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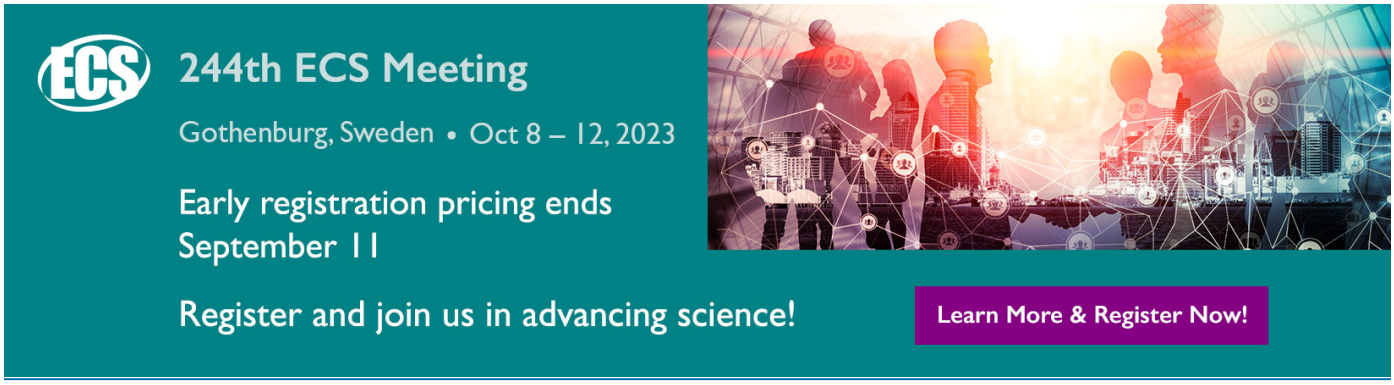

Antibacterial Efficacy and Molecular Docking of Leaf Extract of *Laurus nobilis L* Against some Isolated Pathogenic UTI Bacteria

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Abstract. The objective of the current study was to analyze the chemical compositions and antibacterial properties of *Laurus nobilis*. The bacterial strain was isolated from urine sample of female patients have urinary tract infection in Al-Basrah Teaching Hospital. Two solvents (hot and cold aqueous and ethanol) were used to extract the dried leaves of *L. nobilis*. While there were differences in the inhibition zones that solvent extracts demonstrated against bacterial pathogens, all of them significantly inhibited pathogens. The diameters of the inhibition zones on *Staphylococcus aureus* where the alcoholic extract was in the range of 17-29 mm, 22-28 mm for hot water and 12-14 mm for cold aqueous extract. The diameters of the inhibition zones on *Klebsiella pneumoniae* for alcoholic extract were 18-20 mm, 19-21.5 mm for hot aqueous extract and 12-17 mm for cold water extract. The GC-MS analysis demonstrated the presence of different phytochemical compounds in the extract of Laurus nobilis. A total of 60 compounds were identified, for ethanolic extract, tris (2-methylenecyclopropyl)methanol, (3aS,6aR,9aR,9bS)-3,6,9-trimethylenedecahydroazuleno[4,5-b]furan-2(3H)-one and (3aS,6aR,9aR,9bS)-6-methyl-3,9-dimethylene-3a,4,6a,7,8,9,9a,9b-octahydroazuleno[4,5-b]furan-2(3H)-one were the major compounds with percentage values 9.64%, 8.86% and 7.43%, respectively. For hot water extract, the major three compounds were 5-(hydroxymethyl)furan-2-carbaldehyde 11.64%, 2-methyl-5-nitro-2H-1,2,3-triazol-4-amine 8.39% and tris(2-methylenecyclopropyl)methanol 6.81%. Whereas, for cold water extract, the major compounds were n-Hexadecanoic acid 26.05%, Bis(2-ethylhexyl) phthalate 22.94% and Octadecanoic acid 8.25%. Molecular docking showed that these nine major compounds had an excellent binding affinity -4.25 to -8.56 kcal/mol against *S. aureus* using protein 1JIJ. The binding affinity of these compounds against *K. pneumoniae* (protein 6PIB) were in the range -4.03 to -8.22 kcal/mol.

Keywords. Plant extract, Antibacterial activity, Molecular docking, GC-MS instrument, Phytochemical analysis.

1. Introduction

A variety of biological activity, including antibacterial, anti-inflammatory, and antioxidant ones, have been identified for extracts extracted from medicinal plants [1]. The antimicrobial compounds from

medicinal plants may inhibit the growth of bacteria, fungi, viruses, and protozoa by different mechanisms than those of currently used antimicrobials, and they may have significant clinical value in the treatment of microbial strains that are resistant to antimicrobials [2]. While not functioning as antibiotics by themselves, several of those active compounds exhibit both intrinsic antibacterial activity and antibiotic resistance-modifying capabilities. When combined with other antibiotics, some of these compounds can aid in the reduction of bacterial antibiotic resistance. Chemically complex substances offer excellent therapeutic potential since they are less likely to cause side effects than synthesized medications and are also more unlikely to cause resistance [3-5]. Additionally, the synergistic interaction between the active chemicals in the extracts is a factor in how well medicinal plant extracts limit bacterial growth. A wide range of chemical compounds present in medicinal plants have been shown to have antibacterial activity in vitro [6,7].

In recent years, the main applications of gas chromatography-mass spectrometry (GC-MS) have been to detect functional groups and identify a variety of bioactive therapeutic phytocompounds found in medicinal plants [8,9]. Alkaloids, nitro compounds, asters, alcohols, organic acids, steroids, long-chain hydrocarbons, and amino acids are just a few of the substances that can be found using the most efficient, quick, and accurate method, GC-MS, which also uses a little quantity of plant extracts [10].

Computer-aided drug discovery methods have developed as more advanced technologies that can be used to search for drugs made from phytochemicals found in a number of therapeutic plants. For technological and pharmaceutical research, computational prediction models play a crucial role in directing approach choice [11]. Currently, molecular docking is a successful and economical method for creating and evaluating medications. Additionally, by non-covalently introducing a molecule into a target macromolecule's binding site, this method makes systemic investigation easier. This particular binding occurs at each ligand's active site [12–14].

In this regard, the phytochemical components present in the *Laurus nobilis* plant were detected and identified using the GC-MS method in the current study. Three different crude extracts (ethanolic, hot and cold water) were used with different concentration to evaluate the antibacterial activity against pathogenic *Staphylococcus aureus* and *Klebsiella pneumoniae* isolated from urine of female patients with UTI disease. Finally, the molecular docking of the major three compounds identified in three extracted media was studied using MOE software on proteins ID: 1JIJ and 6PIB.

2. Experimental Part

2.1. Materials and Reagents

None of the chemicals used in this experiment were further purified; instead, they were all of the reagent grade. They came from Sigma-Aldrich.

2.2. Collection and Identification of Plant Materials

Bay laurel leaves (*Laurus nobilis L*) were exported from Latakia city (Syria). The leaves were divided into smaller pieces and rinsed in distilled water after first being washed in tap water. Then, at room temperature, the clean parts were dried. The dried leaves were then put to a home grinder for processing. The extraction process used the powder.

2.3. Preparation of the Plant Extracts

Using a magnetic starrier, 250 mL of cold water was used to extract 25 g of powdered laurus nobilis leaf for 48 hours at room temperature. In contrast, the Soxhlet device was employed to extract the plant using hot water and ethanol as solvents. The laurus nobilis solutions were concentrated under decreased pressure using a rotary evaporator at 50°C after the supernatant was filtered through Whatman filter paper. The unprocessed extracts were gathered and allowed to air dry [15].

2.4. Primarily Phytochemical Screening

The phytochemical components of *laurus nobilis* leaves extract were identified using conventional extraction and screening techniques.

