Bull. Chem. Soc. Ethiop. **2025**, 39(2), 351-366.
DOI: https://dx.doi.org/10.4314/bcse.v39i2.13

ISSN 1011-3924
Printed in Ethiopia
Online ISSN 1726-801X

GC-MS PROFILING AND IN SILICO PHARMACOKINETIC PROPERTIES OF ESSENTIAL OILS HYDRODISTILLED FROM LEAVES OF *CAPPARIS TOMENTOSA* AND *CADABA ROTUNDIFOLIA*

Teshome Degfie[1,2*], Milkyas Endale[3], Tekalign Begna[4,5], Chuleui Jung[4,5] and Aman Dekebo[1,2*]

[1]Department of Applied Chemistry, Adama Science and Technology University, P.O. Box 1888, Adama, Ethiopia
[2]Institute of Pharmaceutical Sciences, Adama Science and Technology University, P.O. Box 1888, Adama, Ethiopia
[3]Traditional and Modern Medicine Research and Development Directorate, Armauer Hansen Research Institute, Ethiopia, P.O.BOX 1005, Addis Ababa4Agricultural Science and Technology 4Research Institute Andong National University, Republic of Korea
[5]Department of Plant Medicals, Andong National University, Andong GB 36729, Republic of Korea

(Received June 11, 2024; Revised October 25, 2024; Accepted October 28, 2024)

ABSTRACT. In Ethiopian traditional medicine *Capparis tomentosa* treats tuberculosis, diarrhea, epilepsy, and malaria, while *Cadaba rotundifolia* for arthritis, tonsillitis and snake bites. Essential oils from the plant leaves were hydro-distilled using Clevenger apparatus and analyzed by GC-MS. SwissADME and ProTox-II assessed drug-likeness and ADMET of major compounds. Leaf extracts were tested against three bacterial strains using agar disc-diffusion method. GC-MS identified 25 compounds (89.7%) in *C. tomentosa* and 23 (95.47%) in *C. rotundifolia*. Major compounds (**1-15**) followed Lipinski's and Veber's rules, with compounds **2**, **7**, **9**, and **12** in the Boiled-Egg's yellow region. Compounds **3**, **4**, **7**, **11**, and **12** had LD50 >5000 mg/kg, indicating lower toxicity than chloramphenicol (LD_{50} = 1500 mg/kg). At 5 µg/mL, *C. tomentosa* oil showed stronger inhibition against *E. coli* (10±0.0 mm) and *P. aeruginosa* (9.0±0.25 mm), its methanol and n-hexane extracts against *E. coli* (9.85±0.14 mm) and *P. aeruginosa* (8.1±0.19 mm), respectively. *C. rotundifolia* oil was more effective against *P. aeruginosa* (8±0.5 mm) than chloramphenicol (6.9±0.51 mm), while its n-hexane and methanol extracts inhibited *P. aeruginosa* (8.1±0.17 mm) and *E. coli* (8.0±0.31 mm), respectively. These findings support traditional medicinal use of the studied plants, and highlight their potential as sources of bioactive compounds.

KEY WORDS: *Capparis tomentosa*, *Cadaba rotundifolia*, Essential oils, GC-MS, *In silico* pharmacokinetic

INTRODUCTION

The *Capparidaceae* family (Caper family), contains around 700 flowering plant species growing in temperate and tropical regions. The well-known genera within the family include *Capparis*, represented by species like *Capparis tomentosa* [1], and *Cadaba*, which includes species like *Cadaba rotundifolia* [2]. *Capparis* is estimated to include around 250 species found across tropical and subtropical regions [3]. *Capparis tomentosa Lam*., known locally as Gmero or Gimero (Amharic) in Ethiopia [4]. It can grow up to 10 meters tall, with elliptic to ovate leaves [5]. *C. tomentosa* is widely distributed in Ethiopia, Namibia, Eritrea, Botswana, Lesotho, South Africa, and Swaziland [6]. In South Africa, it is valued for treating sexual and reproductive health issues and HIV-related conditions like tuberculosis, herpes simplex, herpes zoster, and chronic diarrhea [7]. Additionally, it is used in infusions to aid with epilepsy, sterility, threatened abortion, gonorrhea, syphilis, and postpartum bleeding. Decoctions made from its roots, leaves, and bark are employed to alleviate coughs, fever, and asthma [8]. The plant is also used for diverse

*Corresponding authors. E-mail: teshome2degfie@yahoo.com, amandekeb@gmail.com

medicinal purposes across Africa, including as an aphrodisiac [9], cancer treatment [10], and management of diabetes, goiter, and high blood pressure [11]. In Ethiopia, the plant's root serves as therapeutic agents to treat many ailments such as epilepsy, postpartum bleeding [12], toothaches, and wounds [13, 14]. In Eastern Ethiopia's Dengego valleys, a root and leaf concoction is ingested to facilitate nipple pore opening [15]. The powdered root's smoke is inhaled to treat malaria, "Mich", and the evil eye near Debre Libanos monastery in Ethiopia [16]. Extracts of *Capparis tomentosa* aerial parts exhibited *in-vitro* antimicrobial activity against *Staphylococcus aureus* and *Bacillus cereus*, and showed fungal growth inhibition against *Aspergillus flavus* and *Candida albicans* [5]. Different classes of secondary metabolites, namely alkaloids, anthranoids, flavonoids, glycosides, polyphenols, saponins, steroids and tannins were reported from extracts of different parts of the *C. tomentosa* [17].

Cadaba rotundifolia Forssk, locally known as "Delensisa" in Afan Oromo [15, 18], is an evergreen shrub reaching heights of 2-4 meters [19, 20]. It grows in Sudan, Somalia, Socotra, Saudi Arabia, northern Kenya, and in various Ethiopian regions [20]. It is densely branched shrub produces a strong scent from its small glandular-hair-covered twigs. Its cylindrical capsule fruit matures from green to darker shades, eventually splitting to reveal dark brown seeds encased in a bright orange-red lining [19]. In traditional medicine, leaves and roots extracts of *C. rotundifolia* have been used for treating abscesses and tumors in Sudan [10], while in Djibouti, it is employed as an antibiotic after soaking crushed leaves in water [21]. In Eastern Ethiopia, a concoction of its bark or leaves, combined with *Withania somnifera*, is taken orally to treat prolonged menstruation [15]. The plant's leaves and young branches are utilized for external injuries, wounds, and skin infections [18]. Various parts of *C. rotundifolia* are utilized for the treatment of human ailments such as arthritis (stems), eye sickness (leaves), tonsillitis (leaves), flue "Mitch" (leaves), broken head (leaves), snake bite (leaves); and for livestock ailments, including retained placenta, external parasite, brucellosis for livestock, in Yalo Woreda of Afar region, Ethiopia [22]. The cold water infusion of leaves of *C. rotundifolia* is also orally administered for the handling malaria around Awash Fentale, district of the Afar Region, Ethiopia [4]. Phytochemical studies of extracts of the different parts *Cadaba rotundifolia* led to isolation of secondary metabolites, such as alkaloids and flavonoid [23]. Although *C. tomentosa* and *C. rotundifolia* are widely used in ethno-medicine, there is limited scientific research on the analysis of essential oils of these plants in Ethiopia. Essential oils are complex mixtures of volatile compounds found in low concentrations in various plant parts, including flowers, leaves, and roots [24]. They are recognized for their diverse bioactivities, including antibacterial [25]. Thus, the present study is designed to investigate the essential oil composition and in vitro biological activity of essential oils and crude extracts from leaves *C. tomentosa* and *C. rotundifolia*.

