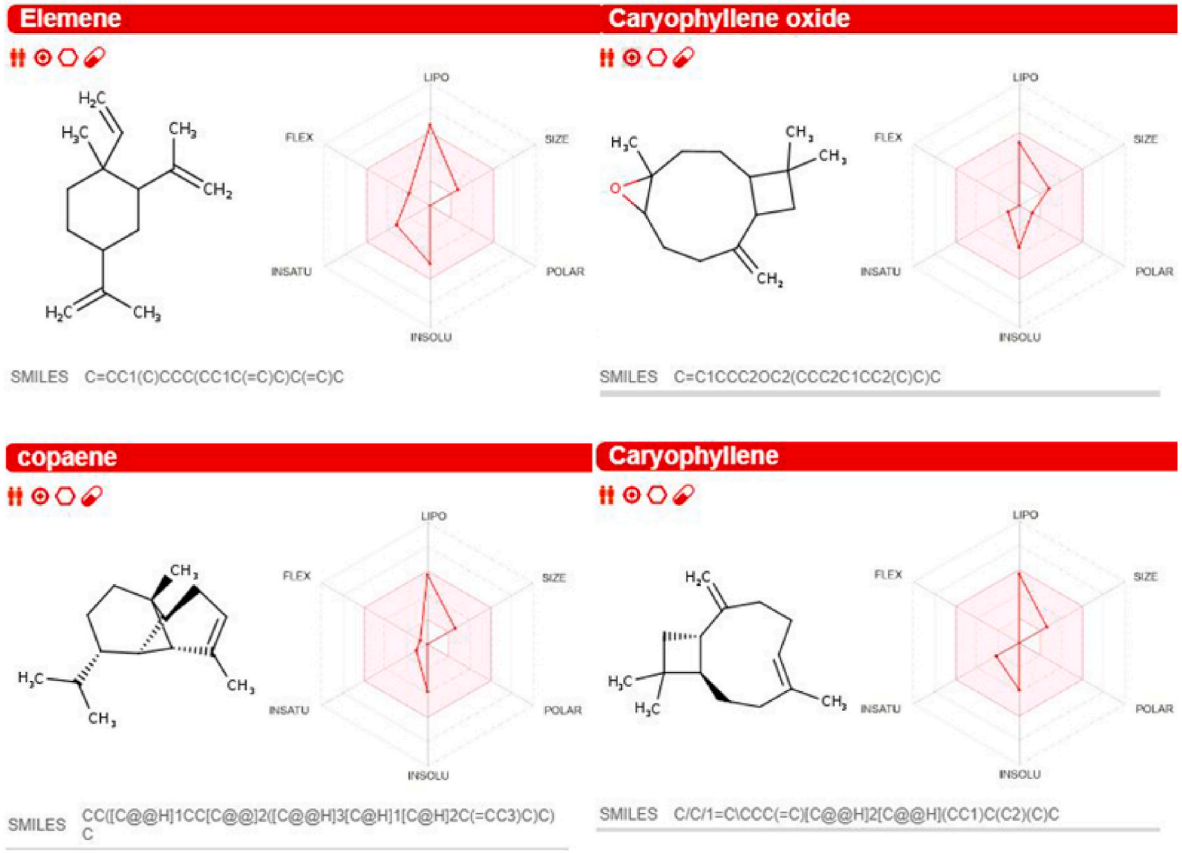


Fig. 8. Bioavailability radars of the phytochemicals tested (elemene, caryophyllene oxide, copaene, and caryophyllene).

attack and spread the damage all over the body, causing serious damage to almost all the cells. Some important biomolecules susceptible to free radical oxidation are Lipids, Proteins, Nucleic acids, and Carbohydrates. Thus, the need for antioxidant therapy arises.

Antioxidants are compounds that neutralize and interact with free radicals, thus preventing them from causing cell damage. The presence of these antioxidants can prevent the types of free radical damage that have been associated with cancer development and other diseases. The antioxidants work in different parts of cells and contribute to different chemical reactions in the body. As a first line of defense, some antioxidants suppress the formation of free radicals, while others work to remove them before they do damage to cells or repair damage once it has been done. Numerous plants have phytochemical properties that act as antioxidants. In addition to some familiar nutrients that act as antioxidants, such as vitamins C and E and B-carotene, there are many others that are phytochemicals, such as quercetin and other flavonoids [107].

Sehrawat and Soni [108] found that the plant could be a source of natural antioxidants because it has a number of bioactive substances that neutralize free radicals, which can damage cell membranes and DNA and have other pharmacological effects. In the DPPH test, the ability of a compound to act as a donor for hydrogen atoms or electrons was measured spectrophotometrically. The results showed that the *D. regia* extract had a high level of antioxidant activity (IC50 = 5.95 μg/ml) and was more effective at getting rid of DPPH radicals than the other plant extracts, which were less effective. This could be credited to the presence of more phytochemicals (22 compounds) than the other three studied plant extracts (Fig. 6), including flavonoids, phenolics, fatty acids, terpenes, and alkanes. This is in agreement with the findings of Mariajancyrani, Chandramohan [109], who revealed the presence of tannin, terpenoids, flavonoids, steroids, and fatty acids in the chloroform extract of *D. regia* leaves.

Moreover, the leaves of *D. regia* are valuable as drugs [110]. The leaves are accounted for their antimicrobial and antioxidant impacts [111]. It was reported that *D. regia* is utilized in numerous nations for the preparation of extracts having antifungal and antimicrobial activities [112].

Natural sources of bioinsecticides include pheromones, bacteria, fungi, viruses, and protozoa, as well as bioactive plant compounds, pheromones, and microbes. Phytochemicals, microbiological pesticides, plant-incorporated protectants, and pheromones are the four primary categories of bioinsecticides based on their source [113]. They have been employed to control pests with success [114]. They are better than synthetic molecules because they are biodegradable, less poisonous, target-specific, and very powerful in small quantities.

Plants are biological factories that produce various chemicals collectively known as secondary metabolites. Secondary metabolites like alkaloids, carbohydrates, flavonoids, saponins, tannins, and terpenoids are what give medicinal plants their pharmacological effects. Many diverse groups of bioactive substances extracted from or included in botanical insecticides can have the potential to cause adverse effects on pests or organisms that consume or are exposed to them.

In this work, the analysis of organic compounds in the acetone and aqueous extracts of *B. glabra, D. regia, L. camara,* and *P. orientalis* revealed that the acetone extract showed a higher number of different organic compounds, with a higher chemical abundance of the terpene compounds, while fatty acid compounds were most common in the aqueous extract, followed by terpenes. The extraction yield, phytochemical content, and antioxidant properties were influenced by the polarity of the extracting solvents [115]. The different solvents resulted in various extraction yields. This is because differences in the polarity of the solvents could cause a wide variation in the level of bioactive compounds in the extract due to the plant materials containing high levels of polar compounds that are soluble in solvents with high polarity. The results revealed that alkanes, flavonoids, terpenes, ketone, and

phenols were among the phytochemicals identified in acetone more than in aqueous extract [116].

