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RESEARCH ARTICLE

Synthesis, characterization, and studying the biological activity, Theoretical Study by Molecular Docking of new Derivatives from Eugenol with different drug

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ABSTRACT

For potential therapeutic uses against resistant microbial strains, this study aims to synthesize, characterize, and evaluate new (H1-H4) eugenol (2-methoxy-4-prop-2-enylphenol, 4-Allyl-2-methoxyphenol compounds, eugenol / phthalic anhydride) functionalized with medications like paracetamol, sulfamethoxazole, and phenylephrine. Due to growing antimicrobial resistance, synthesis and analytical characterization of medicinal molecules from natural sources, such as eugenol, must continue.

Methodology: For antifungal and antibacterial purposes, the compounds (H2-H4) were docked against the enzymes dihydrofolate reductase and UDP-N-acetylenolpyruvoylglucosamine reductase. The GOLD program was used to retrieve crystal structures and carry out docking. Discovery Studio Visualizer was used to study complex protein-ligand interactions. After six hours of reflux, compound H1 emerged as a reddish-brown gelatinous solid due to the interaction between phthalic anhydride and eugenol. It was necessary to activate many grams of the material H1 by treating it with the reagent $SOCl_2$ until the intermediate H2 was generated. H2, phenylephrine, sulfamethoxazole, and paracetamol reacted to produce H3, H4, and H5. The physical properties of the synthesized compounds, such as color and melting point ranges of 147–210°C and yield between 70% and 70%, were evaluated by laboratory researchers. The spectroscopic tests corroborated the compounds' characteristics and their medicinal potential, while a structural analysis verified the successful synthesis of the compounds.

Results: Compound H3 formed several hydrophobic and hydrogen interactions and had a high PLP fitness score to both DHFR and UDP-N-acetylenolpyruvoylglucosamine reductase (104.14 and 92.32, respectively). With the two enzymes, H2 likewise had a high PLP fitness score. The laboratory procedure effectively yielded pure chemicals H1, H2, H3, H4, and H5, according to structural confirmation using FTIR and ^{1}H-NMR measurements. Functional group bond vibrations through O-H, N-H, aromatic C-H, aliphatic C-H, ester C=O, amide C=O, and aromatic C=C bonds were demonstrated using FTIR spectroscopy. The accuracy of the experiments was confirmed by a number of structural integrity tests that were checked using ^{1}H-NMR spectroscopy. These compounds exhibited moderate to considerable antibacterial and antifungal activity against the infection-causing organisms Candida albicans, Escherichia coli, and Staphylococcus aureus, according to biological testing.

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Conclusion: Eugenol and phthalic anhydride were used in the research study to create novel chemicals that were integrated with pharmaceuticals like sulfamethoxazole and paracetamol. Compound H26, which has the highest binding affinity, is the main inhibitor of the DHFR and MurB enzymes. The proper structure and purity were verified by FTIR and 1H-NMR spectroscopy. Sulfamethoxazole and phenylephrine architectures improved the compounds' antibacterial and antifungal activities against pathogenic microorganisms.
Keywords: Paracetamol, Sulfamethoxazole, Phenylephrine, FTIR and H-MNR

1. Introduction

Due to the growing global concern about anti-microbial resistance, conventional therapeutic agents have lost their efficacy. The continuous emergence of resistant microbial strains demands the development of new drugs with improved anti-microbial activity. So, researchers gradually focus on natural products, an abundant source of structurally diverse compounds with inherent bioactivities [1-3].

Natural compounds with strong antimicrobial, antifungal, analgesic, and anti-inflammatory characteristics, such as eugenol (4-allyl-2-methoxyphenol), which is mostly derived from clove oil (Syzygium aromaticum), have great potential for therapeutic uses. However, in order to improve the bioavailability, specificity, and effectiveness of the pharmacological therapy, the original biological features of this natural molecule usually require chemical alterations. These chemical transformations are often accompanied by reactions like esterification, amidation, or substitution, which are determined accurately by analytical methodologies [4-6].

Eugenol is one example of a biogenic molecule that can be chemically modified to increase biological activity and create a medication with specific pharmacological characteristics for therapeutic use. To increase potency, selectivity, and pharmacokinetic characteristics, these chemical alterations mostly involve the addition of additional functional groups or connected biologically active pharmacophores. One common synthetic route comprises esterification, amidation, and substituting reactions with phthalic anhydride reagents. Because of its high electrophilic character, Phthalic anhydride easily enters nucleophilic addition to hydroxyl and amino groups, opening efficient structural dissension of bioactive natural compounds [7, 8].

Phthalic anhydride, often employed in organic chemistry as a reagent, easily participates in nucleophilic additions owing to its strong electrophilic properties. Its activity towards hydroxyl and amino groups has converted it into an important one in synthesizing structurally extremely different and bioactive derivatives. This reactivity can be traced and controlled with the help of analytical methods like Fourier Transform Infrared Spectroscopy (FT-IR) and Nuclear Magnetic Resonance (NMR) spectroscopy so that the precision of the produced accumulations can be easily acknowledged [9, 10].

Natural products, including Eugenol (4-allyl-2-methoxyphenol) extracted mainly from clove oil (Syzygium aromaticum), have potential as therapeutic agents because of their proven anti-microbial, antifungal, analgesic, and anti-inflammatory properties. As a well-elucidated phenolic compound, Eugenol is an ideal scaffold for chemical modification to improve therapeutic efficacy and decrease toxicity [11].

Strongly inclined to operate as a substrate in any nucleophilic reaction involving functional groups such as hydroxyl and amino groups, phthalic anhydride is an electrophilic moiety with a diverse reactivity.

This reaction flexibility bridges diversely structured derivatives systematically monitored and optimized through FTIR and NMR spectroscopy to attain reaction accuracy with precision in the manufacturing process and correct structural purity [12, 13].

Molecular Docking is an important component of computer-assisted drug discovery. It helps in predicting the intermolecular framework formed between a protein and ligand and outputs the appropriate binding between the molecules [14].