Methodology

Collection and identification of plant material

Leaves the plant *C. tomentosa* and *C. rutondifolia* were collected from the surrounding areas of Adama and Dire Dawa cities, Ethiopia, in the period of October to November 2013. The plants were confirmed by the Botanist Mr. Shambel Alemu and specimens of each plant were placed at the National Herbarium, Addis Ababa University, Ethiopia with voucher codes of TCT11/17 for *C. tomentosa*, and TCR10/17 for *C. rotundifolia*. The pictures of *C. tomentosa* (a) and *C. rotundifoli* (b) are shown in Figure 1.

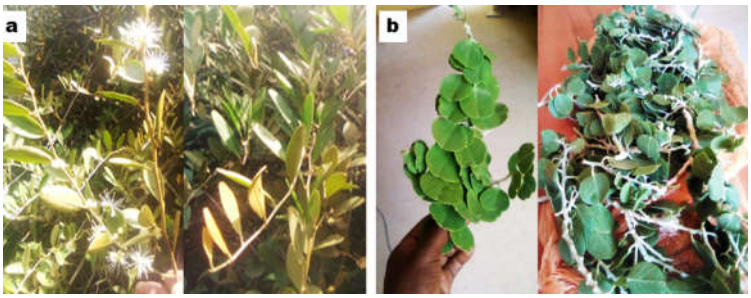

Figure 1. Arial part of *C. tomentosa* (a) and *C. rotundifolia* (b) (Photo taken by Teshome D., September, 2021).

Preparation of crude leaf extracts

Air-dried and ground leaves of *C. tomentosa* and *C. rotudifolia* (0.5 kg, each) were consecutively extracted by n-hexane, dichloromethane:methanol (1:1), and methanol (1.5 L, each) by maceration for 72 h, thrice at ambient temperature. The extract solutions were filtered by Whatman No. 1 filter paper and filtrates were concentrated in vacuo on a rotary evaporator at 40 °C to obtain 31 g, and 24 g of crude extracts, respectively.

Essential oil extraction

The air-dried and ground leaves of *C. tomentosa* and *C. rotudifolia* (500 g, each) were separately subjected to hydro-distillation for 3 h using Clevenger apparatus [26]. Essential oils were collected, dried under anhydrous sodium sulfate, filtered and concentrated using rotary evaporator which afforded 0.29% and 0.22% v/w, respectively. The hydrodistilled oils were then stored at 4 °C until further analysis. Each extraction was performed at least three times.

Essential oils analysis by GC-MS

GC-MS analysis was performed using a GC (7890B, Agilent Technologies, USA) coupled with an MS (5977A Network, Agilent Technologies). An HP 5MS non-polar column (30 m × 250 µm internal diameter, 0.25 µm film thickness, Agilent Technologies) was used. Helium was employed as the carrier gas at a flow rate of 1 mL/min. The injector temperature was set to 230 °C, and injections were made in split mode with a 10:1 split ratio. The oven temperature was initially held at 40 °C for 5 min, then increased to 250 °C at a rate of 6 °C/min, where it was maintained for 20 min, with a total run time of 60 min. Mass spectra were recorded in EI mode at 70 eV, scanning the 50–500 m/z range. Volatile compounds were identified by comparing their spectra with those in the NIST11 GC-MS library and consulting relevant literature [27].

In-silico drug-likeness and ADMET prediction

In this work, drug likeness and ADMETs of major compounds from essential oils hydrodistilled from *C. tomentosa* and *C. rotundifolia* leaves were predicted. The structures of these compounds were converted to canonical SMILES format and analyzed with SwissADME and PreADMET tools to predict their drug-likeness and ADMET pharmacokinetic properties [28, 29]. The Lipinski's rule of five [30] was employed to evaluate drug-likeness property of the compounds, and those that do not violate more than two of the criteria are considered to possess drug-likeness

properties. Veber's rule was employed to predict the oral bioavailability of the major compounds, suggesting that compounds with fewer than ten rotatable bonds (RTB) and a polar surface area (TPSA) <140 Å^2 are expected to demonstrate good oral bioavailability [31]. Furthermore, some of the ADMET parameters, such as gastrointestinal absorption (GIA), blood-brain barrier (BBB) permeability, permeability glycoprotein (P-gp) interaction, cytochrome P450 (CYP) inhibitory effects, lethal dose 50 (LD_{50}), and organ toxicities were predicted [28]. Toxicological endpoints, including the lethal dose 50 (LD_{50}) and organ toxicities, were also predicted utilizing the Pro Tox II tool [29, 32]. Boiled-Egg plot was set to evaluate the human intestinal absorption, brain access and P-gp score [33]. Besides, bioavailability radar based on six properties (lipophilicity, size, polarity, solubility, saturation, and flexibility) was carried out to study the suitable physicochemical properties for oral bioavailability of the major components of the essential oils.

In-vitro antibacterial activity of essential oils and crude leaf extracts

In-vitro bacterial growth inhibitions essential oil, and n-hexane, dichloromethane/methanol and methanol crude extracts of leaves of *C. tomentosa* and *C. rotundifolia* were carried out towards *S. aureus* (ATCC 25923), *E. coli* (ATCC 25922), and *P. aeruginosa* (ATCC 27853) strains obtained from the Public Health Institute of Ethiopia. The experiments were conducted at microbiology laboratory, Haramaya University in collaboration with microbiologists. The agar medium disc-diffusion method was employed following standard protocols [34]. Careful inoculation of fresh colonies (2-4) of the mincrobes to a salty solution and adjustment to a 0.5 McFarland standard (108 CFU/mL) was done. Mueller Hinton Agar plates were speckled with bacterial solutions using a cotton swab. Samples were prepared in sterilized Whatman No. 1 filter paper discs (6 mm in diameter). Concentrations of essential oil and extracts ranging from 1000 to 50 µg/mL were prepared from stock solutions in 4% DMSO. Chloramphenicol discs and DMSO served as positive and negative controls. Each 100 µL solution was loaded onto 6 mm paper discs, placed on MHA plates with bacterial cultures, and incubated at 37 ºC for 18-24 hours. Inhibition zones were measured, and results, expressed as mean ± standard deviation, were based on duplicate experiments under aseptic conditions.

RESULTS AND DISCUSSION

Essential oils analysis

The essential oils hydrodistilled from dried and grounded leaves of *C. tomentosa* and *C. rotundifolia* were examined using gas chromatography-mass spectrometry (GC-MS). Based on the obtained GC-MS data, the chemical composition of the essential oils of *C. tomentosa* and *C. rotundifolia* revealed the presence of 25 components (comprising 89.7% of the total) and 23 components (constituting 95.47% of the total), respectively. The chemical profiles and their percentage composition, retention times (RT) and retention index (RI) of the essential oils of *C. tomentosa* and *C. rotundifolia*) are presented in Tables 1 and 2, respectively. The GC chromatogram of the major components of each essential oil is depicted in Figure 2.

The essential oil hydrodistilled from the leaves of *C. tomentosa* contains major constituents, including 2-tetradecene (E) (3.8%) (**1**), 2,4-bis(1,1-dimethylethyl)phenol (21.03%) (**2**), cetene (10.11%) (**3**), 1-octadecene (12.07%) (**4**), cycloeicosane (10.15%) (**5**), cyclotetracosane (6.55%) (**6**), 4-methylpentan-2-yl pentyl phthalate (3.55%) (**7**), and bis(2-ethylhexyl) phthalate (8.38%) (**8**) (Figure 2 and Table 1). These compounds considered to represent the constituents within the essential oil contributing distinct properties. The structures of these major chemical components (**1-8**) are presented in Figure 3. The essential oils previously reported by [35] from both leaves and fruits of *C. tomentosa*, obtained via steam distillation using a Clevenger type apparatus, was noted to contain β-phellandrene and β-pinene as major components. This differs from the major component 4-methylpentan-2-yl pentyl phthalate-(21.03%) reported in the current study. Such

variations can be attributed to different environmental factors including soil type, climatic, stage of growth, among others, that may affect the chemical compositions of essential oils of the same plant species [36].