Our results are in conformity with previous studies supporting the use of acetone as the best solvent to recover higher extractable compounds from various medicinal plants [117]. Similarly, previous studies have shown that the high polarity of acetone was found to exhibit better efficiency in extracting various polar phytocompounds, such as phenolics, from the leaves of *L. camara* [118]. Also, the results showed that acetone extracts of plant materials were more toxic to mosquito larvae, *Cx. pipiens* than aqueous extracts. This is in line with the study of Bosly [70], who seemed to rank the leaf extracts in order of their toxicity to mosquito larvae as follows: acetone > methanol > aqueous > hexane. It was mentioned that the activities of the plant extracts against mosquito species depend on the solvent used in extracting the phytochemicals responsible for the responses [119]. Results of GC-MS analysis in our study led to the identification of various compounds such as terpenes, fatty acids, esters, ketone, alkane, steroids, aliphatic amines, and phenols in the leaves of *B. glabra, D. regia, L. camara, and P. orientalis* by using two different solvents (acetone and aqueous). This agrees with Park IlKwon, Lee HoiSeon [120], who reported that the leaves of *B. glabra* contain a wide variety of secondary metabolites such as phenols, flavonoids, tannins, saponins, and proteins.

The qualitative analyses of the ethanolic extracts from *D. regia* bark and *Carica papaya* leaf showed the presence of phytochemical constituents, including flavonoids, alkaloids, triterpenoids, steroids, tannins, and glycosides [121]. The most significant phytochemical groups in *L. camara* are flavonoids, carbohydrates, proteins, alkaloids, glycosides, iridescent phenylethanoids, oligosaccharides, quinine, saponins, steroids, triterpenes, sesquiterpenoids, and tannin. Pavela and Vrchotová [122] reported that *Thuja orientalis* contains bioflavonoids, terpenoids, fatty acids, and cytotoxic principles. In this study, all ornamental plant extracts tested showed strong insecticidal effectiveness against mosquito larvae (moderate to high larvicidal activities) and antibacterial activity, but the most effective plant extracts against mosquito larvae were *P. orientalis* and *L. camara*, followed by *B. glabra* and *D. regia*, and this may be due to the presence of insecticide and antimicrobial activity and other organic compounds such as fatty acids and esters, alkanes, flavonoids, ketone, phenols, monoterpenes, and sesquiterpenes. Also, data showed that the chemical parts of the *P. orientalis* plant do not overlap with those of *B. glabra, D. regia,* or *L. camara*, either in acetone or water extracts.

Thuja orientalis previously acquired cytotoxic principles and contained terpenoids, fatty acids, aliphatic compounds like alkanes, and bioflavonoids [123]; this is in line with our results. Fatty acids and esters are one of the secondary metabolites that gave our tested plants their insecticidal effect. In other studies, saturated and polyunsaturated acids (particularly C8, C9, and C10) showed toxic effects against houseflies, horn flies, and stable flies, respectively. A similar study proved that a fatty acid mixture (C8910) has been shown to be both toxic and refractive to an insecticide-resistant Anopheles mosquito strain. Our results also agree with Yousef, EL-LAKWAH [124], who found that the larvicidal activity of linoleic acid was active against S. littorals and that the larval weight was reduced.

The common monoterpenes and sesquiterpenes that were highly present in the tested four plant leaf extracts were cedrol, caryophyllene, caryophyllene oxide, phytol, squalene, and Caryophyllene. The main components, such as Caryophyllene which is known as Isocaryophyllene; eucalyptol; and caryophyllene oxide, might be responsible for the observed insecticidal activity, and this agrees with Zoubiri and Baaliouamer [125], who reported that the main components, e.g., b-caryophyllene and caryophyllene oxide, had insecticidal activity. Also, Caryophyllene oxide, spathulenol, and germacrene-D are known to possess anticarcinogenic, anti-inflammatory, insecticide, pesticide, and antibacterial properties [102].

Elemene refers to a class of sesquiterpene compounds found in certain medicinal plants, such as *Curcuma wenyujin* and *Rhizoma zedoariae*. The bioactivity of elemene, has been studied in the context of its anti-cancer, anti-inflammatory and immunomodulatory effects [126]. Caryophyllene oxide is a sesquiterpene oxide, a type of organic compound found in many plants, particularly in essential oils. Caryophyllene oxide has shown antioxidant activity and has been investigated for its various biological activities such as anti-inflammatory, antimicrobial, and anticancer effects [127]. Copaene is a sesquiterpene hydrocarbon found in various essential oils. This compound has been investigated for its potential to reduce pain perception and cytotoxic effects on certain cancer cells in addition to anti-inflammatory, antimicrobial properties [128]. Caryophyllene is a bicyclic sesquiterpene that belongs to the class of compounds known as terpenes. It is commonly found in the essential oils of various plants, particularly in spices such as black pepper, cloves, and cinnamon, as well as in cannabis. Caryophyllene is unique among terpenes because it can also act as a cannabinoid by interacting with the endocannabinoid system. Caryophyllene is known for its anti-inflammatory effects. It interacts with the CB2 receptors of the endocannabinoid system, which are primarily found in immune cells and has shown analgesic properties, potentially contributing to pain relief. Some studies suggest that caryophyllene may have anxiolytic, antidepressant-like effects, antioxidant, gastroprotective and neuroprotective potential [129].

HPLC analysis showed the presence of flavonoids and phenolic compounds in *L. camara* and *P. orientalis* acetone extracts, whereas polyphenolic flavonoid (Sylimarine) and flavonoid glycoside (Rutin) were the most abundant constituents in *L. camara* and *P. orientalis*. This result agrees with Ahmed, Al-Sagheer [130], who reported that both species of *Lantana (L. camara* and *L. montevidensis)* contained flavonoid glycosides. In some cases, the antibacterial activities of flavonoid glycosides were equal to or higher than those of ciprofloxacin used as a reference antibiotic, suggesting that they might be effective antibiotics against these pathogenic bacteria [131]. Considering the medical importance of the test microbial species, the result can be considered promising for the development of new antimicrobial drugs.

Rutin (3, 3, 4, 5, 7-pentahydroxyflavone-3-rhamnoglucoside), also called rutoside, quercetin-3-rutinoside, or sophorin, is a flavonol category of flavonoid [132]. Chemically, rutin is a glycoside combining the flavonol quercetin with the disaccharide rutinose (rhamnose and glucose) [133]. Phytochemistry analyses of *P. orientalis* shed light on many chemical constituents, such as diterpenes and flavonoids [134]. Rutin has significant antioxidant capabilities due to its reducing characteristics on various oxidizing species such as superoxide, peroxyl, and hydroxyl radicals [135]. Besides, it has pharmacological properties such as anticancer, antibacterial, and anti-inflammatory properties [136]. Due to its several pharmacological qualities, such as its anti-inflammatory, anticancer, antioxidant, analgesic, and antibacterial actions, thymol has been utilized in traditional medicine in many countries. Additionally, its safety as a natural plant chemical has also been shown [137].

Secondary metabolites are produced in amazing diversity in all plants. Phenolic compounds are one of the most important categories of these metabolites. Many of phenolic compounds have antioxidant properties [138]. There have been numerous instances of an increased buildup of phenolic compounds and peroxide activity in plants exposed to high metal concentrations. Phosphonic' antioxidant action is mostly owing to their redox characteristics, which allow them to operate as reducing agents, hydrogen donors, and singlet oxygen quenchers [139].