Several previous researches have shown the role of analytical chemistry in steering synthesis and characterization of bioactive derivatives. By way of example, a preceding study by Silva et al. (2024) [15] confirmed that FTIR and NMR spectroscopy merited it to create a novel anti-microbial complex achieved from the natural phenolic molecules. Research demonstrated that systematic spectroscopic analysis validated structural stability and systematically optimized chemical reactions, making Chemical compounds more effective in therapeutic drug-resistant bacterial strains.

Similarly, Rehman et al. (2024) [16] very closely employed proton nuclear magnetic resonance (1H-NMR) spectroscopy Fourier transform infrared (FTIR) spectroscopy for characterization of the sulfonamide-based complexes. Their work demonstrated the utility of those analytical methods in determining and confirming successful sulfonamide conjugations and linking structural features to bacterial activity against resistant microorganisms. These discoveries highlight the extensive usage of analytical chemistry to examine the relationship between chemical frameworks and biological behavior.

Currently, the research project concentrates on synthesizing new eugenol derivatives through reaction with phthalic anhydride and subsequent interaction with paracetamol, sulfamethoxazole, and phenylephrine pharmaceutical compounds. Paracetamol is commonly used for its analgesic and antipyretic actions, with the antibacterial activity of sulfamethoxazole, and as an effective sympathomimetic agent, a nasal decongestant phenylephrine.

This study's primary goal is to synthesize, physiochemically characterize, and evaluate the biological activity of novel eugenol compounds—complexes of eugenol and phthalic anhydride—that have been further functionalized with medications (phenylephrine, sulfamethoxazole, and paracetamol). In order to identify novel candidates against resistant microbial strains for their possible therapeutic applications, the research attempts to establish structural and biological correlations of these derivatives utilizing thorough analysis techniques and biological activity measurements.

2. Material and methods

All intermediates came from Hyper-chem, which is situated on Hangxing Road in Hangzhou, China. FTIR on Japanese Shimazu 8400s, 1HNMR equipment with 500 and 125 MHz quality, respectively, from Varian/Aligant USA, and the capillary tube method for melting point recording on an electric melting point device from the Stuart company in England

2.1. Molecular docking

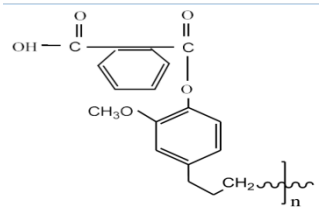
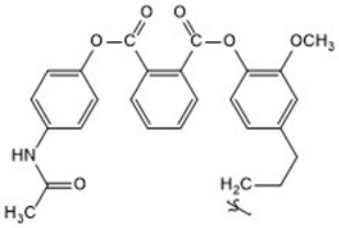
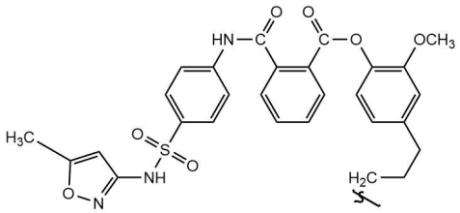
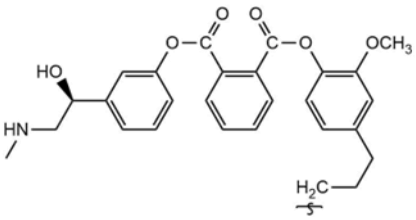
The full license version of Genetic Optimization for Ligand Docking (GOLD) was used to carry out the molecular docking. The Hermes visualizer application in GOLD is used to provide the docking procedure. Protein residues and nucleotides within 10 A served as the binding location for the docking. udp-n-acetylenolpyruvoylglucosamine reductase and dihydrofolate reductase were obtained from the PDB website [PDB: 1AI9 and 1HSK, respectively]. PLP fitness is used to carry out the scoring function. The GOLD docking technique employed default values for all parameters, and the Fitness function of Piecewise Linear Potential (CHEMPLP) was used to grade each solution. The ligand's interaction with the active site's protein residues was evaluated using the docking results, which included the docked pose, binding mode, and binding free energy.

2.2. Chemical synthesis

In Scheme 1, The following methods, which are shown in Scheme 1, were used to create several novel compounds of eugenol using various drugs.

The physical properties of prepared H1, H2, H3, and H4 compounds are shown in Table 1

Table 1. Some physical properties of prepared H1, H2, H3, and H4 compound

	Structure	Color	Melting point^{0}C	
H1		Brown- Reddish	147-155	70
H2		Dark-yellow	155-167	70
H3		Orange-Reddish	180-210	70
H4		Orange-yellowish	160-175	70

2.3. Synthesis (4-allyl-2-methoxy phenol) (Eugenol) with Phthalic anhydride(H1)

In a 50 ml round flask fitted with a magnetic stirrer, 1 gm of (4-allyl-2-methoxy phenol) (Eugenol) was dissolved in (10 ml) of DMSO, and (2) ml of (0.5% NaOH) was added to the mixture, and it was heated for a (1/2 hr.) at (75-80) °C. Then, 1gm of phthalic anhydride was dissolved in (10 ml) of DMSO and mixed with (4-allyl-2-methoxy phenol) (Eugenol), then heated for a (6 hr) at (75-80) °C [12, 17]. The Reddish-brown gelatinous material was collected and washed with (10 ml) diethyl ether, Lastly, they were dried overnight at 60 °C in a vacuum oven.

compound, H1, was activated by adding 1 mL of thionyl dichloride ($SOCl_2$) the mixture was heated under stirring at 75-80 °C for 30 minutes. The resulting solution mixed with (1 gm, 0.0066mol) of paracetamol was dissolved in 10 mL of DMSO and 4 hours of heated at 75-80 °C. Dark-yellow, gelatinous compound (compound H2) was obtained, which was collected, washed with 10 mL of diethyl ether, and dried overnight in a –vacuum oven at 60 °C.

The same procedure of H3, H4 is used to prepare (4-allyl-2-methoxy phenol) (Eugenol) with Drugs of Sulfamethoxazole (H3) and Phenylephrine (H4) [18].