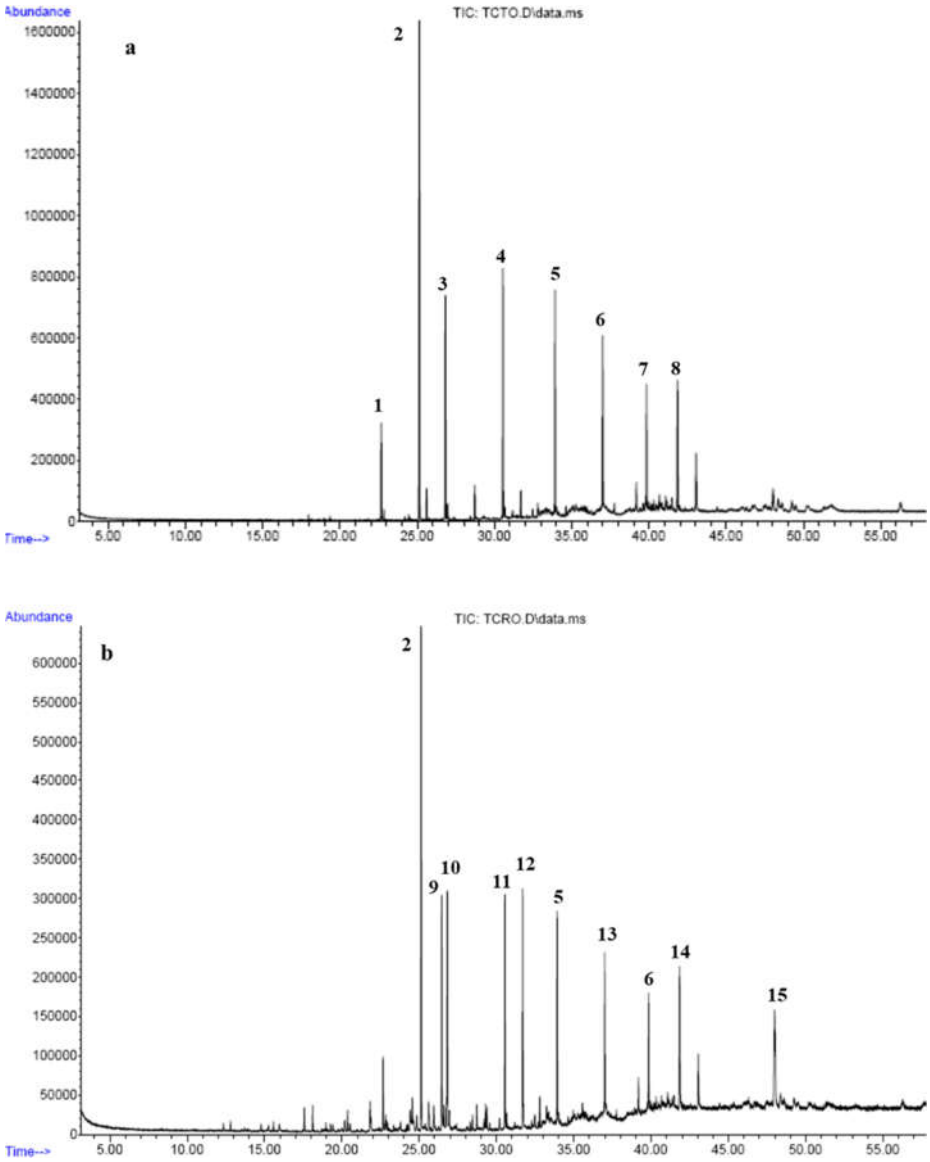

Figure 2. GC profile of essential oils of leaves of *C. tomentosa* (a), and *C. rotundifolia* (b).

Based on the results obtained from GC-MS analysis, the major chemical components identified in the essential oil hydrodistilled from the leaves of *C. rotundifolia* were found to be 4-methylpentan-2-yl pentyl phthalate (15.6%) (**2**), cycloeicosane (10.15%) (**5**), cyclotetracosane (6.55%) (**6**), (Z)-hex-3-en-1-yl benzoate (8.01%) (**9**), cyclohexadecane (8.34%) (**10**), 1-nonadecene (7.47) (**11**), diisobutyl phthalate (8.24%) (**12**), behenic alcohol (5.33%) (**13**), diisooctyl phthalate (6.03%) (**14**) and bis(2-ethylhexyl) decanedioate (9.34%) (**15**) (Figure 2). The structures of these major components (**2**, **5**, **6** and **9-15**) are shown in Figure 3. Prior to the completion of this study, there were no reports on the essential oil analysis of *C. rotundifolia*. The GC-MS analysis of ethanolic extract of roots of another Cadaba species, *Cadaba trifoliate*, identified 1,2-benzenedicarboxylic acid, diisooctyl ester, and 1-methyl-pyrrolidine-2-carboxylic acid as major compounds [37], differing from the findings of this study.

Table 1. Percentage composition of essential oil hydrodistilled from leaves of *C. tomentosa*.

S.No.	Identified chemical components	RT	MW	% Total	RI [38]
1	2-Tetradecene, (E)-	22.66	196.219	3.89	1497
2	Tetradecane	22.83	198.235	0.42	1504
3	Phenol, 2,4-bis(1,1-dimethylethyl)-	25.13	206.167	21.03	1614
4	Xyloidone	25.60	240.079	1.41	1638
5	Cetene	26.81	224.25	10.11	1698
6	Hexadecane	26.96	226.266	0.66	1706
7	2-Propenoic acid, pentadecyl ester	28.72	282.256	1.45	1799
8	1-Octadecene	30.54	252.282	12.07	1900
9	Octadecane	30.66	254.297	0.51	1907
10	2H-Pyran, tetrahydro-4-methyl-2-(2-methyl-1-propenyl)-	31.17	154.136	0.65	1937
11	Phthalic acid, butyl isohexyl ester	31.69	306.183	1.42	1967
12	7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione	32.46	276.173	0.81	2012
13	Hexadecanoic acid, methyl ester	32.79	270.256	0.24	2033
14	Cycloeicosane	33.91	280.313	10.15	2101
15	2-Hexyldodecan-1-ol	34.61	270.292	0.44	2146
16	1-Dodecanol, 2-hexyl-	37.75	270.292	0.53	2400
17	[1,1'-Biphenyl]-2,3'-diol, 3,4',5,6'-tetrakis(1,1-dimethylethyl)-	39.17	410.318	1.64	2470
18	Phthalic acid, isobutyl 2-methylpent-3-yl ester	39.76	306.183	0.49	2558
19	Cyclotetracosane	39.83	336.376	6.55	2504
20	Phthalic acid, 2-ethylbutyl nonyl ester	40.30	376.261	0.47	2537
21	4-Methylpentan-2-yl pentyl phthalate	40.66	320.199	3.55	2562
22	Phthalic acid, 5-methylhex-2-yl pentyl ester	41.06	334.214	0.84	2590
23	Phthalic acid, hexadecyl pentyl ester	41.48	460.355	0.73	2616
24	Bis(2-ethylhexyl) phthalate	41.84	390.277	8.37	2637
25	Phthalic acid, 4-methylhept-3-yl nonyl ester	49.25	404.293	1.18	2941
	Total			89.7 %	

Note: MW: Molecular weight; RT: Retention time in min, RI-Retention index.

In-silico prediction of drug-likeness and ADMET properties

Drug-likeness properties

The SwissADME tool was used to predict the drug-likeness properties of the major chemical components found in the essential oils hydrodistilled from the leaves of *C. tomentosa* (**1-8**) and *C. rotundifolia* (**2**, **5**, **6**, **9**, **10-15**), with the results displayed in Table 3.