2.4.1. Tannins Test
To determine the content of tannins, 500 mg of the crude extract of laurus nobilis leaf was mixed with 10 mL of distilled water before being filtered. As a confirmatory tannin test, the addition of FeCl3 to the filtrate caused the production of a blue, blue-black, green, or blue-green color [16,17].

2.4.2. Flavonoids Test, Shinoda Test
When a small amount of magnesium was added, followed by the dropwise addition of concentrated hydrochloric acid, a few pink scarlet, crimson red, or occasionally green to blue color appearances developed that were thought to indicate the presence of flavonoids [16,17].

2.4.3. Phenolic Compounds Test, $FeCl_3$ Test
Add a few drops of a 10% ferric chloride solution to 1 ml of the filtered plant extract sample. The presence of phenolic compounds is indicated by the appearance of green, blue, or violet color [16,17].

2.4.4. Saponins Test
To verify the presence of saponins, 500 mg of the crude extract were shook with water in a test tube. The presence of saponin was confirmed by the production of froth that endures heating [16,17].

2.5. Gas Chromatography-Mass Spectrometry (GC–MS) Analysis
The Perkin-Elmer Clarus 680 system (Perkin-Elmer, Inc. U.S.A.) equipped with a fused silica column, packed with Elite-5MS) capillary column (30 m in length, 250 m in diameter, and 0.25 m in thickness) was used to conduct GC-MS studies of leaf extracts. The carrier gas was employed, which had a purity of 99.99 percent, at a constant flow rate of 1 mL/min. An electron ionization energy approach with a high ionization energy of 70 eV (electron Volts), 0.2 s of scan duration, and fragments spanning from 40 to 600 m/z was selected for GC-MS spectrum detection. The injector temperature was kept at 250 °C, and the injection quantity was 1 L (split ratio: 10:1). (constant). The column oven's temperature was initially set at 50 °C for three minutes, then increased by 10 °C per minute up to 280 °C before being elevated to 300 °C for ten minutes. Based on a comparison of the retention time (min), peak area, peak height, and mass spectral patterns of the test samples with the spectral databases of real compounds kept in the National Institute of Standards and Technology (NIST) library, the phytochemicals present in the samples were identified.

2.6. Isolation and Identification of Bacteria
In this investigation, urine samples from female patients with urinary tract infections were collected. *Staphylococcus aureus* and *Klebsiella pneumonia* were isolated using culture media (Mannitol salt agar and MacConkey agar) and identified biochemically and by vitek2 compact auto analyzer system, and the bacteria were then incubated at 37°C for 24 hours. The isolates were maintained in nutrient agar slants at 4°C for antibacterial study [18].

2.7. Antibacterial Activity Test
Antibacterial activity was assessed by agar well diffusion method of Kirby Bauer where in nutrient agar plates were prepared and spread with 20 ul of the available pathogenic cultures. Wells of 5 mm diameter were bored using sterile borer. Wells were loaded with antimicrobial , (DMSO) and distilled water as control.
An agar well diffusion test was used to assess the antibacterial activity of alcohol, cold, and hot extracts of Laurus nobilis. The extract concentrations used were 1000, 500, 250, and 125 mg/mL DMSO. After that, all of the plates were incubated for 24 hours at 35 2 ^{o}C. The inhibition zone against an isolated bacterial strain was measured in millimeters to test the extracts' antibacterial activity [19, 20].

2.8. Molecular Docking Studies
Molecular docking of the five first major compounds of the three different extract was performed using MOE 2015 v10 and all water and ligand molecules were removed. Crystal structure of

Staphylococcus aureus (protein ID: 1JIJ) and *Klebsiella pneumonia* (proteins ID: 6PIB) was obtained from RCSB protein data bank.

3. Results and Discussion

3.1. Preliminary Phytochemical Screening

The phytochemical detection of the aqueous extracts (cold and hot) and alcoholic extract of bay laurel leaves showed the presence of tannins, phenols, and saponins, as well as flavonoids clearly appeared in the alcoholic extract and cold aqueous extract, while it did not appear in the hot aqueous. The pH of the three types of extracts was determined, as shown in Table 1.

Table 1. Phytochemical prescreening of extracts from bay laurel leaves. The symbols "+" and "-" stand for "present" and "absent," respectively.

Phytochemicals	Cold Water	Hot water	Ethanol
Flavonoids	+	-	+
Tannins	+	+	+
Saponins	+	+	+
Phenols	+	+	+
pH	3.6	5.2	4.6

3.2. GC–MS Analysis

The GC-MS chromatogram of bay laurel leaf extracts in aqueous (hot and cold) and ethanol revealed a total of 60 peaks that were identified as the bioactive compounds by comparing their peak retention time, peak area (percent), peak height (percent), and mass spectral fragmentation patterns to those of the well-known compounds listed in the NIST library.

Tables 2-4 shows the GC-MS results for the three different extracted media according to the identified compounds with decreasing sort of peak area percentage. Results revealed that compounds 1e, 2a and 3c were identified in the three extracted media, whereas, the compounds 1d and 3j were identified in cold and hot water, respectively. Another view, the isolation showed that there are many bioactive compounds such fatty acids with good concentrations such as 1a, 1c, 1h and 2f, vitamin E (2j) and heterocyclic compounds as 1g, 2b, 2c, 2d, 2g, 2l, 3b, 3d, 3e, 3g, 3h, 3i and 3n, as shown in Tables 2-4.

The following are the three major phytoconstituents and their peak area percentages in the cold-water leaf extract of bay laurel: n-Hexadecanoic acid (26.0592%), Bis(2-ethylhexyl) phthalate (22.9483%) and Octadecanoic acid (8.2588%), as shown in Table 2 and Figure 1. The ethanol extract gave many phytoconstituents, the three major bioactive compounds were: Methanol, tris(methylenecyclopropyl)- (9.6424%), Azuleno[4,5-b]furan-2(3H)-one, decahydro-3,6,9-tris(methylene)-, [3aS-(3a.alpha.,6a.alpha.,9a.alpha.,9b.beta.)]-, (8.8636%) and Azuleno[4,5-b]furan-2(3H)-one, 3a,4,6a,7,8,9,9a,9b-octahydro-6-methyl-3,9-bis(methylene)-, [3aS-(3a.alpha.,6a.alpha.,9a.alpha.,9b.beta.)]- (7.4323%). On the other hand, hot-water extract showed many phytoconstituents, the first three were: 5-Hydroxymethylfurfural (11.6419%), 2H-1,2,3-Triazol-4-amine, 2-methyl-5-nitro- (8.3914%) and Methanol, tris(methylenecyclopropyl)- (6.8122%).

Table 2. Phytochemical compounds identified in the cold-water of bay laurel leaf extract using GC-MS. CAS chemical abstract service.