2.4. Fourier Transform Infrared (FT-IR) Spectra

Using FT-IR spectroscopy on the generated compounds, the structural characteristics of the chemical bonds (functional groups) dividing the molecules were examined. A Shimadzu FT-IR 8400S (Japan) with a wave number range of 400–4000 cm-1 was used to measure this FT-IR. Samples were made by combining 1% of chemicals with 99% KBr that had been compressed onto a disk.

2.5. Proton-Nuclear magnetic resonance (1H-NMR)

DMSO-d6 was used as a solvent to produce the 1H-NMR spectra of a few polymers.

2.6. Biological efficacy

Muller Hinton agar (38 g in 1L distilled water) was autoclaved at 121°C and 15 psi pressure after being totally dissolved by swirling over a hot plate apparatus. The slurry was aseptically put into Petri dishes and allowed to harden after being gently chilled. A sterile spreader was used to equally distribute the prepared isolates across the surface of the medium after they were added to the plates, and they were then allowed to dry overnight. The polymer was applied in different concentrations (ppm) and then incubated for a whole day at 37 °C. Using a ruler, the diameter of inhibition was measured in millimeters in order to document the findings [19, 20].

3. Results and Discussion

This step involves opening the phthalic anhydride ring through a nucleophilic attack by the hydroxyl group of the Eugenol on the carbonyl group to produce (H1). The reaction mechanism is illustrated Scheme in shown in Figure 1.

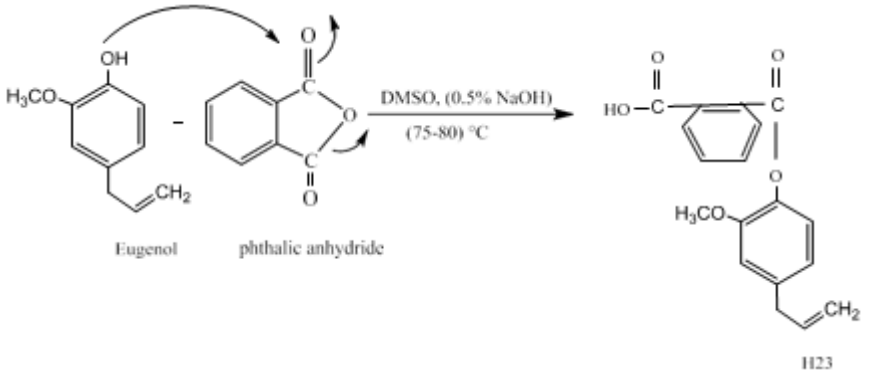


Figure 1. Mechanism of ring opening of phthalic anhydride with Eugenol (H1).

The second step is activating compound H1 using thionyl chloride, converting it into compound H2. After that activation, compound H2 was incubated alone or in mixtures with several drugs: paracetamol, sulfamethoxazole, and phenyl abrin. These combinations yielded three products (identified as H2, H3, and H4). This synthetic pathway is shown explicitly in the reaction sequence contained in Figure 2.

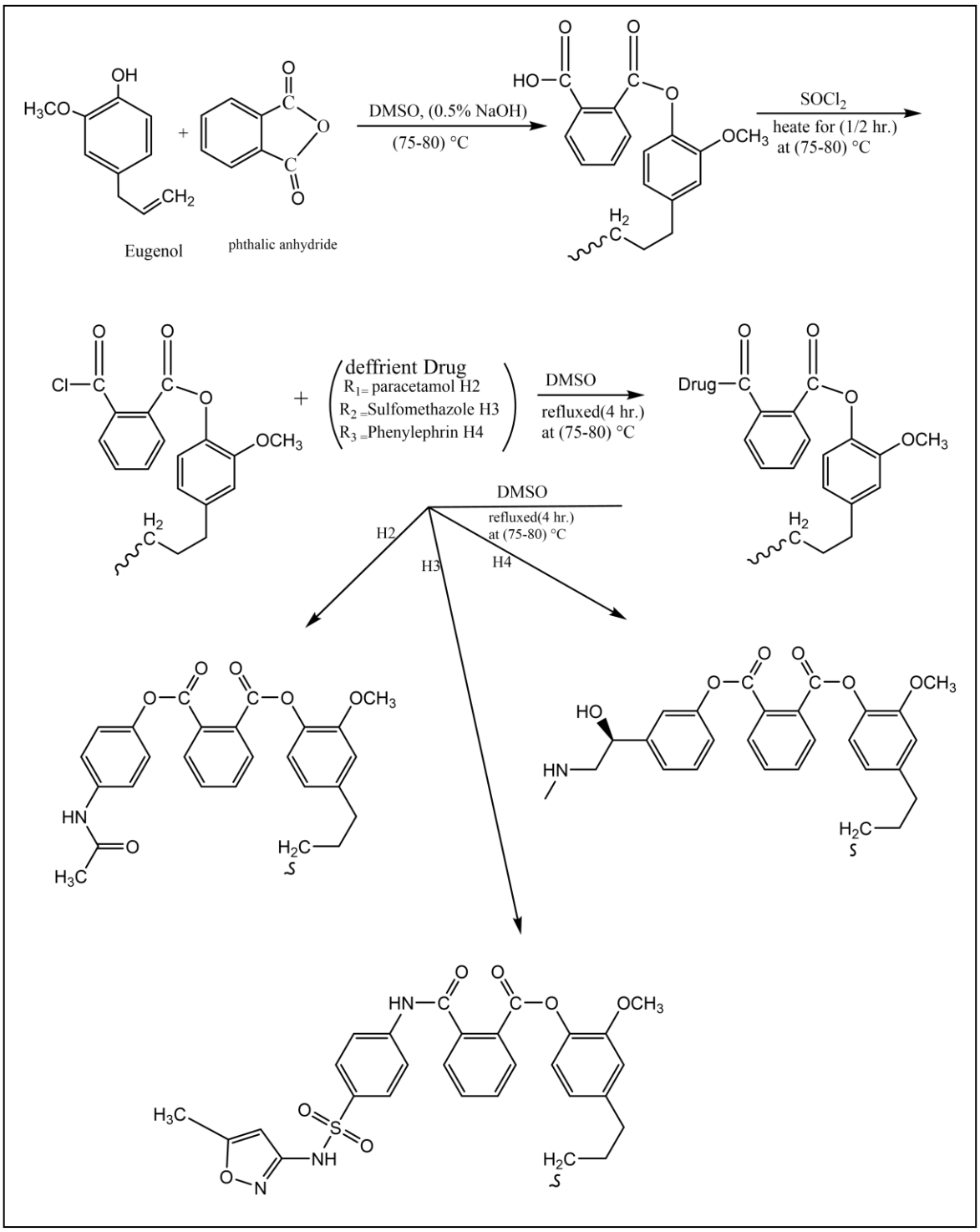


Figure 2. Scheme for the Synthesis of Compound (H1, H2, H3, H4,).