Based on the outcome, all tested compounds showed zero violation to the Lipinski's rule of five, except compounds **4**, **11**, **13** and **14** that violated one rule (iLogP > 5. All the compounds

scored far larger iLogP value (3.04 < lop < 5) than the standard chloramphenicol (1.17) suggesting smaller absorption and distribution property relative to the drug. Number of rotatable bonds (NRB) less than ten have been scored by compounds **2**, **5**, **6**, **9**, **10**, and **12**, indicating their higher degree of conformational stability advantageous for their structural integrity and interactions within biological systems [39]. All tested compounds exhibit topological polar surface area (TPSA) of less than 140 Å². This indicates their potential for excellent absorption in the intestine. Considering both NRB and TPSA values, Veber's Rule is obeyed by all compounds with no violations shown by **1**, **2**, **5**, **6**, **9**, **10**, and **12**. The drug-likeness prediction outcome revealed that most of the tested compounds possess favorable oral pharmacokinetic properties.

Table 2. Percentage composition of essential oils hydrodistilled from leaves of *C. rotundifolia.*

S. No.	Identified chemical components	RT	MW	% Total	RI [38]
1	Methyl 2-phenylacetate	17.57	150.07	1.09	1281
2	L-α.-Terpineol	18.11	154.14	0.91	1302
3	1-(2,4-dimethoxy-3-methylphenyl)ethan-1-one	20.37	194.09	0.78	1395
4	Eugenol	21.82	164.08	1.86	1459
5	2-Tetradecene, (*E*)-	22.66	196.22	2.55	1497
6	*trans*-β-Ionone	24.55	192.15	1.31	1586
7	Phenol, 2,4-bis(1,1-dimethylethyl)-	25.12	206.17	15.62	1614
8	1H-2-Benzopyran-1-one, 3,4-dihydro-8-hydroxy-3-methyl-	25.93	178.06	1.54	1654
9	(Z)-Hex-3-en-1-yl benzoate	26.45	204.12	8.01	1680
10	*n*-Hexyl benzoate	26.60	206.13	0.87	1688
11	Cyclohexadecane	26.81	224.25	8.34	1698
12	2-Propenoic acid, pentadecyl ester	28.73	282.26	0.88	1799
13	1,7-di-iso-propylnaphthalene	29.29	212.16	0.77	1831
14	1-Nonadecene	30.54	266.30	7.47	1951
15	Diisobutyl phthalate	31.69	278.15	8.24	1984
16	Hexadecanoic acid, methyl ester	32.79	270.26	1.16	2033
17	Isoxazole, 5-methoxy-3-phenyl-	33.23	175.06	0.90	2059
18	Cycloeicosane	33.91	280.31	6.50	2101
19	Behenic alcohol	37	326.36	5.33	2306
20	[1,1'-Biphenyl]-2,3'-diol, 3,4',5,6'-tetrakis(1,1-dimethylethyl)-	39.1	410.31	1.85	2467
21	Cyclotetracosane	39.83	336.38	4.11	2504
22	Diisooctyl phthalate	41.84	390.28	6.02	2637
23	bis(2-Ethylhexyl) decanedioate	47.98	426.37	9.34	2905
	Total			95.47 %	

Note: MW - Molecular weight; RT: Retention time in min, RI - Retention index.

ADME properties

The ADME factors, including logKp, GIA, BBB permeability, transporter P-gp binding, and the CYP450 isoforms (CYP1A2, 2C9, 2C19, 2D6 and 3A4) inhibition, were also predicted by SwissADME and obtained results are presented in Table 3. Based on the results, the tested compounds scored logKp values of -0.42 to -5.08 cm/s, unlike that of the standard chloramphenicol (-7.46 cm/s). A molecule is less permeable to skin when the logKp (cm/s) is higher negative [28]. Compounds **2**, **7**, **8**, **9**, **12**, and **14** scored high GIA, which is consistent with the logKp values. Compounds **2**, **7**, **9**, and **12** exhibited blood brain barrier (BBB) permeation, which is fundamental for the distribution of central nerves system-acting molecules. Good absorption and distribution characteristics of pharmacological molecules can be attributed to high gastrointestinal (GI) and blood-brain barrier (BBB) penetration [39]. The obtained ADME

prediction revealed that all the tested major components of the essential oils, except **6** and **8**, were determined to be P-gp negative, and thus don't inhibit of most of the selected cytochromes (CYP). Prediction of cytochromes (CYP) inhibitor interaction indicated that compounds **5**, **6**, and **14** showed non-inhibitory effect against each of the tested cytochromes, similar to that of chloramphenicol.

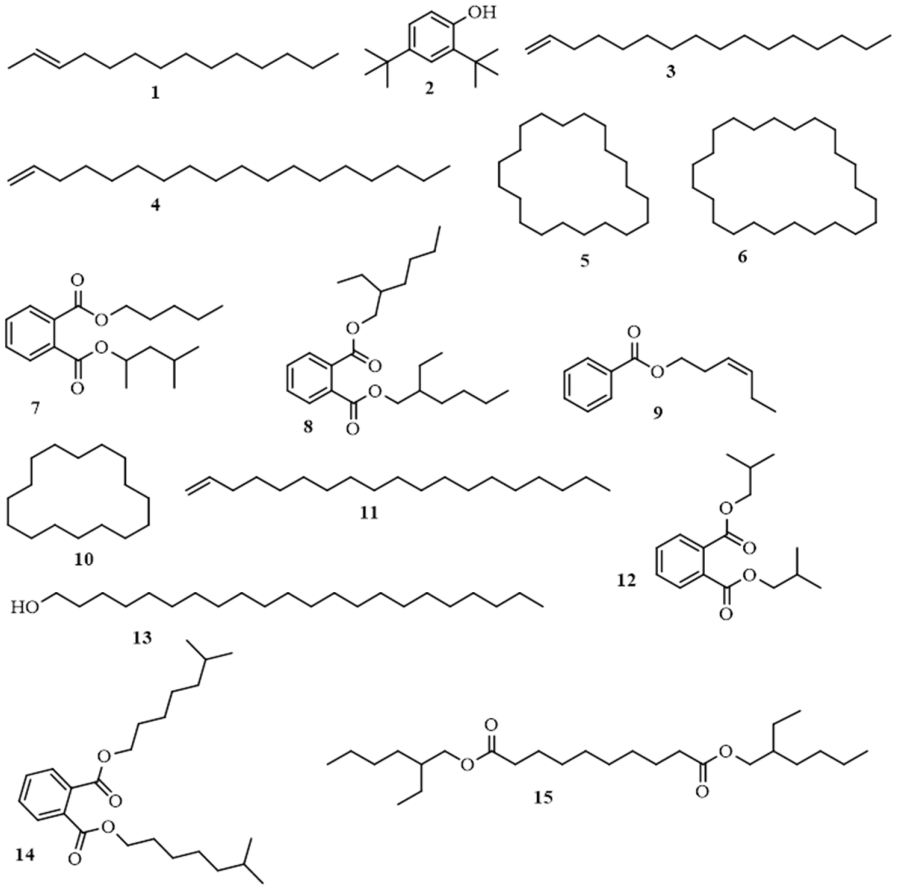

Figure 3. Structures of major constituents of essential oils of leaves of *C. tomentosa* (**1-8**) and *C rotundifolia* (**2**, **5**, **6** and **9-15**).

Toxicity property perdition

The toxicity property of the major components identified in essential oils (**1-15**) was predicted using ProTox II, and presented in Table 4. Based on the result, compounds **3**, **4**, **7**, **11** and **12** scored LD_{50} > 5000 mg/kg, predicting that the compounds are nontoxic when administered orally, and are better relative to the standard chloramphenicol (LD_{50} = 1500 mg/kg). Compounds **1**, **9**, and **15** have been categorized under the toxicity class of 5 (LD_{50} = 5000 mg/kg) but still better than the standard. None of the compounds were predicted to have hepatotoxicity, implying that they have no adverse effects to organs such as liver or kidney. Compounds **1**, **2**, **3**, **4**, **11**, and **13**

demonstrated no carcinogenicity property. All the compounds displayed non-immunotoxicity, mutagenicity, and cytotoxicity properties, indicating no adverse effects on the immune system, no potential for inducing DNA alterations leading to mutations, and typically resulting in no cell death or damage, respectively. The standard drug chloramphenicol was found to be mutagenic unlike the tested compounds. These findings collectively contribute valuable information for assessing the safety and pharmacological profile of the compounds.