No.	CAS	Name of the compound	Molecular formula	Molecular weight	Peak area (%)	RT (min)
1a	000057-10-3	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256.43	26.0592	22.3481
1b	000117-81-7	Bis(2-ethylhexyl) phthalate	$C_{24}H_{38}O_4$	390.56	22.9483	27.3633
1c	000057-11-4	Octadecanoic acid	$C_{18}H_{36}O_2$	284.48	8.2588	24.1845
1d	023074-10-4	5-Ethyl-2-furaldehyde	$C_7H_8O_2$	124.14	3.1158	20.5485
1e	1000152-74-7	Methanol, tris(methylenecyclopropyl) -	$C_{13}H_{16}O$	188.27	3.0969	24.7451

No.	CAS	Name of the compound	Molecular formula	Molecular weight	Peak area (%)	RT (min)
1f	1000383-17-7	Carbonic acid, but-3-yn-1-yl undecyl ester	$C_{16}H_{28}O_3$	268.4	3.0586	17.355
1g	000591-11-7	2(5H)-Furanone, 5-methyl-	$C_5H_6O_2$	98.1	2.8985	8.4014
1h	001851-90-7	2-Decenoic acid	$C_{10}H_{18}O_2$	170.25	1.8121	22.0973

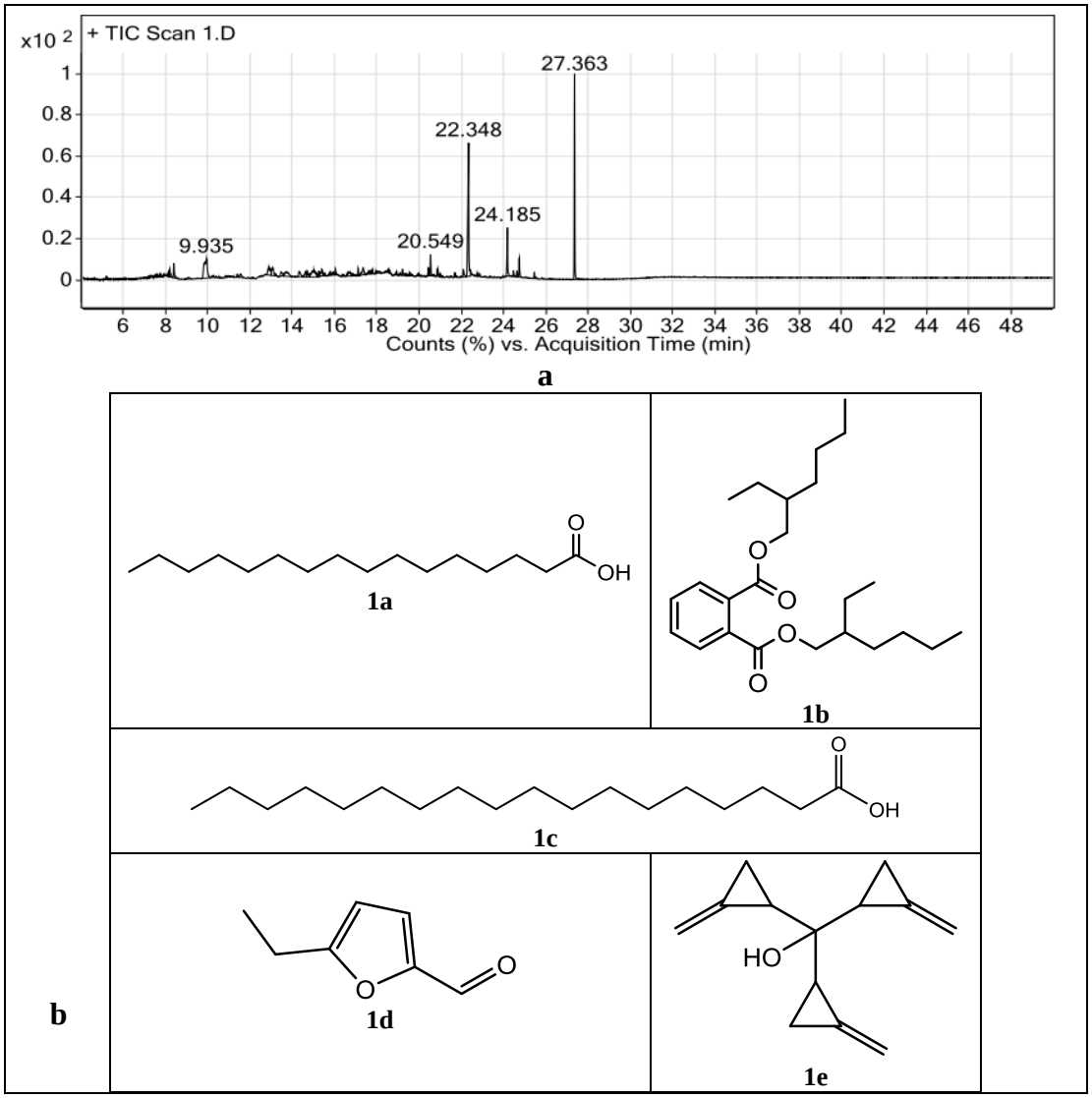


Figure 1. (a) GC-MS chromatogram of cold-water leaf extract of bay laurel. (b) Chemical structures of the first three phytocompounds.

Table 3. Phytochemical compounds identified in the ethanol of bay laurel leaf extract using GC-MS. CAS chemical abstract service.

No.	CAS	Name of the compound	Molecular formula	Molecular weight	Peak area (%)	RT (min)
2a	1000152-74-7	Methanol, tris(methylenecyclopropyl)-	$C_{13}H_{16}O$	188.27	9.6424	24.8114
2b	000477-43-0	Azuleno[4,5-b]furan-2(3H)-one, decahydro-3,6,9-tris(methylene)-, [3aS-(3a.alpha.,6a.alpha.,9a.alpha.,9b. beta.)]-	$C_{15}H_{18}O_2$	230.31	8.8636	22.798

No.	CAS	Name of the compound	Molecular formula	Molecular weight	Peak area (%)	RT (min)
2c	037936-58-6	Azuleno[4,5-b]furan-2(3H)-one, 3a,4,6a,7,8,9,9a,9b-octahydro-6-methyl-3,9-bis(methylene)-, [3aS-(3a.alpha.,6a.alpha.,9a.alpha.,9b.beta.)]-	$C_{15}H_{18}O_2$	230.31	7.4323	22.9012
2d	001838-94-4	2-Methyl-2-vinyloxirane	C_5H_8O	84.12	6.9896	25.5785
2e	1000191-76-5	2-Isopropylidene-3-methylhexa-3,5-dienal	$C_{10}H_{14}O$	150.22	4.7797	24.686
2f	000057-10-3	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256.43	4.6144	22.3407
2g	004290-13-5	Santamarine	$C_{15}H_{20}O_3$	248.32	4.2523	24.4943
2h	005794-04-7	Bicyclo[2.2.1]heptane, 2,2-dimethyl-3-methylene-, (1S)-	$C_{10}H_{16}$	136.24	2.8844	15.3563
2i	000504-96-1	Neophytadiene	$C_{20}H_{38}$	278.52	2.7829	21.0648
2j	000059-02-9	Vitamin E	$C_{29}H_{50}O_2$	430.72	2.5937	31.4861
2k	000150-86-7	Phytol	$C_{20}H_{40}O$	296.54	2.4801	23.7199
2l	000496-16-2	Benzofuran, 2,3-dihydro-	C_8H_8O	120.15	2.39	13.6378