These phenolic chemicals, often known as polyphenols, include a wide variety of components, including simple flavonoids, phenolic acids, complex flavonoids, and colorful anthocyanins. These phenolic chemicals are usually associated with plant defense responses. However, phenolic metabolites play an essential role in other processes, such as incorporation of attractive chemicals to aid in pollination, coloration for masking and protection from herbivores, and antibacterial and antifungal activity [140,141].

Our data revealed that the ornamental plant extracts contain many

biologically active compounds with antimicrobial and antiparasitic activity, as shown in the GC-MS results of *B. glabra* and *P. orientalis* plants, which contained antimalarial bioactive compounds such as halofantrine and retinol. They also contain caryophyllene (14.61 %) and cedrol (41.58 %), which have insecticidal effects. *D. regia* had E,E,Z-1,3,12-Nonadecatriene-5,14-diol (3.46 %); Isochiapin (1.88 %); and 1-Heptatriacotanol (1.38 %); *L. camara* plant had 2-Hydroxy-3-(palmitoyloxy) propyl (9E)-9-octadecenoate (16.28 %); Tricyclo [20.8.0.0 (7,16)] triacontane,1(22),7(16)-diepoxy- (7.91 %), and Squalene (1.88 %), where these compounds all have antimicrobial effects. Beside that the chemical analysis with HPLC of *L. camara* and *P. orientalis* plants' acetone extracts revealed the presence of phenolic and flavonoids. The presence of these metabolites in conjunction with fatty acids, tannins and terpenoids confers antibacterial and antioxidant activity to these extracts. Intriguingly, flavonoids can form compounds with biological components and microbial cell walls, potentially impairing their function and inhibiting microbial development. Many researchers have extensively studied *L. camara* for its antibacterial properties. Besides, *L. camara* possesses many important biological activities, namely antipyretic, antimicrobial, antimutagenic, antimicrobial, fungicidal, insecticidal, anthelmintic, etc. [142,143]. It is believed that the lantadines present in all *L. camara* are responsible for almost all the biological activity. Moreover, some of these biological activities can be partially attributed to other secondary metabolites such as alkaloids, terpenoids, and phenolics [93].

The ADME profile of the monoterpenoids (elemene, caryophyllene oxide, caryophyllene, and copaene) that have been found in plants has rarely been studied alongside in vitro antimicrobial effectiveness studies against pathogenic microbes. The Swiss ADME server was utilized in this work to analyze various ADME characteristics such as physiochemical properties, pharmacokinetics, solubility, lipophilicity, drug-likeness based on Lipinski's rule of five, and medicinal chemistry [55]. The four phytochemical compounds in silico ADME prediction proved drug-likeness, as indicated by no violation of Lipinski's rule of five and the derived bioavailability score (0.55). Furthermore, the compound's red line in the bioavailability radar map must be inside the pink area to be considered drug-like. All compounds' radar plots were totally within the pink area. Furthermore, the ADME data, together with the boiled egg model, demonstrated that all the investigated phytochemicals had superior gastrointestinal absorption and permeability of the blood-brain barrier [55].

P-gp and cytochrome P450 (CYP) are known to aid in the biotransformation of xenobiotics to protect tissues. The phytochemicals in this investigation did not have any P-gp substrates. The P-gp transporter is identified as the most important member of the ATP-binding cassette transporter family, which is critical for assessing the protective efflux of biological membranes (GI tract or brain) from xenobiotics [55]. Furthermore, the three phytochemicals evaluated interacted only with the CYP1A2 isoenzyme, delivering efficiency with minimal toxicity [144].

To study the in-silico toxicity parameters, the machine learning programs Protox-II [64]were utilized. The projected LD50 (mg/kg) for the three phytochemicals evaluated varied from 3700 to 5300, putting them in Protox-II toxicity class 5. Furthermore, StopTox software determined that all the investigated phytocompounds were non-cardiotoxic based on hERG liability prediction, with confidence levels ranging from 50 to 90 %. However, before being assessed in appropriate laboratory animal models, the resulting toxicity findings must be correlated with the in vitro safety assessments.

Finally, our research has shown that the extracts of *B. glabra, D. regia, L. camara,* and *P. orientalis* are full of bioactive organic compounds that make them work better and more effective against harmful insects. These compounds include terpenes, phenols, and flavonoids. We therefore recommend their use in mosquito control programs and many other natural pests.

5. Conclusion

Mosquitoes are an important vector of deadly diseases that threaten human health, and their dangers extend beyond eradication. The emergence or recurrence of mosquitoes in endemic, non-endemic, and new parts of the world has led to the widespread use of synthetic pesticides to reduce the transmission of mosquito-borne diseases. With the emergence of resistant mosquitoes and concerns about the toxicity of synthetic pesticides to both target and non-target organisms, safer, biodegradable alternatives, Eco-friendly [145] and more efficient methods of controlling mosquitoes and other medical and veterinary pests have been sought. As phytochemicals are gaining popularity in mosquito control because they are natural, environmentally safe, less toxic, less expensive, and, most importantly, less susceptible to insect resistance, selected ornamental plants were evaluated for the detection of effective chemicals used as insecticides and against many microbes and pests. This was proven in the research, as the results of the research showed the efficiency of ornamental plants as insecticides, antimicrobials, and antioxidants, and the four phytochemical compounds in the ADME predicted silico test showed similarity and the possibility of the intervention of that plant in the manufacture of medicine. Our data revealed that ornamental plant extracts of *B. glabra, D. regia, L. camara, and P. orientalis* are rich with bioactive organic compounds in addition to phenolics and flavonoids. There is no doubt that more bioactive chemicals must be discovered, and future research should focus on the discovery of botanical products with the goal of disseminating them as a reliable treatment to reduce mosquito risks and prevent mosquito-borne diseases.

Funding

The study did not receive fund

Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Benha University, and approved by Ethics Committee of Faculty of Science, Benha University (Code: BUFS 2023-16Ent).

Informed consent statement

Not applicable.

Consent for publication

Not applicable.

Preprint publishing

The manuscript was published as preprint on Research square [146], entitled Evaluation of four ornamental plant extracts as insecticidal, antimicrobial, and antioxidant against the West Nile vector, Culex pipiens (Diptera: Culicidae) and metabolomics screening for potential therapeutics.

CRediT authorship contribution statement

Reham M. Mostafa: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Data curation, Conceptualization. **Mohamed M. Baz:** Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization. **Heba Talat Ebeed:** Writing – original draft, Supervision, Methodology, Formal analysis, Data curation. **Heba S. Essawy:** Writing – original draft, Visualization, Supervision, Project administration, Funding acquisition, Data curation. **Ghada E. Dawwam:** Writing – original draft, Visualization, Resources, Investigation, Formal analysis,

Conceptualization. **Ahmed B. Darwish:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Data curation. **Abdelfattah Selim:** Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Nancy M. El-Shourbagy:** Writing – original draft, Validation, Resources, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no competing interests.

Data availability

Data will be made available on request.

Acknowledgments

We are grateful to the Entomology and Botany Departments of the Faculty of Science at Benha University, where this study was conducted. We also thank Dr. Heba Ebeed, Botany and Microbiology Department, Faculty of Science, Damietta University, for metabolomics and chemo-informatic analysis and her strong and effective contributions to research development. We also thank Dr. Ahmed Darwish, Zoology Department, Faculty of Science, Suez University, for his valuable support and advice.