Figure 3 displays the FT-IR spectrum of chemical (H1). comprises specific bands of characteristic days at definite wavenumbers. A wide absorption band at about 3363 cm^{-1} showed the hydroxyl groups (O–H). Two separated bands were present within the region 2850–2920 cm^{-1} due to the aliphatic carbon-hydrogen (C–H) stretching mode vibrations. Besides, the band at 3002 cm^{-1} was associated with aromatic carbon-hydrogen (C–H) stretching modes. The spectrum also contained the ester C=O stretching band at 1605 cm^{-1} and a second C=O band for a carboxylic acid at 1709 cm^{-1}. Sharp bands around 1435 cm^{-1} were associated with the stretching bands of (C=C) of benzene rings [21].

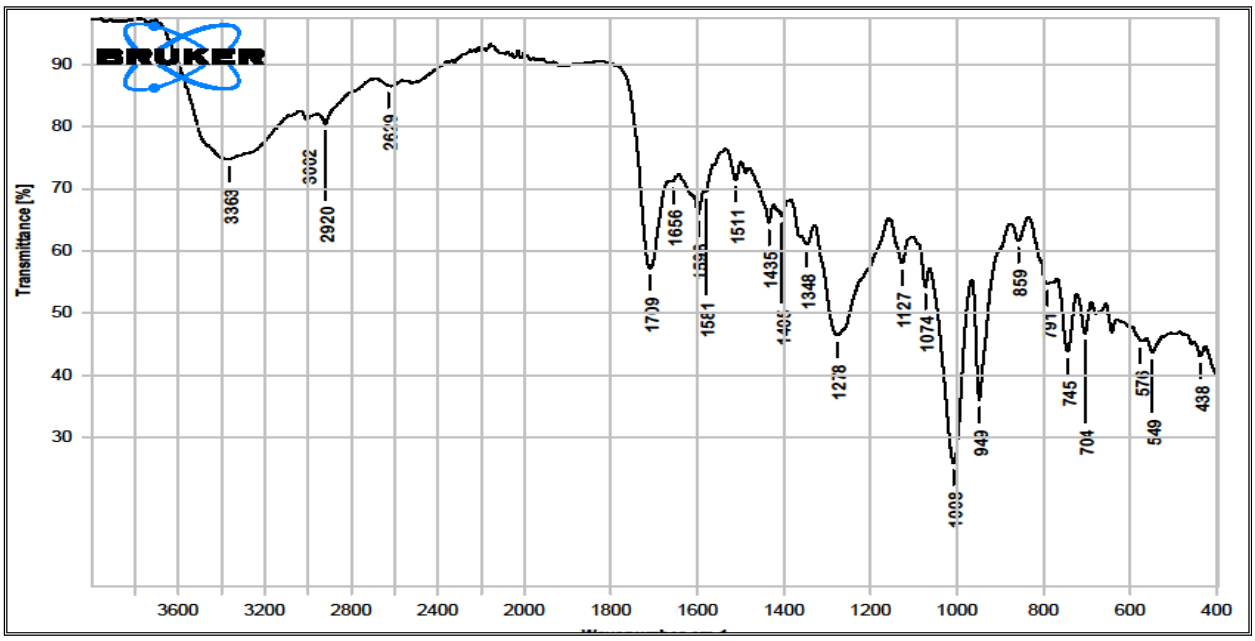


Figure 3. The compound of H1 results from FTIR

So far, the FI-IR spectrum of compound (H2), displayed in Figure 4, exhibited a strong O–H stretching vibration near 3339 cm. Aromatic bands of carbon-hydrogen (C–H) stretching bonds existed between the wavenumbers of 2926–2973 cm^{-1} and an aromatic C–H band occurred at about 3248 cm^{-1}. The ester C=O stretching vibration appeared at 1629 cm^{-1}, and the C=O stretching vibration of carboxylic acid appeared at 1704 cm^{-1}. Additionally, to compound H1, C=C vibrations of the benzene ring (about 1435 cm^{-1}) were found.