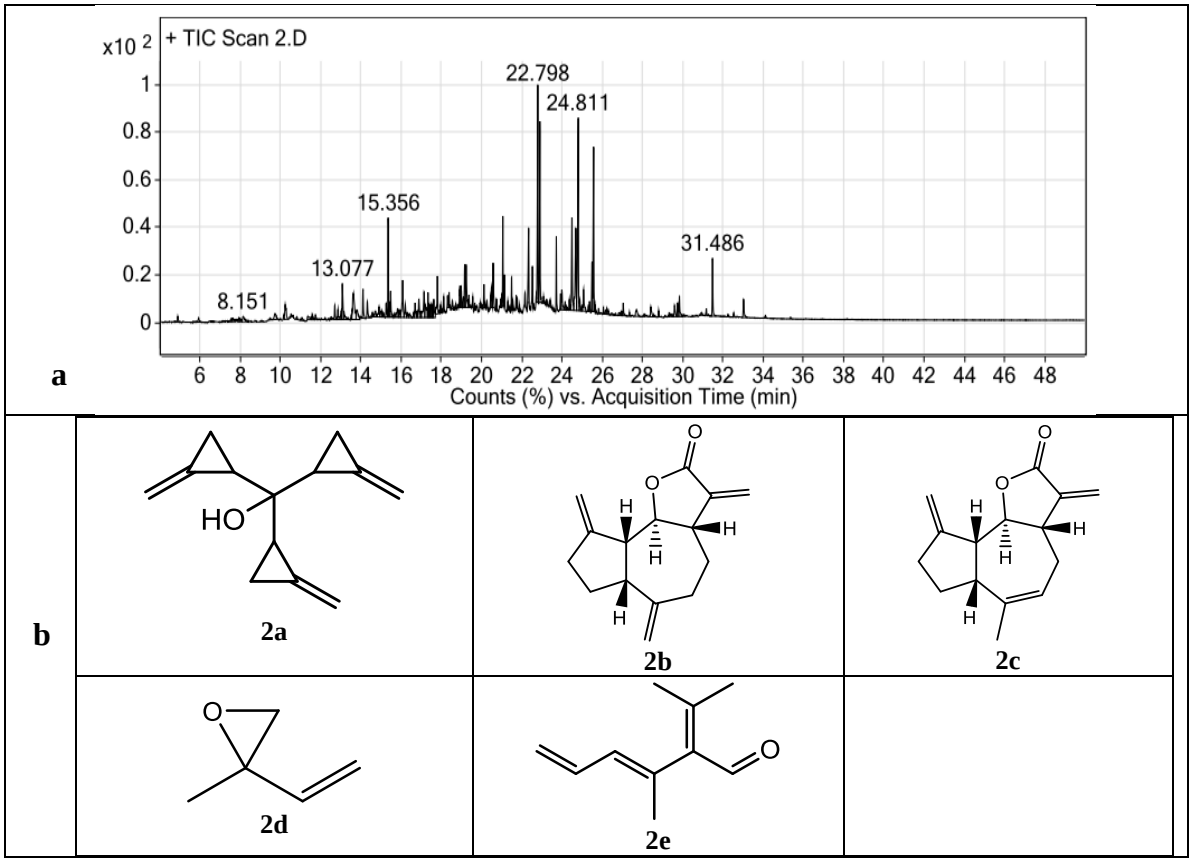


Figure 2. (a) GC-MS chromatogram of ethanolic leaf extract of bay laurel. (b) Chemical structures of the first three phytocompounds.

Table 4. Phytochemical compounds identified in the hot water of bay laurel leaf extract using GC-MS. CAS chemical abstract service.

No.	CAS	Name of the compound	Molecular formula	Molecular weight	Peak area (%)	RT (min)
3a	000067-47-0	5-Hydroxymethylfurfural	$C_6H_6O_3$	126.11	11.6419	14.0584
3b	1000258-90-5	2H-1,2,3-Triazol-4-amine, 2-methyl-5-nitro-	$C_3H_5N_5O_2$	143.11	8.3914	25.586
3c	1000152-74-7	Methanol, tris(methylenecyclopropyl)-	$C_{13}H_{16}O$	188.27	6.8122	24.8337
3d	1000195-02-5	1-Allylazetidine	$C_6H_{11}N$	97.16	5.4767	14.3682
3e	1000294-64-4	Preg-4-en-3-one, 17.alpha.-hydroxy-17.beta.-cyano-	$C_{20}H_{27}NO_2$	313.44	4.7892	24.7305
3f	004290-13-5	Santamarine	$C_{15}H_{20}O_3$	248.32	4.7114	24.5166
3g	000120-80-9	Catechol	$C_6H_6O_2$	110.11	4.1641	13.638
3h	028564-83-2	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	$C_6H_8O_4$	144.13	3.6734	12.7308
3i	1000362-61-6	2-Furanbutanoic acid, .gamma.-oxo-	$C_8H_8O_4$	168.15	3.4994	14.7738
3j	023074-10-4	5-Ethyl-2-furaldehyde	$C_7H_8O_2$	124.14	3.2219	20.6593
3k	000502-61-4	.alpha.-Farnesene	$C_{15}H_{24}$	204.36	3.0039	21.4189
3l	001569-60-4	5-Hepten-2-ol, 6-methyl-	$C_8H_{16}O$	128.22	2.8519	11.4549
3m	007642-09-3	3-Hexene, (Z)-	C_6H_{12}	84.16	2.6809	9.9356
3n	000497-23-4	2(5H)-Furanone	$C_4H_4O_2$	84.07	2.5331	8.3647

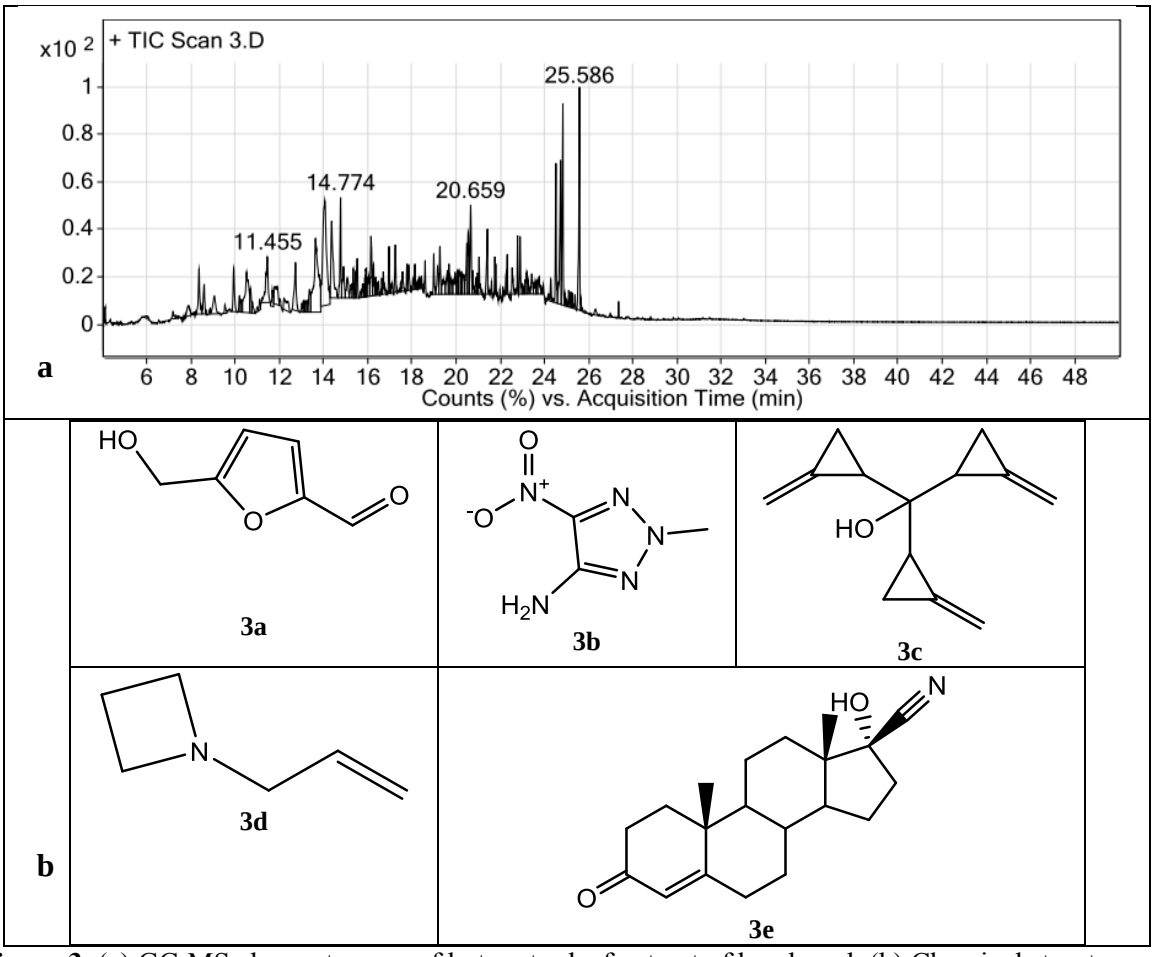


Figure 3. (a) GC-MS chromatogram of hot-water leaf extract of bay laurel. (b) Chemical structures of the first three phytocompounds.