References

[1] S.-S. Cheng, C.-G. Huang, Y.-J. Chen, J.-J. Yu, W.-J. Chen, S.-T. Chang, Chemical compositions and larvicidal activities of leaf essential oils from two eucalyptus species, Bioresour. Technol. 100 (2009) 452–456.
[2] A. Selim, A. Radwan, Seroprevalence and molecular characterization of West Nile virus in Egypt, Comp. Immunol. Microbiol. Infect. Dis. 71 (2020) 101473.
[3] A. Selim, A. Radwan, F. Arnaout, H. Khater, The recent update of the situation of West Nile fever among equids in Egypt after three decades of missing information, Pak. Vet. J. 40 (2020).
[4] M.M. Baz, A.M. Selim, I.T. Radwan, H.F. Khater, Plant oils in the fight against the West Nile vector, Culex pipiens, Int. J. Trop. Insect Sci. 42 (2022) 2373–2380.
[5] A. Selim, A. Abdelhady, The first detection of anti-West Nile virus antibody in domestic ruminants in Egypt, Trop. Anim. Health Prod. 52 (2020) 3147–3151.
[6] V. Prajapati, A. Tripathi, K. Aggarwal, Khanuja S. Insecticidal, Repellent and oviposition-deterrent activity of selected essential oils against Anopheles stephensi, Aedes aegypti and Culex quinquefasciatus, Bioresour. Technol. 96 (2005) 1749–1757.
[7] A. Selim, A. Megahed, S. Kandeel, A. Alouffi, M.M. Almutairi, West Nile virus seroprevalence and associated risk factors among horses in Egypt, Sci. Rep. 11 (2021) 20932.
[8] P. Hemalatha, D. Elumalai, A. Janaki, M. Babu, K. Velu, K. Velayutham, et al., Larvicidal activity of Lantana camara aculeata against three important mosquito species, J. Entomol. Zool. Stud. 3 (2015) 174–181.
[9] WHO, Evaluation of Genetically Modified Mosquitoes for the Control of Vector-Borne Diseases: Position Statement, October 2020, 2020.
[10] A. Selim, A.D. Alanazi, A. Sazmand, D. Otranto, Seroprevalence and associated risk factors for vector-borne pathogens in dogs from Egypt, Parasites Vectors 14 (2021) 1–11.
[11] A. Selim, M. Marzok, K. Alkashif, M. Kandeel, M. Salem, M.Z. Sayed-Ahmed, Bluetongue virus infection in cattle: serosurvey and its associated risk factors, Trop. Anim. Health Prod. 55 (2023) 285.
[12] A. Selim, S. Shoulah, A. Abdelhady, A. Alouffi, Y. Alraey, W.S. Al-Salem, Seroprevalence and risk factors associated with canine leishmaniasis in Egypt, Veterin. Sci. 8 (2021) 236.
[13] M. Marzok, K. Alkashif, M. Kandeel, M. Salem, M.Z. Sayed-Ahmed, A. Selim, Seroprevalence of Rift Valley Fever virus in one-humped camels (Camelus dromedaries) in Egypt, Trop. Anim. Health Prod. 55 (2023) 345.
[14] N. Jirakanjanakit, P. Rongnoparut, S. Saengtharatip, T. Chareonviriyaphap, S. Duchon, C. Bellec, et al., Insecticide susceptible/resistance status in Aedes (Stegomyia) aegypti and Aedes (Stegomyia) albopictus (Diptera: Culicidae) in Thailand during 2003–2005, J. Econ. Entomol. 100 (2014) 545–550.
[15] F. Bakkali, S. Averbeck, D. Averbeck, M. Idaomar, Biological effects of essential oils–a review, Food Chem. Toxicol. 46 (2008) 446–475.
[16] M.M. Baz, A. Selim, I.T. Radwan, A.M. Alkhaibari, H.F. Khater, Larvicidal and adulticidal effects of some Egyptian oils against Culex pipiens, Sci. Rep. 12 (2022) 4406.
[17] M.M. Baz, M.M. Hegazy, H.F. Khater, Y.A. El-Sayed, Comparative Evaluation of Five Oil-Resin Plant Extracts against the Mosquito Larvae, Culex pipiens Say (Diptera: Culicidae), 2021.
[18] B. Chapagain, Z. Wiesman, Larvicidal effects of aqueous extracts of Balanites aegyptiaca (desert date) against the larvae of Culex pipiens mosquitoes, Afr. J. Biotechnol. 4 (2005).
[19] N. Chowdhury, A. Ghosh, G. Chandra, Mosquito larvicidal activities of Solanum villosum berry extract against the dengue vector Stegomyia aegypti, BMC Compl. Alternative Med. 8 (2008) 1–8.
[20] C. Joseph, M. Ndoile, R. Malima, M. Nkunya, Larvicidal and mosquitocidal extracts, a coumarin, isoflavonoids and pterocarpans from Neorautanenia mitis, Trans. Roy. Soc. Trop. Med. Hyg. 98 (2004) 451–455.
[21] E.S.B. Cavalcanti, S.M.d. Morais, M.A.A. Lima, E.W.P. Santana, Larvicidal Activity of Essential Oils from Brazilian Plants against Aedes aegypti L, vol. 99, Memórias do Instituto Oswaldo Cruz, 2004, pp. 541–544.
[22] Gutierrez R. Martha Perez, Neira Gonzalez A. Maria, C. Hoyo-Vadillo, Alkaloids from piper: a review of its phytochemistry and pharmacology, Mini Rev. Med. Chem. 13 (2013) 163–193.
[23] Y.-C. Yang, E.-H. Lee, H.-S. Lee, D.-K. Lee, Y.-J. Ahn, Repellency of aromatic medicinal plant extracts and a steam distillate to Aedes aegypti, J. Am. Mosq. Control Assoc. 20 (2004) 146–149.