Table 3. In-silico drug-likeness and ADME predictions of major compounds from essential oils hydrodistilled from leaves of *C. tomentosa* (**1-8**) and *C. rotundifolia* (**2**, **5**, **6**, **9-15**).

Predicted	Compounds															
Parameter	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**CA**
Drug likeness																
MW (g/mol)	196.4	206.3	224.4	252.5	280.5	336.6	320.4	390.6	204.3	224.4	266.5	278.3	326.6	390.6	426.7	323.1
NHD	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	3
NHA	0	1	0	0	0	0	4	4	2	0	0	4	1	4	4	5
LogP (iLogP)	4.11	3.08	4.61	5.05	4.43	4.97	4.09	4.77	3.04	3.68	5.28	3.31	5.73	5.42	6.36	1.17
Lipinski's RO5	0	0	0	1	0	0	0	0	0	0	1	0	1	1	1	0
NRB	10	2	13	15	0	0	11	16	6	0	16	8	20	16	23	7
TPSA (A°2)	0	20.23	0	0	0	0	52.6	52.6	26.3	0	0	52.6	20.23	52.6	52.6	115.4
Veber's rule	0	0	1	1	0	0	1	1	0	0	1	0	1	1	1	0
ADME																
log Kp cm/s	-1.99	-3.87	-1.31	-0.72	-2.03	-0.83	-4.03	-3.39	-4.68	-3.22	-0.42	-5.08	-0.94	-2.71	-2.77	-7.46
GIA	Low	High	Low	Low	Low	Low	High	High	High	Low	Low	High	Low	High	Low	High
BBB	No	Yes	No	No	No	No	Yes	No	Yes	No	No	Yes	No	No	No	No
P-gp substrate	No	No	No	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No
Inhibitory interaction																
CYP1A2	Yes	No	Yes	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	No	Yes	No
CYP2C19	No	No	No	No	No	No	Yes	No	Yes	No	No	Yes	No	No	No	No
CYP2C9	Yes	No	No	No	No	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No
CYP2D6	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No
CYP3A4	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	Yes	No

Formula: **1**: $C_{14}H_{28}$; **2**: $C_{14}H_{22}O$; **3**: $C_{16}H_{32}$; **4**: $C_{18}H_{36}$; **5**: $C_{20}H_{40}$; **6**: $C_{24}H_{48}$; **7**: $C_{19}H_{28}O_4$; **8**: $C_{24}H_{38}O_4$; **9**: $C_{13}H_{16}O_2$; **10**: $C_{16}H_{32}$; **11**: $C_{19}H_{38}$; **12**: $C_{16}H_{22}O_4$; **13**: $C_{22}H_{46}O$; **14**: $C_{24}H_{38}O_4$; **15**: $C_{26}H_{50}O_4$; **CA**: $C_{11}H_{12}Cl_2N_2O_5$. CA= Chloramphenicol, NHD = Number of hydrogen donor, NHA = Number of hydrogen acceptor, NRB = Number of rotatable bonds, TPSA = total polar surface area, MW = Molecular weight, LogKp = Skin permeation value, G = Gastro-Intestinal, BBB = Blood brain barrier.

Boiled-Egg Model

Based on the Boiled Egg model (Figure 4), compounds **2**, **7**, **9** and **12** appeared in yellow region indicating their capability to permeate brain barrier. Compounds **8** and **14** located in the white region indicating their high probability of passive absorption by the GIT, which is as good as the standard chloramphenicol (CA). Compounds **1**, **3**, **4**, **5**, **8**, **11**, **13**, **14**, and **15** were predicted to have low BBB permeation and GIT absorption probabilities (located outside white or yellow ellipse). All compounds are non-PGP (PGP-), detonating they are not actively pumped into the gastrointestinal lumen.

Table 4. Oral toxicity prediction for major compounds identified in essential oils hydrodistilled from leaves of *C. tomentosa* (**1-8**) and *C. rotundifolia* (**2**, **5**, **6**, **9**, **10-15**).

Compounds	LD_{50} (mg/kg)	Class of toxicty	Organ toxicity	Toxicity end points			
			Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity
1	5000	5	Inactive	Inactive	Inactive	Inactive	Inactive
2	700	4	Inactive	Inactive	Inactive	Inactive	Inactive
3	5050	6	Inactive	Inactive	Inactive	Inactive	Inactive
4	5050	6	Inactive	Inactive	Inactive	Inactive	Inactive
5	750	3	Inactive	Active	Inactive	Inactive	Inactive
6	750	3	Inactive	Active	Inactive	Inactive	Inactive
7	26000	6	Inactive	Active	Inactive	Inactive	Inactive
8	1340	4	Inactive	Active	Inactive	Inactive	Inactive
9	5000	5	Inactive	Active	Inactive	Inactive	Inactive
10	750	3	Inactive	Active	Inactive	Inactive	Inactive
11	5050	6	Inactive	Inactive	Inactive	Inactive	Inactive
12	10000	6	Inactive	Active	Inactive	Inactive	Inactive
13	1000	4	Inactive	Inactive	Inactive	Inactive	Inactive
14	1340	4	Inactive	Active	Inactive	Inactive	Inactive
15	5000	5	Inactive	Active	Inactive	Inactive	Inactive
CA	1500	4	Inactive	Inactive	Inactive	Active	Inactive

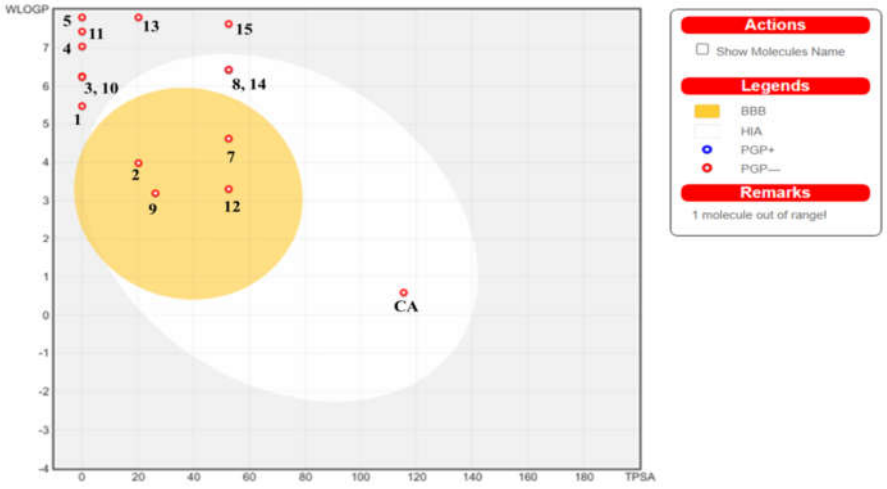

Figure 4. Boiled-Egg overview for brain access and intestinal absorption of major compounds identified from essential oils hydrodistilled from leaves of *C. tomentosa* (**1-8**) and *C. rotundifolia* (**2**, **5**, **6**, **9-15**).

Bioavailability radar

The bioavailability radar visualization assisted in determining the oral bioavailability of the major essential oil compounds. The pink area in the radar represents the optimal zone for each bioavailability property. The result displayed that all the six bioavailability radar properties of compounds **2**, **9**, and **12** positioned in the pink colored region indicating their optimum bioavailability, comparable to the standard chloramphenicol (Figure 5). All of the compounds possess acceptable size, polarity, and unsaturation properties.