3.3. Antibacterial Activity

Tables 5 and 6 summarize the results of the *in vitro* antibacterial activity of the extracts from bay Laurel leaves. The extracts of the three medium indicate variations in how the two bacterial strains' growth is inhibited. The values of the inhibition zone diameter ranged from 12 to 29 mm.

Table 5 shows that the three extracted media displayed very good inhibition zone 29-26 mm at the concentration of 1000 µg/ml against *S. aureus* bacteria and the activity was proportional with the concentrations. The minimum concentration gave good activity was 125 µg/ml for the hot-water extract (20 mm). Table 6 referred the effect of the different extracts on *Klebsiella pneumoniae* which gave good inhibition zone 20-12, 21-12 and 17-12 mm for ethanolic, hot and cold water, respectively. Conversely, the growth of all the examined microorganisms was not inhibited by the negative controls, pure water or DMSO.

According to this study, this kind of plant may be able to treat bacterial resistance to a variety of antibiotics due to its safety, affordability, and impact on a wide range of germs. Since the phytochemical properties of plant families and subfamilies as well as the mode of action greatly influence the antibacterial efficiency of therapeutic plants. These findings demonstrate that, as revealed by the GC-MS results, these pathways differ significantly depending on the types of components found in various plant extracts.

Table 5. Effect of different concentrations of bay laurel leaf extracts on inhibiting *Staphylococcus aureus* estimated by the average inhibition diameters (mm).

Extracts	**Concentration of extract (µg/ml)**			
	1000	**500**	**250**	**125**
	Inhibition Zone (mm)			
Ethanolic extract	29	25	21	17
Hot Water extract	28	24	22	20
Cold water extract	26	20	15	12
Cefalexin	-	37	-	-

Table 6. Effect of different concentrations of bay laurel leaf extracts on inhibiting *Klebsiella pneumoniae*, estimated by the average inhibition diameters (mm).

Extracts	**Concentration of extract (µg/ml)**			
	1000	**500**	**250**	**125**
	Inhibition Zone (mm)			
Ethanolic extract	20	18	13	12
Hot Water extract	21	19	12	14
Cold water extract	17	15	15	12
Cefalexin	-	23	-	-

3.4. Molecular Docking Studies

For testing purposes, the first five compounds from each extraction were docked into the binding sites of the S. aureus TyrRS (PDB ID: 1JIJ) and *K. pneumoniae* LpxH-AZ1 (PDB ID: 6PIB) to see if they might prevent the disease induced by each bacterium. Tables 7 provide an overview of the outcomes.

For the 1JIJ protein, the 15 compounds had molecular docking scores that ranged from -4.25 to -8.56 kcal/mol, and their RMSDs were between 0.79 and 2.32. For 6PIB, these compounds have docking scores between -4.34 and -8.22 kcal/mol and RMSD values between 0.99 and 2.49. The optimum ligand-receptor binding occurs when the RMSD is close to 2 and the energy score is less or equal 7 kcal/mol [21,22]. To validate the molecular docking data, these two values were employed as criteria. Tables 8 and 9 display the findings for just the substances that produced reliable molecular docking scores.

Table 7. Docking scores of the compounds (1a-1e), (2a-2e) and (3a-3e) with largest pocket of active site of *S. aureus* using protein 1JIJ and *K. pneumoniae* using protein 6PIB.

Compound	1JIJ protein		6PIB protein	
	S Score kcal/mol	RMSD Å	S Score kcal/mol	RMSD Å
1a	-7.27	1.22	-8.04	2.12
1b	-8.56	1.88	-8.22	1.45
1c	-7.54	1.83	-7.63	1.59
1d	-4.67	1.02	-4.66	1.26
1e	-5.42	1.32	-5.26	1.08
2a	-5.42	0.79	-5.75	0.99
2b	-5.37	2.32	-5.44	1.34
2c	-5.66	1.98	-4.76	1.33
2d	-4.25	0.79	-4.03	1.63
2e	-5.26	1.54	-5.12	1.23
3a	-4.53	1.62	-4.34	2.25
3b	-5.45	1.81	-4.57	1.77
3c	-5.38	1.66	-5.75	0.99
3d	-4.48	1.45	-4.42	1.12
3e	-5.77	1.23	-5.18	2.49
Cefalexin	-7.27	1.63	-7.59	1.45

Table 8. Molecular docking score, RMSD, and binding affinity for the compounds showed valid molecular docking scores with 1JIJ.

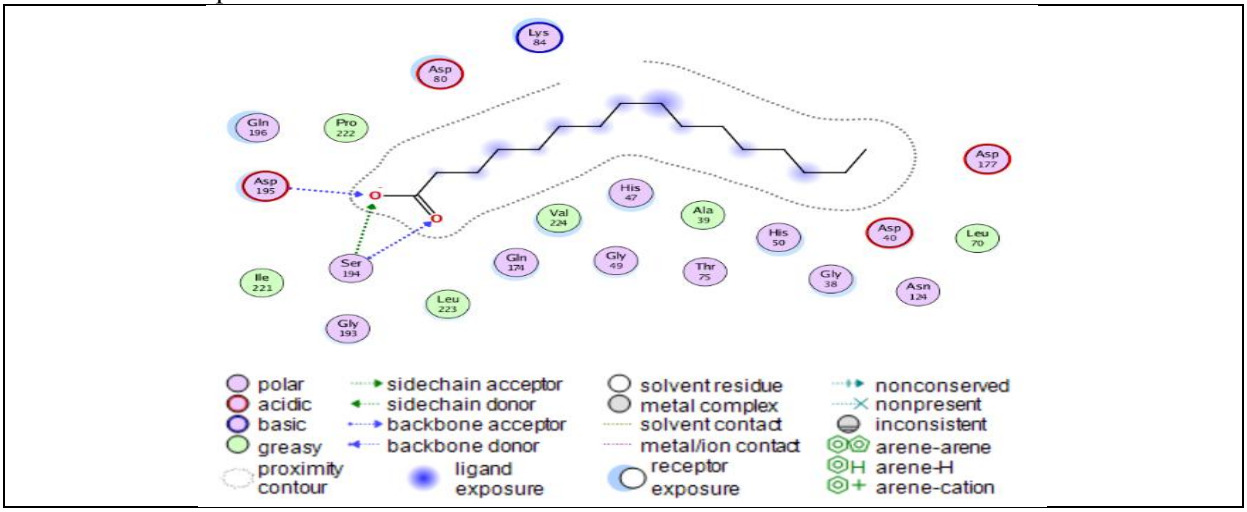
Compound	S Score kcal/mol	RMSD Å	Bonds between Atoms of Compounds and Residues of Active Site of 1JIJ					
			Compd Atoms	Receptor Atoms	Receptor Residues	Interaction	d (Å)	E (kcal/mol)
1a	-7.27	1.22	O-48	CB	SER 194	H-Acceptor	3.44	-0.6
			O-48	N	ASP 195	H-Acceptor	3.45	-0.7
			O-49	N	SER 194	H-Acceptor	3.16	-3.1
1b	-8.56	1.88	O-13	NZ	LYS 84	H-Acceptor	3.25	-1.4
1c	-7.54	1.83	O-54	NZ	LYS 84	H-Acceptor	3.05	-2.6
			O-54	NZ	LYS 84	Ionic	3.05	-4.1
1d	-4.67	1.02	-	-	-	-	-	-
1e	-5.42	1.32	O-2	O	GLY 38	H-Donor	3.02	-1.3
2a	-5.42	0.79	O-2	O	GLY 38	H-Donor	3.03	-1.3
2b	-5.37	2.32	O-22	SG	CYS 37	H-Donor	3.46	-1.0
2c	-5.66	1.98	-	-	-	-	-	-
2d	-4.25	0.79	O-1	N	GLY 38	H-Acceptor	3.00	-1.4
2e	-5.26	1.54	-	-	-	-	-	-
3a	-4.53	1.62	O-14	OD2	ASP 40	H-Donor	3.25	-0.7
3b	-5.45	1.81	N-6	OD1	ASP 177	H-Donor	2.92	-3.9
			N-3	OH	TYR 36	H-Acceptor	3.22	-0.7
3c	-5.38	1.66	O-2	O	GLY 38	H-Donor	2.98	-1.5
			N-1	OE1	GLN 174	H-Donor	2.93	-3.4
3d	-4.48	1.45	C-12	OD2	ASP 40	H-Donor	3.16	-1.7
			N-1	OD2	ASP 40	Ionic	3.39	-2.3
3e	-5.77	1.23	O-31	SG	CYS 37	H-Donor	3.54	-2.3
			O-37	NZ	LYS 84	H-Acceptor	2.96	-1.1

Table 9. Molecular docking score, RMSD, and binding affinity for the compounds showed valid molecular docking scores with 6PIB.