[24] G.M. Lengai, J.W. Muthomi, E.R. Mbega, Phytochemical activity and role of botanical pesticides in pest management for sustainable agricultural crop production, Sci. Afr. 7 (2020) e00239.
[25] S. Buchmann, The Reason for Flowers: Their History, Culture, Biology, and How They Change Our Lives, Simon and Schuster, 2015.
[26] Demirak M.Ş. Şengül, E. Canpolat, Plant-based bioinsecticides for mosquito control: impact on insecticide resistance and disease transmission, Insects 13 (2022) 162.
[27] M.F. Maia, A. Robinson, A. John, J. Mgando, E. Simfukwe, S.J. Moore, Comparison of the CDC Backpack aspirator and the Prokopack aspirator for sampling indoor-and outdoor-resting mosquitoes in southern Tanzania, Parasites Vectors 4 (2011) 1–10.
[28] M.M. Baz, A.T. Alfagham, L.A. Al-Shuraym, A.F. Moharam, Efficacy and comparative toxicity of phytochemical compounds extracted from aromatic perennial trees and herbs against vector borne Culex pipiens (Diptera: Culicidae) and hyalomma dromedarii (Acari: ixodidae) as green insecticides, Pak. Vet. J. 44 (2024).
[29] Z. Pava, I. Handayuni, L. Trianty, R.A. Utami, Y.K. Tirta, A.M. Puspitasari, et al., Passively versus actively detected malaria: similar genetic diversity but different complexity of infection, Am. J. Trop. Med. Hyg. 97 (2017) 1788.
[30] S. Elumalai, K. Saravanan, D. Rajesh, B. Ravichandran, Medicinal plants used ethno botanically by Thenu kuruba tribes of Coorg District, Karnataka, India, J. Tree Sci. 38 (2019) 46–58.
[31] K. Girish, Antimicrobial activities of lantana camara Linn, Asian J. Pharmaceut. Clin. Res. 10 (2017) 57–67.
[32] G. Thamotharan, G. Sekar, T. Ganesh, S. Sen, R. Chakraborty, S. Kumar, Antiulcerogenic effects of Lantana camara Linn. leaves on in vivo test models in rats, Asian J. Pharmaceut. Clin. Res. 3 (2010) 57–60.
[33] K.M. Sathish, S. Maneemegalai, Evaluation of larvicidal effect of Lantana camara Linn. against mosquito species Aedes aegypti and Culex quinquefasciatus, Adv. Biol. Res. 2 (2008) 39–43.
[34] A. Alagić, B. Baxerres, F. Berger, A.M. Bindewald, S. Bouquet, G. Brundu, et al., Identification Handbook for Non Native Tree Species in the Alpine Space, The Alptrees project, 2022.
[35] P. Srivastava, P. Kumar, D. Singh, V. Singh, Biological properties of Thuja orientalis Linn, Adv. Life Sci. 2 (2012) 17–20.
[36] M. Bortolotti, A. Bolognesi, Polito L. Bouganin, An attractive weapon for immunotoxins, Toxins 10 (2018) 323.
[37] R. Abarca-Vargas, V.L. Petricevich, Bougainvillea genus: a review on phytochemistry, pharmacology, and toxicology, Evid. base Compl. Alternative Med. 2018 (2018).
[38] V. Gupta, M. George, L. Joseph, M. Singhal, H. Singh, Evaluation of antibacterial activity of Bougainvillea glabra 'snow white'and Bougainvillea glabra 'choicy', J. Chem. Pharmaceut. Res. 1 (2009) 233–237.
[39] H. Saikia, A. Lama, Effect of Bougainvillea Spectabilis Leaves on Serum Lipids in Albino Rats Fed with High Fat Diet, 2011.
[40] B. Deepa, O. Remadevi, Larvicidal Activity of the Flowers of Delonix Regia (Bojer Ex Hook.) Rafin.(Fabales: Fabaceae) against the Teak Defoliator, Hyblaea Puera Cramer, 2011.
[41] G. Shabir, F. Anwar, B. Sultana, Z.M. Khalid, M. Afzal, Q.M. Khan, et al., Antioxidant and antimicrobial attributes and phenolics of different solvent extracts from leaves, flowers and bark of Gold Mohar [Delonix regia (Bojer ex Hook.) Raf.], Molecules 16 (2011) 7302–7319.
[42] K. Cheirmadurai, P. Thanikaivelan, R. Murali, Highly biocompatible collagen–Delonix regia seed polysaccharide hybrid scaffolds for antimicrobial wound dressing, Carbohydr. Polym. 137 (2016) 584–593.
[43] M. Rahman, N. Hasan, A.K. Das, T. Hossain, R. Jahan, A. Khatun, et al., Effect of Delonix regia leaf extract on glucose tolerance in glucoseinduced hyperglycemic mice, Afr. J. Tradit., Complementary Altern. Med. 8 (2011).
[44] V.D. Shewale, T.A. Deshmukh, L.S. Patil, V.R. Patil, Anti-inflammatory activity of delonix regia (boj. Ex. Hook), Adv. Pharmacol. Pharmaceut. Sci. (2012) 2012.
[45] O. Okore, C. Ekedo, B. Ibediugha, G. Ozua, Pest status of thyridopteryx ephemeraeformis (Lepidoptera: Psychidae)(Bagworms) on delonix regia (Fabales: Fabaceae), an ornamental tree, Int. J. Agric. Earth Sci. 2 (2019) 43–51.
[46] S.Z. Heneidy, Y.M. Al-Sodany, A.M. Fakhry, L.M. Bidak, S.A. Kamal, M.W. Halmy, et al., New Records and endemic taxa revealed in the novel Checklist of Alexandria flora: Implications for conservation Prioritization, Egypt. J. Bot. 64 (2024) 387–418.