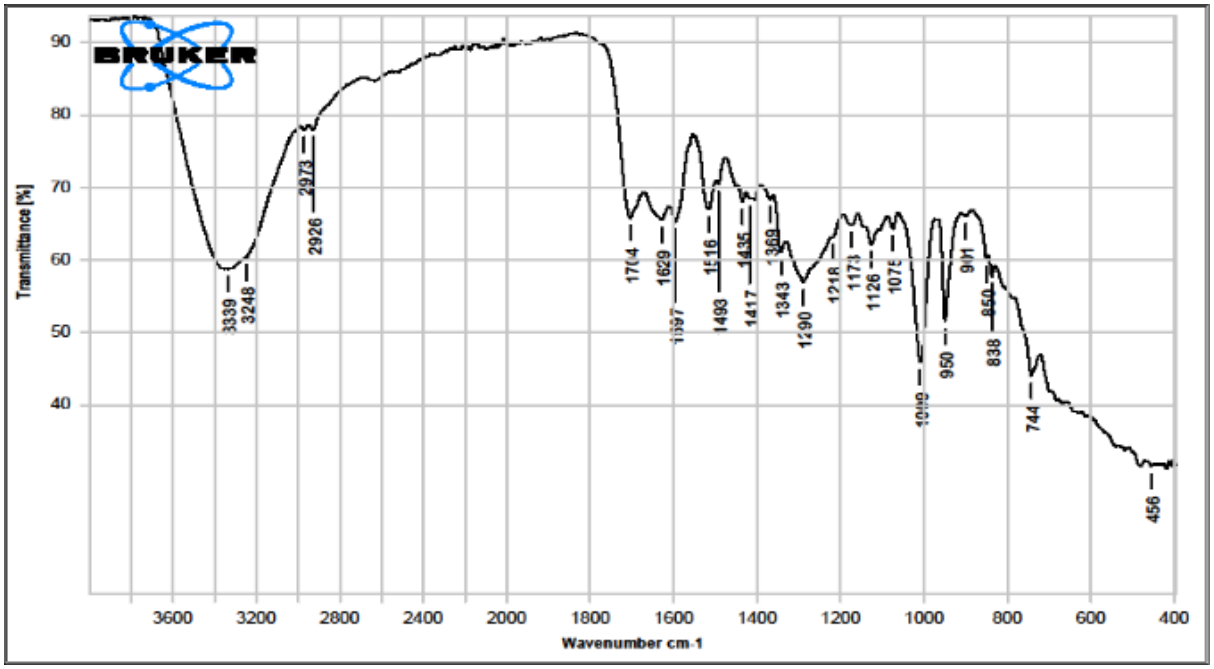


Figure 4. The compound of H2 results from FTIR

Figure 5 for the FT-IR results of compound (H3) showed an O–H band near 3321 cm^{-1} and a further N–H stretching bore near 3255 cm^{-1}. There were two bands of aliphatic C-H stretching at 2880–2989 cm^{-1} and an aromatic C-H stretching at 3107 cm^{-1}. Additionally, two locations (1606 cm-1 and 1650 cm-1) had ester carbonyl vibration bands. The vibrations of the benzene ring (C=C) gave a strong absorption at around 1433 cm^{-1}.

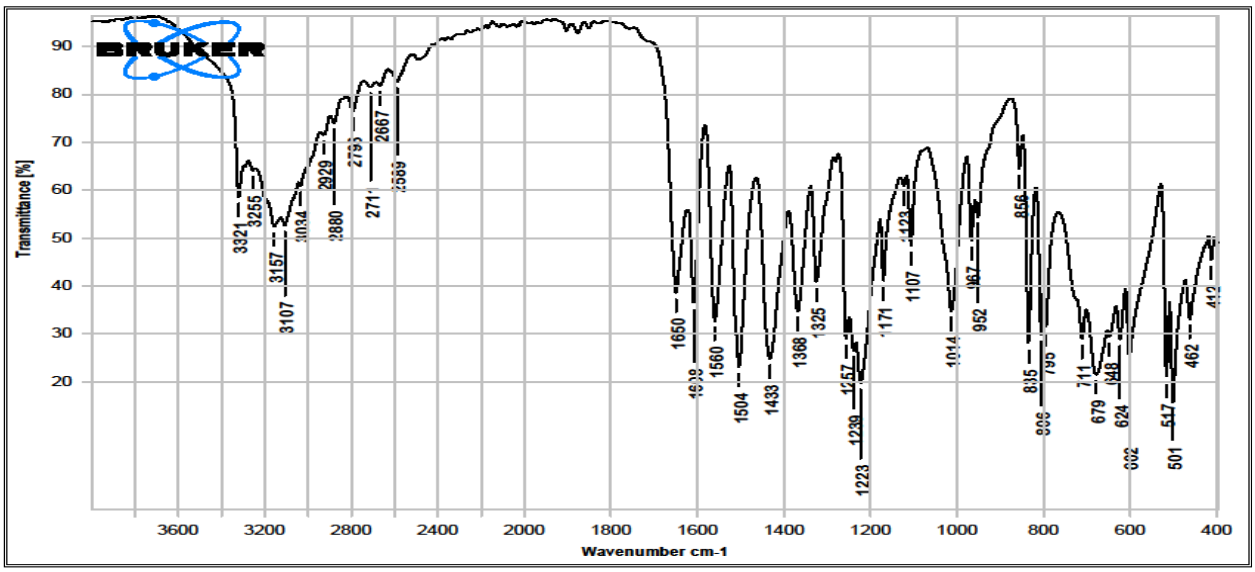


Figure 5. The compound of H3 results from FTIR

The infrared (FT-IR) absorption spectra of compounds H4, presented in Figure 6, display other specific functional groups under unique characteristic absorption features. Both compounds exhibited wide vibrations stretching for OH (-O-H) between 3455-3358 cm^{-1}. Also, separate bands observed at 3361–3228 cm^{-1} represented the bond vibration of the N–H group.

Aromatic carbon-hydrogen (C−H aromatic) stretching absorptions were observed in spectra of compounds H3 for 3057–3001 cm^{-1}. Besides, aliphatic carbon-hydrogen (C–H aliphatic) stretching bands were separated at 2872–2969 cm^{-1} for one compound and 2882–2917 cm^{-1} for another compound. Ester carbonyl (C=O) stretch was present in the 1713–1636 cm^{-1} region. Vibrations of bands related to the skeletal structure related to the benzene ring (1539–1437 cm stew) and C=C bending were easy to observe, and vibrations of bands connected with vibrations of carbon –nitrogen(C—N), that took place, at wavenumbers intervals 1370–1313 cm $^{-1}$ [22, 23].

The FT-IR spectral data for more compounds H1 to H4, in detail, is given in Table 2.