Compound	S Score kcal/mol	RMSD Å	Bonds between Atoms of Compounds and Residues of Active Site of 6PIB					
			Compd Atoms	Receptor Atoms	Receptor Residues	Interaction	d (Å)	E (kcal/mol)
1a	-8.04	2.12	O-49	Mn	Mn 301	Metal	2.54	-1.2
			O-48	ND1	HIS 195	Ionic	3.62	-1.5
			O-49	NE2	HIS 10	Ionic	3.83	-0.9
1b	-8.22	1.45	6-ring	6-ring	PHE 128	pi-pi	3.81	0
1c	-7.63	1.59	O-54	NE2	HIS 195	Ionic	3.32	-2.7
			O-55	ND2	ASN 79	Ionic	3.16	-3.5
			O-55	NE2	HIS 195	Ionic	3.02	-4.4
1d	-4.66	1.26	C-8	SD	MET 156	H-Donor	3.81	-1.2
			5-ring	6-ring	PHE 141	pi-pi	3.96	0
1e	-5.26	1.08	O-2	O	ARG 80	H-Donor	3.18	-0.8
2a	-5.75	0.99	O-2	O	ARG 80	H-Donor	3.27	-1.0
2b	-5.44	1.34	-	-	-	-	-	-
2c	-4.76	1.33	C-9	6-ring	PHE 128	H-pi	3.62	-0.7
2d	-4.03	1.63	-	-	-	-	-	-
2e	-5.12	1.23	-	-	-	-	-	-
3a	-4.34	2.25	O-14	O	ASN 79	H-Donor	3.03	-2.2
3b	-4.57	1.77	N-6	O	MET 156	H-Donor	3.19	-1.0
3c	-5.75	0.99	O-2	O	ARG 80	H-Donor	3.26	-1.0
3d	-4.42	1.12	N-1	O	ARG 80	H-Donor	3.08	-6.2
			C-9	O	TRP 46	H-Donor	3.31	-0.8
3e	-5.18	2.49	C-18	SD	MET 156	H-Donor	3.45	-0.9

The molecular docking of compounds into the binding sites of the *S. aureus* TyrRS showed that the compounds 1a, 1b and 1c gave the highest docking scores of -7.27, -8.56 and -7.54 kcal/mol, respectively, as compared with cefalexin drug which gave -7.27 kcal/mol. The same compounds gave the best values of docking score into *K. pneumoniae* LpxH-AZ1, 1a= -8.04, 1b= -8.22 and 1c= -7.63 kcal/mol compared with standard drug cefalexin -7.59 kcal/mol, as shown in Figures 4-9. Compound 1b interacted with LYS84 of largest pocket of 1JIJ protein with distance of 3.25 Å and interacted with PHE128 of 6PIB as pi-pi interaction with distance of 3.81 Å.

The docking information showed that compound 1a interacted with largest pocket of 1JIJ protein in SER194, ASP195 and SER194 which referred to present of carboxyl group of fatty acid. For this reason, there was good interaction of 1c compound with LYS84 of 1JIJ and with HIS195, ASN79 and HIS195 of 6PIB protein.



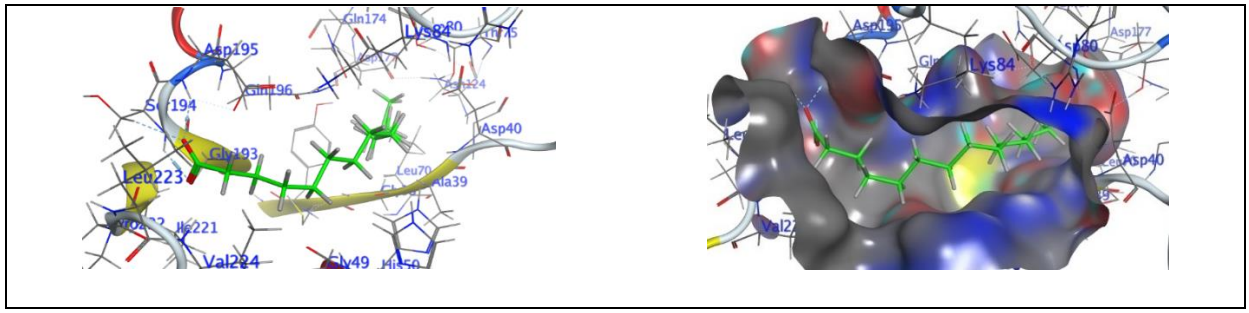


Figure 4. 2D and 3D binding affinity of 1a compound with 1JIJ.