[47] S. Chouhan, K. Sharma, S. Guleria, Antimicrobial activity of some essential oils—present status and future perspectives, Medicines 4 (2017) 58.
[48] S. Ma, R. Jia, M. Guo, K. Qin, L. Zhang, Insecticidal activity of essential oil from Cephalotaxus sinensis and its main components against various agricultural pests, Ind. Crop. Prod. 150 (2020) 112403.
[49] R. Kumar, S. Kranthi, V. Nagrare, D. Monga, K.R. Kranthi, N. Rao, et al., Insecticidal activity of botanical oils and other neem-based derivatives against whitefly, Bemisia tabaci (Gennadius)(Homoptera: Aleyrodidae) on cotton, Int. J. Trop. Insect Sci. 39 (2019) 203–210.
[50] S. Kumar, N. Singh, L.S. Devi, S. Kumar, M. Kamle, P. Kumar, et al., Neem oil and its nanoemulsion in sustainable food preservation and packaging: current status and future prospects, J. Agric. Food Res. 7 (2022) 100254.
[51] N. Jeran, M. Grdiša, F. Varga, Z. Šatović, Z. Liber, D. Dabić, et al., Pyrethrin from Dalmatian pyrethrum (Tanacetum cinerariifolium/Trevir./Sch. Bip.): biosynthesis, biological activity, methods of extraction and determination, Phytochemistry Rev. (2021) 1–31.
[52] A.F. El-Aswad, J. Aisu, M.H. Khalifa, Biological activity of tannins extracts from processed Camellia sinensis (black and green tea), Vicia faba and Urtica dioica and Allium cepa essential oil on three economic insects, J. Plant Dis. Prot. 130 (2023) 495–508.
[53] B.N. Paulino, G.N. Silva, F.F. Araújo, I.A. Néri-Numa, G.M. Pastore, J.L. Bicas, et al., Beyond natural aromas: the bioactive and technological potential of monoterpenes, Trends Food Sci. Technol. 128 (2022) 188–201.
[54] M. Abdullahi, G.A. Shallangwa, A. Uzairu, In silico QSAR and molecular docking simulation of some novel aryl sulfonamide derivatives as inhibitors of H5N1 influenza A virus subtype, Beni-Suef Univ. J. Basic Appl. Sci. 9 (2020) 2.
[55] A. Daina, O. Michielin, V. Zoete, S. Adme, A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules, Sci. Rep. 7 (2017) 42717, 2017.
[56] V. Tackholm, L. Boulos, Students' Flora of Egypt, 1974.
[57] M.M. El-Khalafy, D.A.E.A. Ahmed, K.H. Shaltout, Y.M. Al-Sodany, S.A. Haroun, Re-assessment of the endemic taxa in the egyptian Flora, Afr. J. Ecol. 59 (2021) 784–796.
[58] J. Yuan, L.-J. Hao, G. Wu, S. Wang, J.-a. Duan, G.-Y. Xie, et al., Effects of drying methods on the phytochemicals contents and antioxidant properties of chrysanthemum flower heads harvested at two developmental stages, J. Funct. Foods 19 (2015) 786–795.
[59] M. Baz, Strategies for Mosquito Control: Faculty of Science, Benha University, Egypt, 2013.
[60] S.M.H. Aletayeb, A.D. Khosravi, M. Dehdashtian, F. Kompani, S.M. Mortazavi, M. R. Aramesh, Identification of bacterial agents and antimicrobial susceptibility of neonatal sepsis: a 54-month study in a tertiary hospital, Afr. J. Microbiol. Res. 5 (2011) 528–531.
[61] M. Valko, D. Leibfritz, J. Moncol, M.T. Cronin, M. Mazur, J. Telser, Free radicals and antioxidants in normal physiological functions and human disease, Int. J. Biochem. Cell Biol. 39 (2007) 44–84.
[62] E.-H. Mervat, A.A. Mohamed, M.Z. Salem, M.S. Abd El-Kareem, H.M. Ali, Chemical composition, antioxidant capacity and antibacterial activity against some potato bacterial pathogens of fruit extracts from Phytolacca dioica and Ziziphus spina-christi grown in Egypt, Sci. Hortic. 233 (2018) 225–232.
[63] H.S. Hassan, A.A. Mohamed, M.N. Feleafel, M.Z. Salem, H.M. Ali, M. Akrami, et al., Natural plant extracts and microbial antagonists to control fungal pathogens and improve the productivity of zucchini (Cucurbita pepo L.) in vitro and in greenhouse, Horticulturae 7 (2021) 470.
[64] P. Banerjee, A.O. Eckert, A.K. Schrey, R. Preissner, ProTox-II: a webserver for the prediction of toxicity of chemicals, Nucleic Acids Res. 46 (2018) W257–W263.
[65] R.C. Braga, V.M. Alves, E.N. Muratov, J. Strickland, N. Kleinstreuer, A. Trospsha, et al., Pred-skin: a fast and reliable web application to assess skin sensitization effect of chemicals, J. Chem. Inf. Model. 57 (2017) 1013–1017.
[66] Z.-J. Ni, X. Wang, Y. Shen, K. Thakur, J. Han, J.-G. Zhang, et al., Recent updates on the chemistry, bioactivities, mode of action, and industrial applications of plant essential oils, Trends Food Sci. Technol. 110 (2021) 78–89.
[67] J. Kumar, A. Ramlal, D. Mallick, V. Mishra, An overview of some biopesticides and their importance in plant protection for commercial acceptance, Plants 10 (2021) 1185.
[68] A. Rakshit, V.S. Meena, P.C. Abhilash, B. Sarma, H.B. Singh, L. Fraceto, et al., Biopesticides: Volume 2: Advances in Bio-Inoculants, Woodhead Publishing, 2021.
[69] P.G. Marrone, Pesticidal natural products–status and future potential, Pest Manag. Sci. 75 (2019) 2325–2340.
[70] H.A.E.-K. Bosly, Larvicidal potential of Thuja orientalis leaves and fruits extracts against Culex pipiens (Diptera: Culicidae), J. King Saud Univ. Sci. 35 (2023) 102396.
[71] A. Sanei-Dehkordi, S. Gholami, M.R. Abai, M.M. Sedaghat, Essential oil composition and larvicidal evaluation of Platycladus orientalis against two mosquito vectors, Anopheles stephensi and Culex pipiens, J. Arthropod-borne Dis. 12 (2018) 101.
[72] J.-H. Jeon, S.-H. Lee, M.-K. Kim, H.-S. Lee, Larvicidal activity of Chamaecyparis obtusa and Thuja orientalis leaf oils against two mosquito species, J. Appl. Biol. Chem. 48 (2005) 26–28.
[73] N. Oluah, O. Ezeabiakwa, Evaluation of larvicidal activity of leaf extract of lantana camara (family: verbenaceae) against the Aedes aegypti mosquito, Bio-Research 9 (2012) 768, 74–74.
[74] S.K. Okwute, Plants as potential sources of pesticidal agents: a review, Pesticides–Adv. Chem. Botanic Pestic. 10 (2012) 208–232.