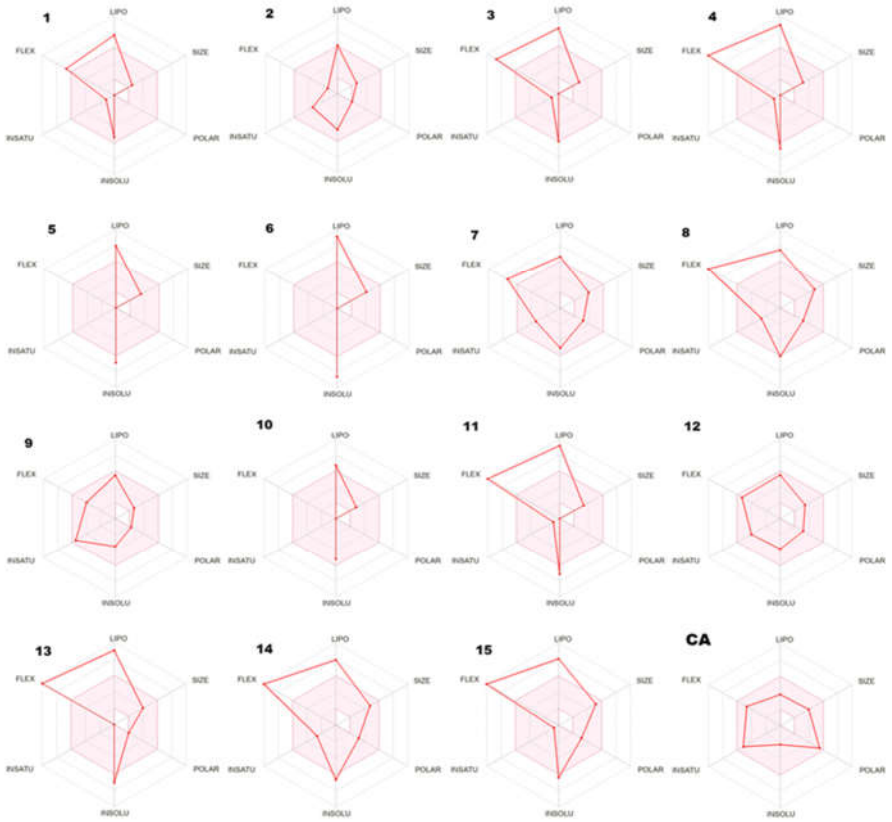

Figure 5. Bioavailability radar of major compounds of the essential oils hydrodistilled from leaves of *C. tomentosa* (**1-8**) and *C. rotundifolia* (**2**, **5**, **6**, **9**, **10-15**).

Antibacterial activity

The in-vitro bacterial growth inhibitions of essential oil and crude extracts from the leaves of *C. tomentosa* and *C. rotundifolia* were tested against *E. coli*, *S. aureus*, and *P. aeruginosa*. The measured mean inhibition zone diameters (in mm) are presented in Table 5. The essential oils and extracts of leaves of *C. tomentosa* were found to cause growth inhibition in a dose dependent manner against *E. coli* and *P. aeruginosa*.

The essential oils hydro-distilled from leaves of *C. tomentosa* inhibited the growth of *E. coli* and *P. aeruginosa* at all tested concentrations, while *S. aureus* inhibited at 1000 µg/mL. At 50 µg/mL, the essential oil collected from leaves of *C. tomentosa* demonstrated superior growth inhibition against *E. coli* with an inhibition zone of 10±0.0 mm, followed by the inhibition against *P. aeruginosa* (9.0±0.25 mm). In this study, the essential oil hydro-distilled from *C. tomentosa* effectively inhibited the growth of gram-negative bacteria (*E. coli* and *P. aeruginosa*) but demonstrated limited activity against the gram-positive *S. aureus* which primarily be attributed to the hydrophobic nature of the essential oil composition. For the extracts, at concentration of 50 µg/mL, the MeOH extract of *C. tomentosa* showed the highest growth inhibition effect against *E.*

coli with a zone of 9.85 ± 0.14 mm, followed by the DCM/MeOH (1:1) extract, which exhibited an inhibition zone of 8.65 ± 0.08 mm. The result generally indicated that the n-hexane, DCM:MeOH and MeOH extracts showed a noticeably lower activity (7.3 ± 0.04, 8.6 ± 0.08, 9.8 ± 0.14 mm, respectively) compared with the standard chloramphenicol (at 30 µg/disc) against the same strain. Whereas against *P. aeruginosa*, the n-hexane extract scored the highest inhibition (8.1 ± 0.19 mm) at 50 µg/mL. Here it is important to note that the n-hexane, DCM:MeOH and MeOH extracts showed more or/equal activity (8.1 ± 0.19, 6.6 ± 0.12, and 7.9 ± 0.05 mm, respectively) with the chloramphenicol at 30 µg/disc (6.9 ± 0.517 mm) against the same bacterium. According to the present findings, the growth inhibition by the essential oil is superior to that of the tested extracts. The extracts were found to be less effective against the gram-positive bacterium *S. aureus*. Up to the completion of this study report, no scientific reports were found on the antibacterial activity of essential oil extracted from *C. tomentosa*. Whereas studies on the ethanol extract from *C. tomentosa* reported to inhibit bacterial growth at 1000 mg/mL and 500 mg/mL, while the hexane extract showed no sensitivity, unlike in this report [40]. In another study, extracts from the aerial parts of *Capparis tomentosa* showed stronger in vitro antibacterial activity than ampicillin against *S. aureus* [5].

Table 5. Bacterial growth inhibition zone (mean ± SD, in mm) of extracts of leaves of *C. tomentosa* and *C. rotundifolia* against *E. coli*, *S. aureus*, and *P. aeruginosa* bacterial strains.

Bacterial strains	Extract conc. (µg/mL)	*C. tomentosa*				*C. rotundifolia*				CA (30 µg/disc
		n-hexane	DCM: MeOH	MeOH	EO	*n*-Hexane	DCM: MeOH	MeOH	EO	
E. coli	50	7.3±0.04	8.6±0.08	9.8±0.14	10±0.0	7.0±0.07	7.3±0.15	8.0±0.31	7.5±0.05	24.8±0.59
	100	8.8±0.08	9.3 ± 0.15	10.0±0.13	11.2±0.25	7.1±0.01	7.7±0.1	8.5±0.05	8.25±0.0	
	300	9.2±.35	9.4 ± 0.5	11.0±0.47	11.8±0.05	7.3±0.1	7.9±0.34	8.8±0.1	9.5±0.5	
	500	9.8±0.11	10.4 ± 0.19	12.7±0.16	12±0.05	8.0±0.02	8.3±0.19	7.9±0.15	10±0.25	
	1000	11.5± 0.03	13.8± 0.05	14.5±0.49	13±0.15	9.9±0.05	10.5±0.02	9.9±0.3	12.5±1	
S. aureus	50	NA	NA	NA	NA	NA	NA	NA	NA	19.4±0.74
	100	NA	NA	NA	NA	NA	NA	NA	6.5.0	
	300	NA	NA	NA	NA	7.0±0.07	6.7±0.25	NA	8.5	
	500	NA	NA	NA	NA	8.0±0.2	7.7±0.6	6.9±0.1	9±0.1	
	1000	NA	NA	NA	7±0.0	9.7±0.55	8.5±0.25	7.9±0.1	10±0.5	
P. aeruginosa	50	8.1±0.19	6.6±0.12	7.9±0.05	9.0±0.25	8.1±0.17	7.1±0.1	7.4±0.03	8±0.5	6.9±0.51
	100	9.6±0.12	6.8±0.05	8.5±0.01	9..5±0.5	9.6±0.14	8.0±0.12	7.3±0.17	8.5±0.05	
	300	9.9±0.37	7.1±0.1	8.6±0.01	10±0.5	10.1±0.16	9.4±0.1	7.9±0.1	10±0.5	
	500	11.6±0.41	7.5±0.02	8.8±0.05	11.9±0.0	11.2±0.10	10.8±0.07	9.3±0.43	13. 5±1	
	1000	12.5±0.05	7.7±0.06	8.9±0.05	13.2±0.5	13.1±0.21	12.2±0.35	10.1±0.4	14.5±0.25	

CA = Chloramphenicol, NA = not available, EO = essential oil.