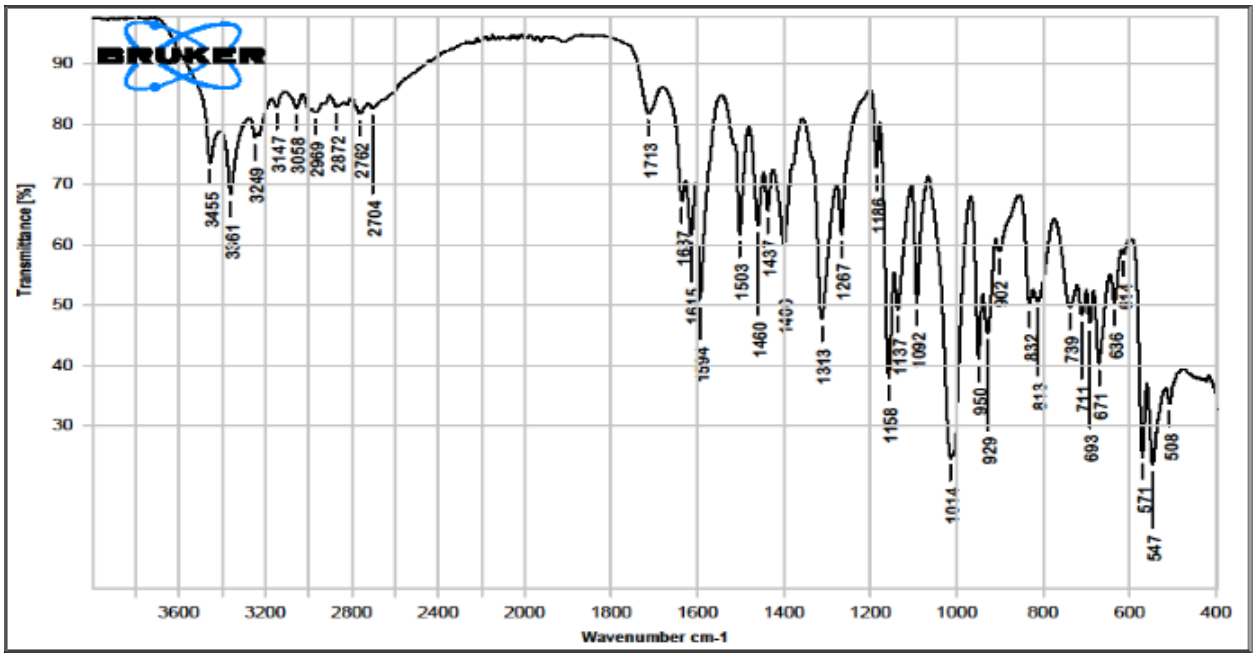


Figure 6. The compound of H4 results from FTIR

Table 2. FT-IR data for the compounds (H1- H4)

Comp.	(O-H) $_{cm}$-1	(N-H) $_{cm}$-1	(C-H) $_{cm}$-1 Aro.	(C-H) $_{cm}$-1 Alph.	(C=O) $_{cm}$-1 amide	(C=O) $_{cm}$-1 ester	(C=O) $_{cm}$-1 carboxylic	(C-N) $_{cm}$-1	(C=C) $_{cm}$-1
H1	3336	-	3002	2850-2920	-	1605	1709	-	1435
H2	3339	-	3248	2926-2973	-	1629	1704	-	1435
H3	3321	3255	3107	2880-2989	1606	1650	-	1366	1433
H4	3455	3361	3057	2872-2969	1615	1637	-	1313	1437

Proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy, TMS as the internal standard, and DMSO-d_4 as the solvent were used to describe the produced compounds (H2, H3, and H4). The spectrum of compound H2 with ^{1}H-NMR (Figure 7) featured specific signals corresponding to different proton groups of its molecular structure. These signals were identified as a singlet at 1.29 ppm associated with methyl protons (CH_3), a singlet at 2.01 ppm related to methylene protons (CH_2), and a singlet at 2.53 ppm versus methoxy protons (OCH_3). Besides, a singlet noted at 3.14 ppm indicated an NH proton. Aromatic proton groups were found in the multiplet way within the fields of 6.5–7.65 ppm and hydroxyl (OH) proton signal as singlet to 6.3 ppm. Additionally, a signal at around 9.71 ppm could be attributed to two protons of the carboxylate group (–COO). Another signal over 7.72 could be due to an amide proton.

Compound H3 (Figure 8) displayed distinct signals at 1.26 and 2.01 ppm in the ^{1}H-NMR spectrum because of the methyl protons. A further signal consisted of a singlet at 3.7 ppm for the NH proton and another at 2.63 ppm for methoxy group protons (OCH_3). The aromatic protons were prominent as multiple peaks in region 6.12–7.65 ppm. Additionally, a corresponding signal at 7.67 ppm was speculated to be from an amide proton, and a signal at 11.1 ppm was surrounded by signals similar to the carboxylate (–COO) protons.

The ^{1}H-NMR spectrum for compound H4 (Figure 9) also displayed a distinct proton resonance signal that matched its predicted structure. Especially in the spectrum, their observed was a singlet for methyl protons (CH_3) (ppm 1.26), singlet for methylene protons (CH_2) (ppm 2.30), and singlet for methoxy protons (OCH_3) (ppm 2.58). The 3.15 ppm upfield singlet was due to the NH proton. Different signals observed in the 6.73–7.94 ppm range were assigned to aromatic protons; a sharp singlet at 6.3 ppm was due to hydroxyl proton (OH). Last, the signal visible at 9.61 ppm was most likely due to the two protons of the carboxylate group (–COO)[24].