[75] A.A. Alghamdi, N.S. Basher, Efficacy of Leaves and Flowers Ethanol Extracts of the Invasive Species Lantana Camara Linn as a Mosquito Larvicidal, 2020.
[76] A. Al-Snafi, Chemical constituents and pharmacological activities of Lantana camara-A review, Asian J. Pharmaceut. Clin. Res. 12912 (2019) 10–20.
[77] E.O. Sousa, C.M. Miranda, C.B. Nobre, A.A. Boligon, M.L. Athayde, J.G. Costa, Phytochemical analysis and antioxidant activities of Lantana camara and Lantana montevidensis extracts, Ind. Crop. Prod. 70 (2015) 7–15.
[78] V. Dua, A. Pandey, A. Dash, Adulticidal activity of essential oil of Lantana camara leaves against mosquitoes, Indian J. Med. Res. 131 (2010) 434–439.
[79] A. Mansoori, N. Singh, S.K. Dubey, T.K. Thakur, N. Alkan, S.N. Das, et al., Phytochemical characterization and assessment of crude extracts from Lantana camara L. for antioxidant and antimicrobial activity, Front. Agron. 2 (2020) 582268.
[80] E. Tadesse, E. Engidawork, T. Nedi, G. Mengistu, Evaluation of the anti-diarrheal activity of the aqueous stem extract of Lantana camara Linn (Verbenaceae) in mice, BMC Compl. Alternative Med. 17 (2017) 1–8.
[81] S. Caruntu, A. Ciceu, N.K. Olah, I. Don, A. Hermenean, C. Cotoraci, Thuja occidentalis L.(Cupressaceae): Ethnobotany, phytochemistry and biological activity, Molecules 25 (2020) 5416.
[82] E. Ghisalberti, Lantana camara L.(verbenaceae), Fitoterapia 71 (2000) 467–486.
[83] S. Jain, A. Vaidya, N. Jain, V. Kumar, A. Modi, Bioactive Compounds of Royal Poinciana (Delonix Regia (Hook.) Raf.). Bioactive Compounds in Underutilized Vegetables and Legumes, 2021, pp. 483–502.
[84] Y. Nagarajan, J. Rongala, S. Luang, A. Singh, N. Shadiac, J. Hayes, et al., A barley efflux transporter operates in a Na+-dependent manner, as revealed by a multidisciplinary platform, Plant Cell 28 (2016) 202–218.
[85] R.S. Baeshen, M.M. Baz, Efficacy of Acacia nilotica, Eucalyptus camaldulensis, and Salix safsafs on the mortality and development of two vector-borne mosquito species, Culex pipiens and Aedes aegypti, in the laboratory and field, Heliyon 9 (2023) e16378.
[86] M.A. Farghali, A.M. Selim, H.F. Khater, N. Bagato, W. Alharbi, K.H. Alharbi, et al., Optimized adsorption and effective disposal of Congo red dye from wastewater: Hydrothermal fabrication of MgAl-LDH nanohydrotalcite-like materials, Arab. J. Chem. 15 (2022) 104171.
[87] H.H. Agus, Terpene Toxicity and Oxidative Stress. Toxicology, Elsevier, 2021, pp. 33–42.
[88] N.R. Larson, S.T. O'Neal, U.R. Bernier, J.R. Bloomquist, T.D. Anderson, Terpenoid-induced feeding deterrence and antennal response of honey bees, Insects 11 (2020) 83.
[89] Z.T. Muhseen, S. Ahmad, G. Li, Structural basis of UDP-N-acetylglucosamine pyrophosphorylase and identification of promising terpenes to control Aedes aegypti, Colloids Surf. B Biointerfaces 204 (2021) 111820.
[90] J. Liu, J. Hua, B. Qu, S. Luo, Insecticidal terpenes from the essential oils of Artemisia nakaii and their inhibitory effects on acetylcholinesterase, Front. Plant Sci. 12 (2021) 720816.
[91] A.K. Srivastava, V.K. Singh, Biological action of essential oils (terpenes), Int. J. Biol. Med. Res. 10 (2019) 6854–6859.
[92] D.A.T. Boncan, S.S. Tsang, C. Li, I.H. Lee, H.-M. Lam, T.-F. Chan, et al., Terpenes and terpenoids in plants: Interactions with environment and insects, Int. J. Mol. Sci. 21 (2020) 7382.
[93] D. Ganjewala, S. Sam, K.H. Khan, Biochemical compositions and antibacterial activities of Lantana camara plants with yellow, lavender, red and white flowers, EurAsia J. BioSci. 3 (2009) 69–77.
[94] K. Priya, G. Deepak, Antibacterial activities and phytochemical analysis of different plant parts of Nyctanthes arbor-tristis (Linn.), Res. J. Phytochem. 4 (2010) 257–263.
[95] F. Guo, Q. Chen, H. Chen, Antimicrobial activity and proposed action mechanism of linalool against Pseudomonas fluorescens, Front. Microbiol. 12 (2021) 562094.
[96] S. Sukul, S. Chaudhuri, Antibacterial natural products from leaves of Lantana camara L. with activity comparable to some therapeutically used antibiotics, Indian J. Pharmaceut. Sci. 63 (2001) 20–23.
[97] S. Basu, A. Ghosh, B. Hazra, Evaluation of the antibacterial activity of Ventilago madraspatana Gaertn., Rubia cordifolia Linn. and Lantana camara Linn.: isolation of emodin and physcion as active antibacterial agents, Phytother Res.: Int. J. Devot. Pharmacol. Toxicol. Eval. Natural Prod. Derivat. 19 (2005) 888–894.
[98] S. Amutha, Phytochemical Investigation and in Vitro Evaluation of Lantana Camara Seed Extracts on Selected Human Pathogenic Bacteria, 2014.
[99] M.B. Gallo, M.J. Sarachine, Biological activities of lupeol, Int. J. Biomed. Pharmaceut. Sci. 3 (2009) 46–66.
[100] R.S. Darwish, H.M. Hammoda, D.A. Ghareeb, A.S. Abdelhamid, F.M. Harraz, E. Shawky, Seasonal dynamics of the phenolic constituents of the cones and leaves of oriental Thuja (Platycladus orientalis L.) reveal their anti-inflammatory biomarkers, RSC Adv. 11 (2021) 24624–24635.
[101] N. Jain, Sharma M. Ethanobotany, Phytochemical and pharmacological aspects of Thuja orientalis. A review, Int. J. Pure Appl. Biosci. 5 (2017) 73–83.
[102] M.K. Swamy, U.R. Sinniah, A comprehensive review on the phytochemical constituents and pharmacological activities of Pogostemon cablin Benth.: an aromatic medicinal plant of industrial importance, Molecules 20 (2015) 8521–8547.
[103] A. Amalia, I. Syafitri, V.D. Prasasty, Antimalarial effect of flamboyant (Delonix regia) bark and papaya (Carica papaya L.) leaf ethanolic extracts against plasmodium berghei in mice, Biomed. Pharmacol. J. 10 (2017) 1081–1089.
[104] L. Kasim, V. Ferro, O. Odukoya, G. Ukpo, V. Seidel, A. Gray, et al., Evaluation of cytotoxic and antimicrobial activities of Struchium sparganophora (Linn.) Ktze Asteraceae, J. Med. Plants Res. 5 (2011) 862–867.