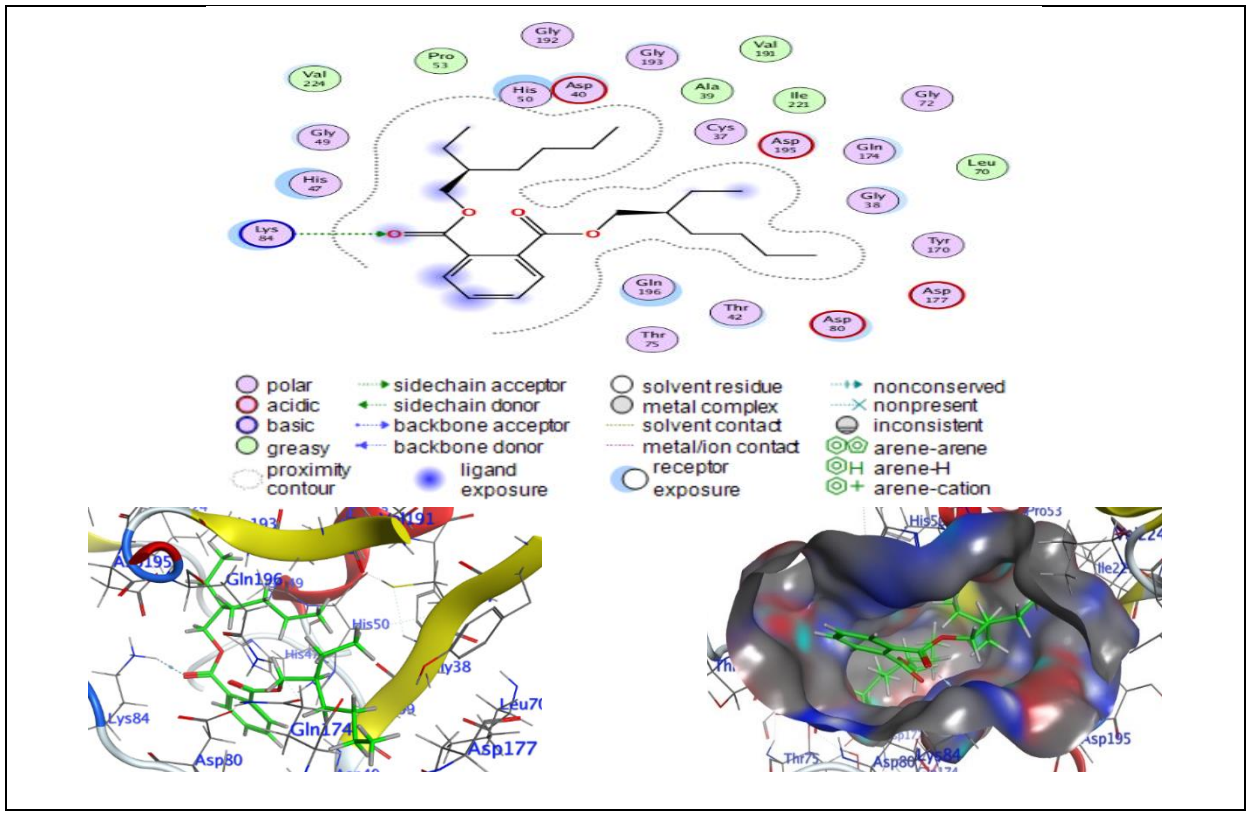
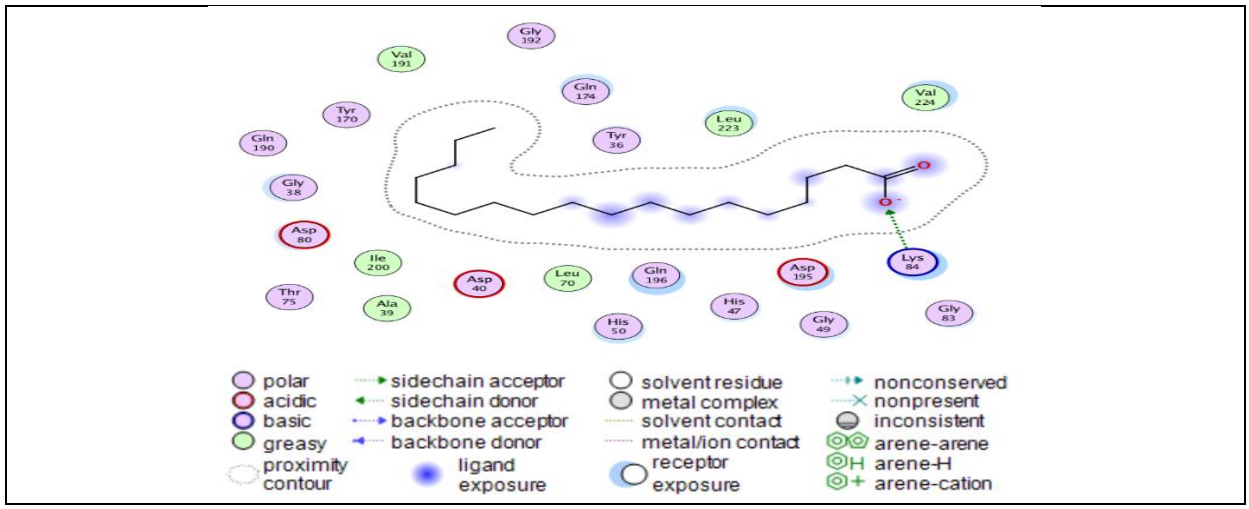


Figure 5. 2D and 3D binding affinity of 1b compound with 1JIJ



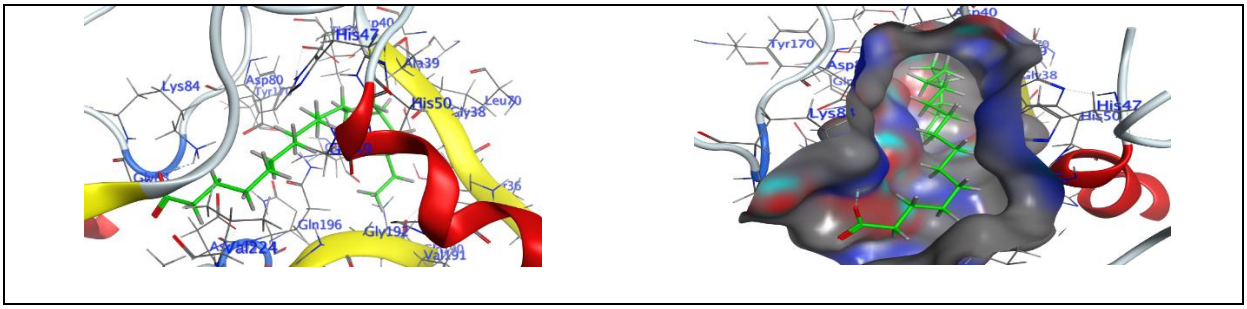


Figure 6. 2D and 3D binding affinity of 1c compound with 1JIJ.

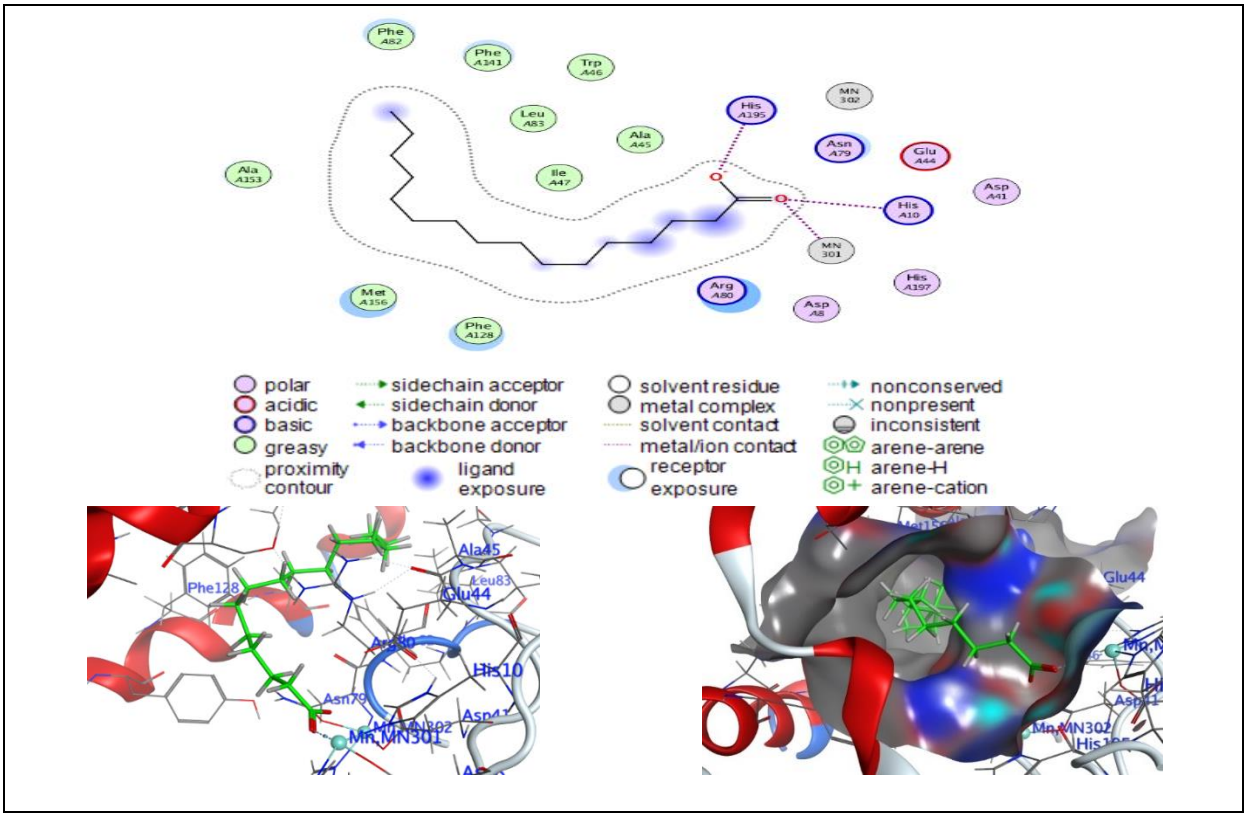
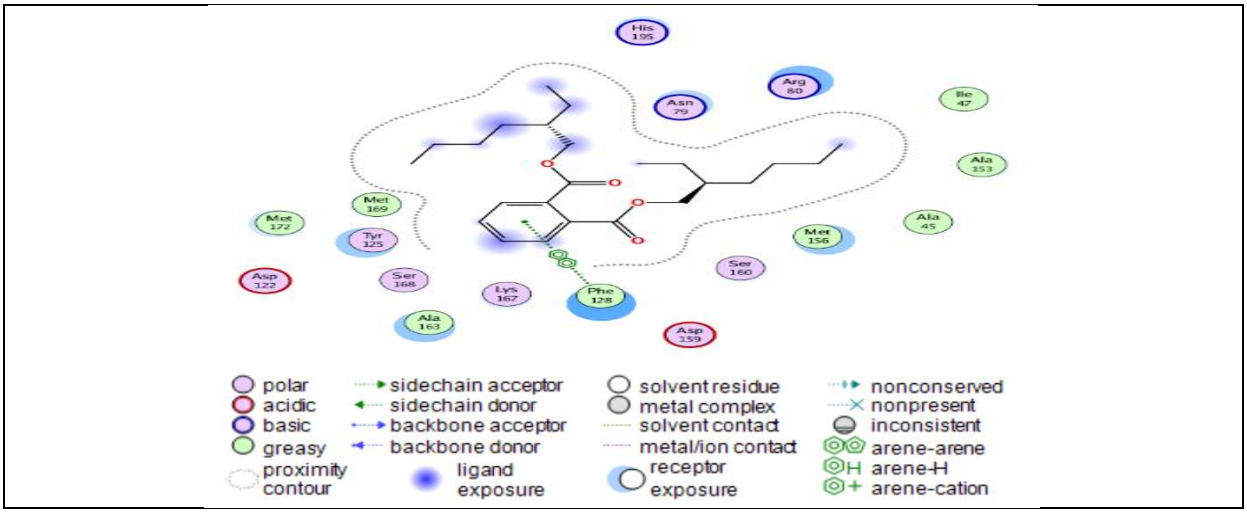