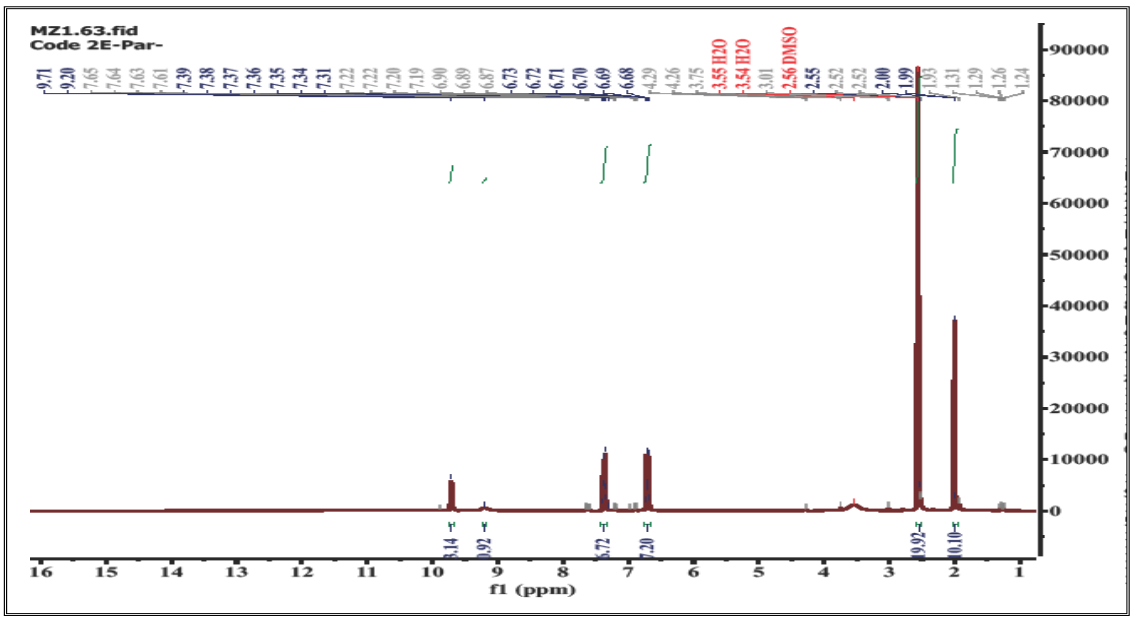


Figure 7. The Compound of H2 resulted from ^{1}H-NMR.

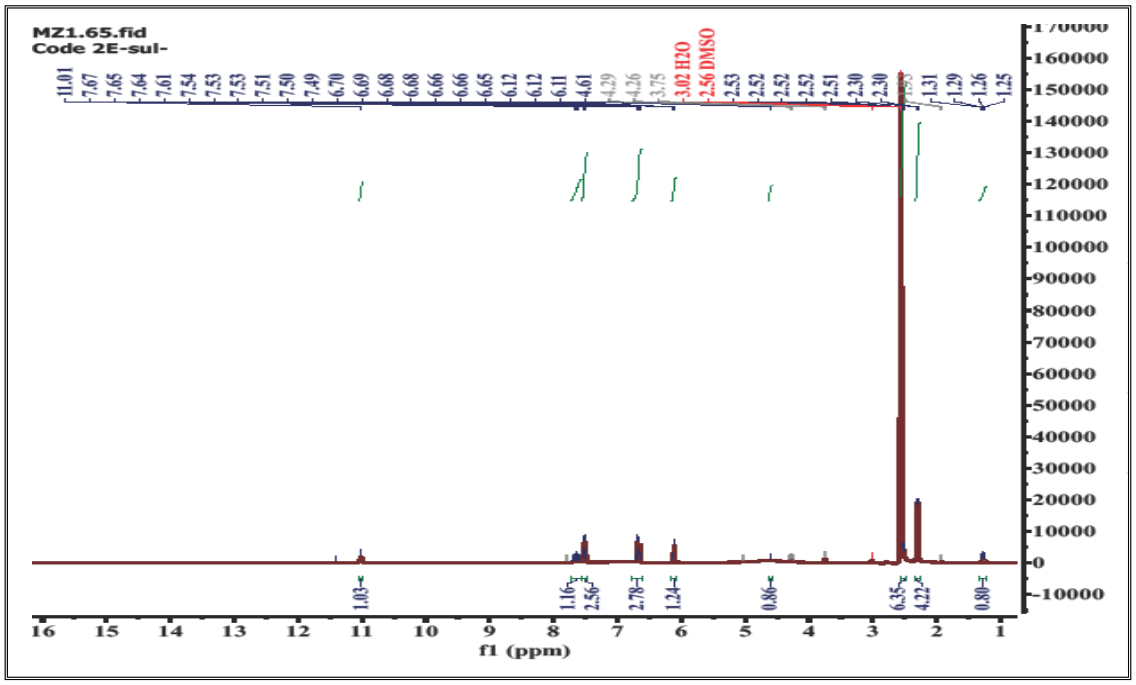


Figure 8. The Compound of H3 resulted from ^{1}H-NMR.

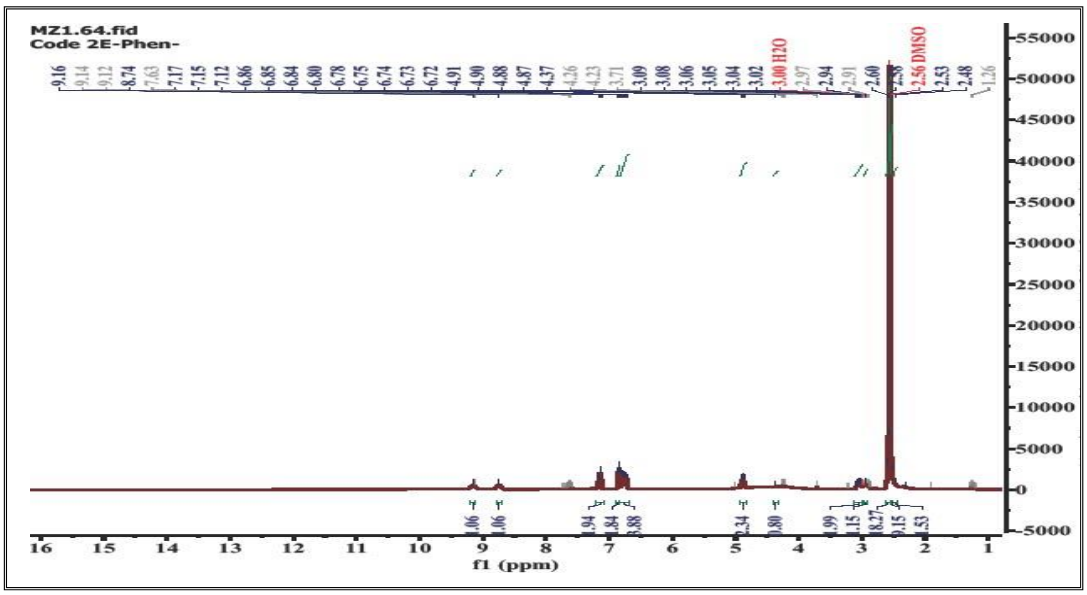
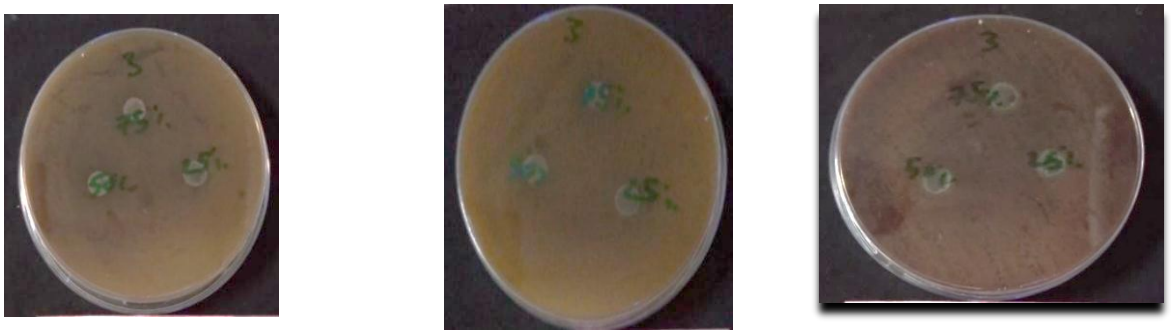