[105] Godstime C. Omojate, Felix O. Enwa, Augustina O. Jewo, Christopher O. Eze, Mechanisms of antimicrobial actions of phytochemicals against enteric pathogens–a review, J. Pharm. Chem. Biol. Sci. 2 (2014) 77–85.
[106] M.V. Ashraf, S. Pant, M.H. Khan, A.A. Shah, S. Siddiqui, M. Jeridi, et al., Phytochemicals as antimicrobials: prospecting Himalayan medicinal plants as source of alternate medicine to combat antimicrobial resistance, Pharmaceuticals 16 (2023) 881.
[107] J. Bouayed, T. Bohn, Exogenous antioxidants—Double-edged swords in cellular redox state: health beneficial effects at physiologic doses versus deleterious effects at high doses, Oxid. Med. Cell. Longev. 3 (2010) 228–237.
[108] S. Sehrawat, H. Soni, Phytopharmacology Profile of Bougainvillea Glabra: an Overview, 2019.
[109] J. Mariajancyrani, G. Chandramohan, P. Saravanan, S. Saivaraj, In-vitro Antioxidant Potential of Delonix Regia Leaves, 2013.
[110] K. Koshimizu, H. Ohigashi, H. Tokuda, A. Kondo, K. Yamaguchi, Screening of edible plants against possible anti-tumor promoting activity, Cancer Lett. 39 (1988) 247–257.
[111] S.M. Ezzat, A. M El-Sayed, M. M Salama, A. A Sleem, Hepatoprotective and Cytotoxic Activities of Delonix Regia Flower Extracts, 2011.
[112] S. Singh, Sonia, Pharmacognostical EVALUATION and phytochemical analysis OF DELONIX regia RAFIN, STEM BARK. Int. J. Pharmaceut. Sci. Res. 9 (2018) 1908–1912.
[113] L. Chengala, N. Singh, Botanical pesticides—a major alternative to chemical pesticides: a review, Int. J. Life Sci. 5 (2017) 722–729.
[114] S. Prabha, A. Yadav, A. Kumar, A. Yadav, H.K. Yadav, S. Kumar, et al., Biopesticides—an alternative and eco-friendly source for the control of pests in agricultural crops, Plant Arch 16 (2016) 902–906.
[115] H. Nawaz, M.A. Shad, N. Rehman, H. Andaleeb, N. Ullah, Effect of solvent polarity on extraction yield and antioxidant properties of phytochemicals from bean (Phaseolus vulgaris) seeds, Brazil. J. Pharmaceut. Sci. 56 (2020) e17129.
[116] R. Mostafa, Rahman R. El, M. Yassin, H. Essawy, Antibacterial, Antivirulence activities and phytochemical screening of some Wild&Wasts plants in Egypt, Egypt. Acad. J. Biol. Sci. G Microbiol. 14 (2022) 65–76.
[117] S.K. Mohanty, K.S. Mallappa, A. Godavarthi, B. Subbanarasiman, A. Maniyam, Evaluation of antioxidant, in vitro cytotoxicity of micropropagated and naturally grown plants of Leptadenia reticulata (Retz.) Wight & Arn.-an endangered medicinal plant, Asian Pac. J. Tropical Med. 7 (2014) S267–S271.
[118] R. Naz, A. Bano, Phytochemical screening, antioxidants and antimicrobial potential of Lantana camara in different solvents, Asian Pacif. J. Tropical Dis. 3 (2013) 480–486.
[119] A. Bukar, Z. Tukur, Adulticidal potentials of dichloromethane extracts of some selected plant leaves against culex mosquitoes, Bayero J. Pure Appl. Sci. 10 (2017) 38–42.
[120] IlKwon P.I. Park, HoiSeon L.H. Lee, SangGil L.S. Lee, P.J. Park JiDoo, A.Y. Ahn YoungJoon, Antifeeding Activity of Isoquinoline Alkaloids Identified in Coptis Japonica Roots against Hyphantria cunea (Lepidoptera: Arctiidae) and Agelastica Coerulea (Coleoptera: Galerucinae), 2000.
[121] T. Venkatachalam, V.K. Kumar, P.K. Selvi, A.O. Maske, V. Anbarasan, P.S. Kumar, Antidiabetic activity of Lantana camara Linn fruits in normal and streptozotocin-induced diabetic rats, J. Pharm. Res. 4 (2011) 1550–1552.
[122] R. Pavela, N. Vrchotová, Growth inhibitory effect of extracts from Reynoutria sp. plants against Spodoptera littoralis larvae, Agrociencia 42 (2008) 573–584.
[123] B. Mehta, M. Sharma, S. Shitut, Identification of Novel Compounds from Thuja Orientalis (Leaves), 1999.
[124] H. Yousef, S.F. El-Lakwah, Y.A. El Sayed, Insecticidal activity of linoleic acid against Spodoptera littoralis (Boisd.), Egypt. J. Agric. Res. 91 (2013) 573–580.
[125] S. Zoubiri, A. Baaliouamer, GC and GC/MS analyses of the Algerian Lantana camara leaf essential oil: effect against Sitophilus granarius adults, J. Saudi Chem. Soc. 16 (2012) 291–297.
[126] B. Zhai, Y. Zeng, Z. Zeng, N. Zhang, C. Li, Y. Zeng, et al., Drug delivery systems for elemene, its main active ingredient β-elemene, and its derivatives in cancer therapy, Int. J. Nanomed. (2018) 6279–6296.
[127] Y.V. Gyrdymova, S.A. Rubtsova, Caryophyllene and caryophyllene oxide: a variety of chemical transformations and biological activities, Chem. Pap. (2022) 1–39.
[128] H. Türkez, K. Celik, B. Toğar, Effects of copaene, a tricyclic sesquiterpene, on human lymphocytes cells in vitro, Cytotechnology 66 (2014) 597–603.
[129] S.S. Dahham, Y.M. Tabana, M.A. Iqbal, M.B. Ahamed, M.O. Ezzat, A.S. Majid, et al., The anticancer, antioxidant and antimicrobial properties of the sesquiterpene β-caryophyllene from the essential oil of Aquilaria crassna, Molecules 20 (2015) 11808–11829.
[130] M.G. Ahmed, A.A. Al-Sagheer, S.Z. El-Zarkouny, E.A. Elwakeel, Potential of selected plant extracts to control severe subacute ruminal acidosis in vitro as compared with monensin, BMC Vet. Res. 18 (2022) 356.
[131] S.J.N. Tatsimo, V.T. Tsague, M. Lamshoft, P. Sarkar, P.K. Bag, M. Spiteller, Antibacterial-guided isolation of constituents from Senna alata leaves with a particular reference against Multi-Drug-Resistant Vibrio cholerae and Shigella flexneri, Int. J. Brain Cognit. Sci. 11 (2017) 46–53.
[132] A. Ganeshpurkar, A.K. Saluja, The pharmacological potential of rutin, Saudi Pharmaceut. J. 25 (2017) 149–164.
[133] S. Sharma, A. Ali, J. Ali, J.K. Sahni, S. Baboota, Rutin: therapeutic potential and recent advances in drug delivery, Expet Opin. Invest. Drugs 22 (2013) 1063–1079.
[134] M.-Q. Shan, J. Shang, A.-W. Ding, Platycladus orientalis leaves: a systemic review on botany, phytochemistry and pharmacology, Am. J. Chin. Med. 42 (2014) 523–542.
[135] A. Imani, N. Maleki, S. Bohlouli, M. Kouhsoltani, S. Sharifi, S. Maleki Dizaj, Molecular mechanisms of anticancer effect of rutin, Phytother Res. 35 (2021) 2500–2513.
[136] R. Negahdari, S. Bohlouli, S. Sharifi, Dizaj S. Maleki, Saadat Y. Rahbar, K. Khezri, et al., Therapeutic benefits of rutin and its nanoformulations, Phytother Res. 35 (2021) 1719–1738.
[137] N.B. Rathod, P. Kulawik, F. Ozogul, J.M. Regenstein, Y. Ozogul, Biological activity of plant-based carvacrol and thymol and their impact on human health and food quality, Trends Food Sci. Technol. 116 (2021) 733–748.
[138] S. Kumar, M.M. Abedin, A.K. Singh, S. Das, Role of phenolic compounds in plant-defensive mechanisms, Plant Phenol. Sustain. Agric. 1 (2020) 517–532.
[139] T. Liang, W. Yue, Q. Li, Comparison of the phenolic content and antioxidant activities of Apocynum venetum L.(Luo-Bu-Ma) and two of its alternative species, Int. J. Mol. Sci. 11 (2010) 4452–4464.
[140] A. Edreva, V. Velikova, T. Tsonev, S. Dagnon, A. Gürel, L. Aktaş, et al., Stress-protective role of secondary metabolites: diversity of functions and mechanisms, Gen. Appl. Plant Physiol. 34 (2008) 67–78.
[141] D. Lin, M. Xiao, J. Zhao, Z. Li, B. Xing, X. Li, et al., An overview of plant phenolic compounds and their importance in human nutrition and management of type 2 diabetes, Molecules 21 (2016) 1374.
[142] Z. Yuan, X.P. Hu, Repellent, antifeedant, and toxic activities of Lantana camara leaf extract against Reticulitermes flavipes (Isoptera: Rhinotermitidae), J. Econ. Entomol. 105 (2012) 2115–2121.
[143] B. Sivakumar, V.G. Va, D.C. Beerappa, K. Nithin, A REVIEW ON MEDICINAL PROPERTIES OF LANTANA CAMARA LINN, 2022.
[144] F. Alminderej, S. Bakari, T.I. Almundarij, M. Snoussi, K. Aouadi, A. Kadri, Antioxidant activities of a new chemotype of Piper cubeba L. fruit essential oil (Methyleugenol/Eugenol): in Silico molecular docking and ADMET studies, Plants 9 (2020) 1534.
[145] Haritha M. Dalavayi, S. Bala, D. Choudhury, Eco-friendly plant based on botanical pesticides, Plant A rchiv. 21 (2021) 2197–2204.
[146] M.M. Baz, R.M. Mostafa, H.T. Ebeed, H.S. Essawy, G.E. Dawwam, A.B. Darwish, et al., Evaluation of Four Ornamental Plant Extracts as Insecticidal, Antimicrobial, and Antioxidant against the West Nile Vector, Culex pipiens (Diptera: Culicidae) and Metabolomics Screening for Potential Therapeutics, 2023.