Figure 7. 2D and 3D binding affinity of 1a compound with 6PIB



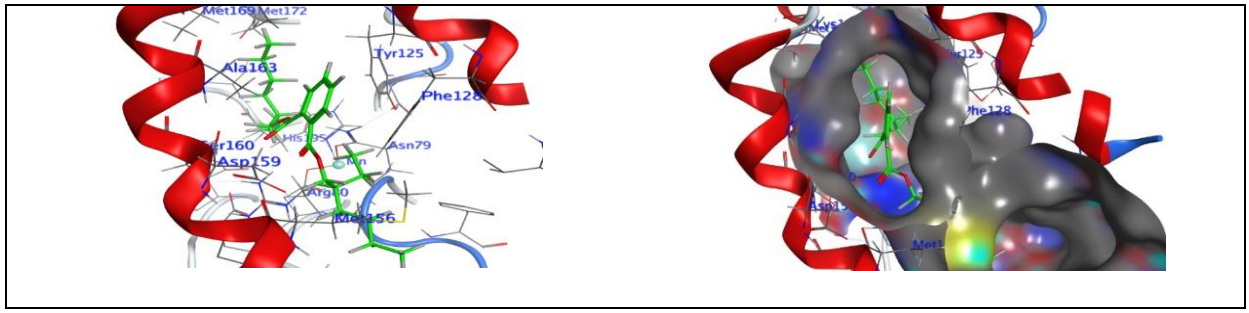


Figure 8. 2D and 3D binding affinity of 1b compound with 6PIB.

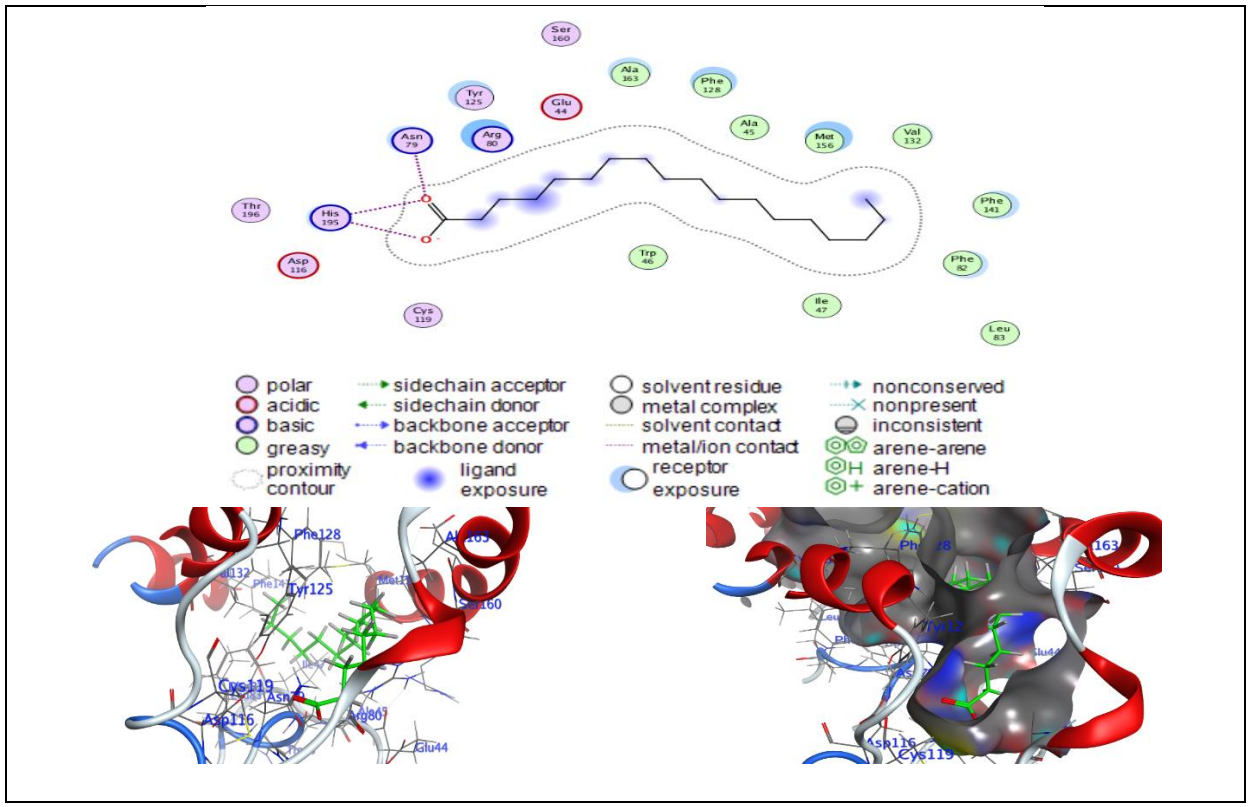


Figure 9. 2D and 3D binding affinity of 1c compound with 6PIB.

Conclusion

Syrians frequently employ the medicinal plant *Laurus nobilis L* for traditional treatment. According to GC-MS study, *Laurus nobilis L* plant extracts in aqueous, ethanolic, and cold, hot forms contain more than 60 different types of active chemicals. Some of these active compounds were in high concentrations as fatty acids, heterocyclic compounds and furfural derivatives. Antibacterial assay of all types of extracted plants showed promising activity against Gram-negative and Gram positive bacteria. In addition, docking studies of the synthesized compounds gave good affinity with the site of protein as compared with the standard drugs.

Conflicts of Interest

There are no conflicts to declare

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