The essential oil, n-hexane, DCM:MeOH and MeOH leaf extracts of *C. rotudofolia* were found to be active at all tested concentrations against *E. coli* and *P. aeruginosa* in a dose dependent manner. At 50 µg/mL concentration of the essential oil hydro-distilled from *C. rotundifolia* was more active against *P. aeruginosa* (8±0.5 mm), which is notable compared to the standard drug chloramphenicol (6.9±0.51 mm). Among the extracts, the n-hexane and MeOH extracts scored highest inhibition diameters against *P. aeruginosa* (8.1±0.17 mm), and *E. coli* (8.0±0.31 mm), respectively, concentration of 50 µg/mL. Generally, the result noted that n-hexane, DCM/MeOH (1:1), and MeOH extracts of *C. rotundifolia* scored better inhibition zone (8.1 ± 0.17, 7.1 ± 0.1, and 7.4 ± 0.03 mm, respectively) than the standard (6.9±0.517 mm) towards P. aeruginosa. Against the Gram positive *S. aurues* bacterium, n-hexane extract showed better activity (7.0 ± 0.07 mm) relative to the remaining two extracts. The essential oil of *C. rotundifolia* demonstrated greater efficacy compared to the extracts (n-hexane, DCM/MeOH, and MeOH). Previous studies

on *C. rotundifolia* extracts showed that the methanol extract inhibited *E. coli* and *P. aeruginosa*, but not *S. aureus*, which is in good agreement with the findings of this study [41].

CONCLUSION

In this study, the GC-MS analysis of essential oils hydro-distilled from leaves of *C. tomentosa* and *C. rotundifolia* plants revealed the presence of 25 (89.7%) and 23 (95.47%) volatile compounds, respectively. The major compounds (1-15) fulfilled the Lipinski's rule of five and Veber's rule, with ADME and toxicity properties showing their favorable oral pharmacokinetic properties. The essential oil hydro-distilled from *C. tomentosa* exhibited *in vitro* antibacterial activity which is higher against *E. coli* followed by *P. aeruginosa*, although it displayed no inhibition zone against *S. aureus* except at the highest concentration. The hydrophobic nature of the essential oil may have contributed to its limited effectiveness against *S. aureus*. The n-hexane, DCM, and MeOH extracts of *C. tomentosa* demonstrated growth inhibition against *E. coli* and *P. aeruginosa*, but showed no activity against *S. aureus*. The essential oil of *C. rotundifolia* demonstrated significant efficacy against both *E. coli* and *P. aeruginosa*, showing stronger inhibition against *P. aeruginosa* (8 ± 0.5 mm, 50 µg/mL) compared to chloramphenicol. The n-hexane extract of *C. rotundifolia* showed better activity against *S. aureus* (7.0 ± 0.07 mm) compared to DCM:MeOH and MeOH extracts. In this study, the extracts of *C. tomentosa* leaves exhibited less activity against *S. aureus*, whereas for *C. rotundifolia* leaves extracts susceptibility was observed at higher concentrations. The findings from SwissADME/T provide valuable insights for evaluating the safety and pharmacological profile of the major compounds of the essential oils. The demonstrated antibacterial activities suggest potential capacity of the studied plants for developing novel antibacterial agents. This study offers compelling evidence supporting the claimed traditional medicinal use of *C. tomentosa* and *C. rotundifolia* leaves. It is recommended to isolate and characterize bioactive compounds from the most potent extracts to identify the constituents responsible for antibacterial activity and explore their therapeutic potential.

ACKNOWLEDGMENTS

Adama Science and Technology University is thankfully acknowledged for funding this research with grant number: ASTU/AS-R/003/2020. We also thankfully acknowledge TWAS and UNESCO for financing this research with funds allocated to AD (TWAS Research Grant RGA No. 20-274 RG/CHE/AF/AC-G - FR3240314163). The Basic Science Research Programme through the National Research Foundation of Korea (NRF), funded by the Ministry of Education (NRF-2018R1A6A1A03024862) provided us fund for the work.

Authors input

AD and ME designed the research, data analysis and critical review of the manuscript. TD carried out the experimental work and drafted the manuscript. TD conducted SwissADME and Protox II studies, TB and CJ conducted the GC-MS analysis. TD, AD and ME organized the manuscript, and also revised it. All authors go through and verified the final manuscript.

Funding

This work was partly supported by National Research Foundation of Korea (NRF-2018R1A6A1A03024862), Adama Science and Technology research grant (ASTU/AS-R/003/2020), TWAS and UNESCO (RGA No. 20-274 RG/CHE/AF/AC-G - FR3240314163).

Availability of data

All data generated or analyzed during this study are included in the article

Declarations

Ethics approval and consent to participate

Not applicable

Conflict of interests

The authors declare no conflict of interests.

REFERENCES

1. Singh, P.; Mishra, G.; Sangeeta, S.; Jha, K.K.; Khosa, R.L. Traditional uses, phytochemistry and pharmacological properties of *Capparis decidua*: An overview. *Der Pharm Lett*. **2011**, 3, 71-82.
2. Demissew, S. Studies a study of the vegetation and floristic composition of Southern Wällo, Ethiopia. *J. Ethiop. Stud.* **2019**, 31, 159-192.
3. Gull, T.; Anwar, F.; Sultana, B.; Alcayde, M.A.C.; Nouman, W. Capparis species: A potential source of bioactives and high-value components: A review. *Ind. Crops Prod*. **2015,** 67, 81-96.
4. Alelign, N.; Giday, M.; Teklehaymanot, T.; Animut, A. Ethnobotanical survey of antimalarial plants in Awash-Fentale District of Afar Region of Ethiopia and in vivo evaluation of selected ones against *Plasmodium berghei*. *Asian Pac. J. Trop. Biomed*. **2018**, 8, 73-78.
5. Aweke, G.; *Capparis tomentosa (PROTA)/Medicinal plants*, PROTA, Wageningen: Netherlands; 2018; *Prota* **2013**, 11, 1-6.
6. Orwa, C.; Mutua, A.; Kindt, R.; Jamnadass, R.; Anthony, S. *Agroforestre Database: A Tree Reference and Selection Guide Version 4.0*, **2009**. Available at: http://www.worldagroforestry.org/sites/treedbs/treedatabases.asp.
7. Chinsembu, K.C.; Syakalima, M.; Semenya, S.S.; Ethnomedicinal plants used by traditional healers in the management of HIV/AIDS opportunistic diseases in Lusaka, Zambia. *South African J. Bot*. **2018**, 122, 369-384.
8. Steenkamp, V.; Traditional herbal remedies used by South African women for gynaecological complaints. *J. Ethnopharmacol*. **2003,** 86, 97-108.
9. Ajao, A.A.; Sibiya, N.P.; Moteetee, A.N.; Sexual prowess from nature: A systematic review of medicinal plants used as aphrodisiacs and sexual dysfunction in sub-Saharan Africa. *South African J. Bot*. **2018**,122, 1-16.
10. Graham, J.G.; Quinn, M.L.; Fabricant, D.S.; Farnsworth, N. R. Plants used against cancer – an extension of the work of Jonathan Hartwell. *J. Ethnopharmacol*. **2000,** 73, 347-77.
11. Wangai, L.N.; Waithera. B.W.; Geoffrey, M. K; Koimburi, N.B.; Ndura, P.K.; Gitau, M.K.; Karanja, R.; Kirira, P. Investigation of the *in vitro* antioxidant activity , *in vivo* antidiabetic efficacy and safety of *Capparis tomentosa* aqueous roots extracts in male alloxanized mice. *J. Med. Plants Stud*. **2015**, 3, 42-47.
12. Teklehaymanot, T.; Giday, M. Ethnobotanical study of medicinal plants used by people in Zegie Peninsula, Northwestern Ethiopia. *J. Ethnobiol. Ethnomed*. **2007**, 11, 1-11.
13. Kefalew, A.; Asfaw, Z.; Kelbessa, E. Ethnobotany of medicinal plants in Ada'a district, East Shewa zone of Oromia regional state, Ethiopia. *J. Ethnobiol. Ethnomed*. **2015**, 11, 1-18.

14. Wondimu, T.; Asfaw, Z.; Kelbessa, E. Ethnobotanical study of medicinal plants around 'Dheeraa' town, Arsi zone, Ethiopia. *J. Ethnopharmacol*. **2007**, 112, 152-561.
15. Belayneh, A.; Bussa, N.F. Ethno-medicinal plants used to treat human ailments in the prehistoric place of Harla and Dengego valleys, Eastern Ethiopia. *J. Ethnobiol. Ethnomed*. **2014,** 10, 1-18.
16. Teklehaymanot, T.; Giday, M.; Medhin, G.; Mekonnen, Y. Knowledge and use of medicinal plants by people around Debre Libanos monastery in Ethiopia. *J. Ethnopharmacol*. **2007**, 111, 271-283.
17. Amusan, O.G.; Sukati, N.; Dlamini, P.S.; Sibandze, F.G. Some swazi phytomedicines and their constituents. *Afr. J. Biotechnol*. **2007**, 6, 267-272.
18. Teklehaymanot, T.; Giday, M. Quantitative ethnobotany of medicinal plants used by Kara and Kwego semi-pastoralist people in lower Omo river valley, Debub Omo zone, Ethiopia. *J. Ethnopharmacol*. **2010**, 130, 76–84.
19. PROTA4U. *Cadaba rotundifolia* Forssk. *PROTA4U*. **2019**. Available at: https://www.prota4u.org/database/protav8.asp.
20. Dagne, E. *Natural Products Database for Africa (NDA)*, **2016**, Version 2.0. Available at: http://www.alnapnetwork.com/SpeciesDetail.aspx.
21. Hassan, A.A.; Merito, A.; Hassan, S.; Aboubaker, D.; Djama, M.; Asfaw, Z.; Kelbessa, E. Medicinal plants and their uses by the people in the region of randa, Djibouti. *J. Ethnopharmacol*. **2013**, 148, 701-13.
22. Teklehaymanot, T. An ethnobotanical survey of medicinal and edible plants of Yalo woreda in Afar regional state, Ethiopia. *J. Ethnobiol. Ethnomed*. **2017**, 13, 1-25.
23. Al-hamoud, G.A.; Orfali, R.S.; Sugimoto, S.; Yamano, Y.; Alothyqi, N.; Alzahrani, A.M.; Matsunami, K. Four new flavonoids isolated from the aerial parts. *Molecules* **2019**, 24, 1-13.
24. Assefa, T.; Tesso, H.; Abdisa, E.; Guta, L.; Melaku, Y. Chemical composition and antibacterial activity of essential oils from selected species of the *Genus Cucumis* in Ethiopia. *Bull. Chem. Soc. Ethiop.* **2023**. 37, 703-715.
25. Gebrehiwot, H.; Dekebo, A.; Shenkute, K.; Ensermu, U.; Endale, M. Chemical composition, antibacterial and antioxidant activities of essential oils from *Cyphostemma Adenocaule* and *Ziziphus Spinachristi*. *Bull. Chem. Soc. Ethiop.* **2024,** 38, 167-186.
26. Bousbia, N.; Abert, M.; Ferhat, M.A.; Petitcolas, E.; Meklati, B.Y.; Chemat, F. Comparison of two isolation methods for essential oil from *Rosemary leaves*: Hydrodistillation and microwave hydrodiffusion and gravity. *Food Chem.* **2009**, 114, 355-362.
27. Linstrom, P.J.; Mallard, W.G. The NIST chemistry webbook: A chemical data resource on the internet. *J. Chem. Eng. Data* **2011**, 46, 1059-1063.
28. Daina, A.; Michielin, O.; Zoete, V. SwissADME: A free web tool to evaluate pharmacokinetics, drug- likeness and medicinal chemistry friendliness of small molecules. *Nat. Publ. Gr*. **2017**, 7, 1-13.
29. Banerjee, P.; Eckert, A.O.; Schrey, A.K.; Preissner, R. ProTox-II: A webserver for the prediction of toxicity of chemicals. *Nucleic Acids Res*. **2018**, 46, W257- W63.
30. Lipinski, C.A.; Lambardo, F. Dominy B.W.; Feeney, P.J. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Acta Petrol. Sin*. **1997**, 28, 1765-84.
31. Veber, D.F.; Johnson, S.R.; Cheng, H.Y.; Smith, B.R.;, Ward, K.W.; Kopple, K.D. Molecular properties that influence the oral bioavailability of drug candidates. *J. Med. Chem*. **2002**, 45, 2615-2623.
32. Degfie, T.; Endale, M.; Tafese, T.; Dekebo, A.; Shenkute, K. *In vitro* antibacterial, antioxidant activities, molecular docking, and ADMET analysis of phytochemicals from roots of *Hydnora johannis*. *Appl. Biol. Chem*. **2022**, 65, 1-13.
33. Daina, A.; Zoete, V. A Boiled-Egg: To predict gastrointestinal absorption and brain penetration of small molecules. *ChemMedChem*. **2016**, 11, 1117-1121.

34. Balouiri, M.; Sadiki, M.; Ibnsouda, S.K. Methods for *in vitro* evaluating antimicrobial activity: A review. *J. Pharm. Anal*. **2016**, 6, 71-79.
35. Mwangi, J.K.; Ndung, M,; Gitu, L. Repellent activity of the essential oil from *Capparis tomentosa* against maize weevil *Sitophilus zeamais*. *J. Resour. Dev. Manag*. **2013**, 1, 9-13.
36. Muhaidat, R.; Al-qudah, M.A.; Al-shayeb, A.; Jacob, J.H.; Al-jaber, H.I.; Hussein, E.; Al-Tarawneh, I.N.; Abu, O.S.T. Chemical profile and antibacterial activity of crude fractions and essential oils of *Capparis ovata* Desf. and *Capparis spinosa* L. (Capparaceae). *Int. J. Integr. Boil.* **2013**, 14, 39-47.
37. Linstrom, P.; Mallard, W. The NIST chemistry webbook: A chemical data resource on the internet. *J. Chem. Eng. Data* **2001**, 46, 1059-1063.
38. Velmurugan, P.; Kamaraj, M.; Prema, D. Phytochemical constituents of *Cadaba. trifoliata* Roxb. root extract. *Int. J. Phytomed*. **2010**, 2, 379-384.
39. Anza, M.; Endale, M.; Eswaramoorthy, R.; Cabedo, N. Cytotoxicity, antimicrobial activity, molecular docking, drug likeness and DFT analysis of benzo phenanthridine alkaloids from roots of *Zanthoxylum chalybeum*. *Biointerface Res. Appl. Chem*. **2021**, 12, 1569-86.
40. Mag, P.; Sama, W.; Ajaiyeoba, E.O. Phytochemical and antimicrobial studies of *Capparis thonningii* and *Capparis tomemtosa*. *Pharmacogn. Mag.* **2006**, 2, 117-122.
41. Alothyqi, N.; Almalki, M.; Albqa'ai, M.; Alsamiri, H.; Alrashdi, S.M.; Ibraheem, O.G. *In vitro* antibacterial activity of four Saudi medicinal plants. *J. Microb. Biochem. Technol*. **2016**, 8, 83-89.