Figure 9. The Compound of H4 resulted from ^{1}H-NMR.

Three different concentrations of the synthesized compounds (H2, H3, and H4) were used to test the antifungal properties against Candida albicans; the results indicated medium to good antifungal activity. utilizing DMSO as a reference at a concentration of 1 mg utilizing the agar spread technique, the plates were incubated for 24 hours at 37°C. Tables 3, 4, and 5 present the findings, accordingly. The inhibition area is measured in millimeters. All compounds were found at a concentration of 75% with a diameter larger than the growth inhibition zone and showed moderate to good activity against *Staphylococcus aureus* and *Escherichia coli* [25].

Table 3. The biological activity of the H2 compound.



Comp.	*Staphylococcus*	*E. Coli*	*Candida*
H2 (75%)	11	10	14
H2 (50%)	10	9	13
H2 (25%)	-ve	-ve	10

Table 4. The biological activity of the H3 compound.

Comp.	*Staphylococcus*	*E. Coli*	*Candida*
H3(75%)	20	21	17
H3 (50%)	18	19	12
H3 (25%)	14	16	10

Table 5. The biological activity of the H4 compound.

Comp.	*Staphylococcus*	*E. Coli*	*Candida*
H4(75%)	19	23	12
H4 (50%)	18	21	10
H4 (25%)	15	17	9

Docking results of (H2-H4) against dihydrofolate reductase, and udp-n-acetylenolpyruvoylglucosamine reductase were showed in table 5 and 6; respectively. Compound H3 exhibited the most favorable binding conformation, displaying the PLP fitness score against dihydrofolate reductase (104.14), and UDP-N-acetylenolpyruvoylglucosamine reductase (92.32). As we shown in (figure 10) it binging by four hydrogen bond with ALA:115, THR:58, ILE:19, ALA:11 amino acid, and different hydrophobic bond with ILE:33, ILE:112, PHE:36, LEU:69, MET:25, VAL:10, TYR:118, GLY:114, ILE:117, ARG:56, LYS:57, GLU:116 amino acid in binding site of 1AI9. While its binding with 1HSK, by two hydrogen bonds with GLY:81, GLY:79 amino acids, and different hydrophobic bond with PRO:141, LEU:231, TYR:42, PHE:274, GLY:145, VAL:198, ILE:192, TYR:77, VAL:199, ILE:84, MET;150, ALA:152 amino acids in binding site showed in (figure 11) [26].

H2 also exhibit high PLP fitness score within both dihydrofolate reductase DHFR (94.21), and with UDP-N-acetylenolpyruvoylglucosamine reductase (71.16), by forming 3 hydrogen bonds with ALA:11, ILE:112, ALA:115 and number of hydrophobic bond with THR:118, ILE:19, MET:25, VAL:10, GLY:114, THR:147, LYS:22, ILE:117, LYS:57, GLU:116. amino acid of DHFR, and by 3 hydrogen bond with SER:82,

ASN:83, ARG:225, and different hydrophobic bond with PRO:141, TYR:149, ARG:310, ILE:84, MET150, GLY:146, ALA:152, ILE:140 amino acids of UDP-N-acetylenolpyruvoylglucosamine reductase as we showed in figure 12 and 13 respectively [27, 28].

Table 6. Docking results of Compounds (H2-H4) with PDB:1AI9

Ligands	PLP fitness score	Hydrogen bonds/Hydrophobic bonds.	
		H- Bonds	Hydrophobic bonds
H2	94.21	ALA:11, ILE:112, ALA:115	THR:118, ILE:19, MET:25, VAL:10, GLY:114, THR:147, LYS:22, ILE:117, LYS:57, GLU:116.
H3	104.14	ALA:115, THR:58, ILE:19, ALA:11	ILE:33, ILE:112, PHE:36, LEU:69, MET:25, VAL:10, TYR:118, GLY:114, ILE:117, ARG:56, LYS:57, GLU:116
H4	73.83	THR:58, SER:61.	ILE:62, LEU:69, LYS:57, TYR:118, ALA:11, VAL:10, ILE:19, MET:25, ILE:112.

Table 7. Docking results of Compounds (H2-H4) with PDB: 1HSK

Ligands	PLP fitness score	Hydrogen bonds/Hydrophobic bonds.	
		H- Bonds	Hydrophobic bonds
H2	71.16	SER:82, ASN:83, ARG:225.	PRO:141, TYR:149, ARG:310, ILE:84, MET150, GLY:146, ALA:152, ILE:140
H3	92.32	GLY:81, GLY:79.	PRO:141, LEU:231, TYR:42, PHE:274, GLY:145, VAL:198, ILE:192, TYR:77, VAL:199, ILE:84, MET;150, ALA:152.
H 4	64.78	ASN:83, TYR:77.	ILE:140, ALA:152, ALA:147, GLY:145, GLY:146, TYR:149, ILE:84, MET:150, ARG:188.

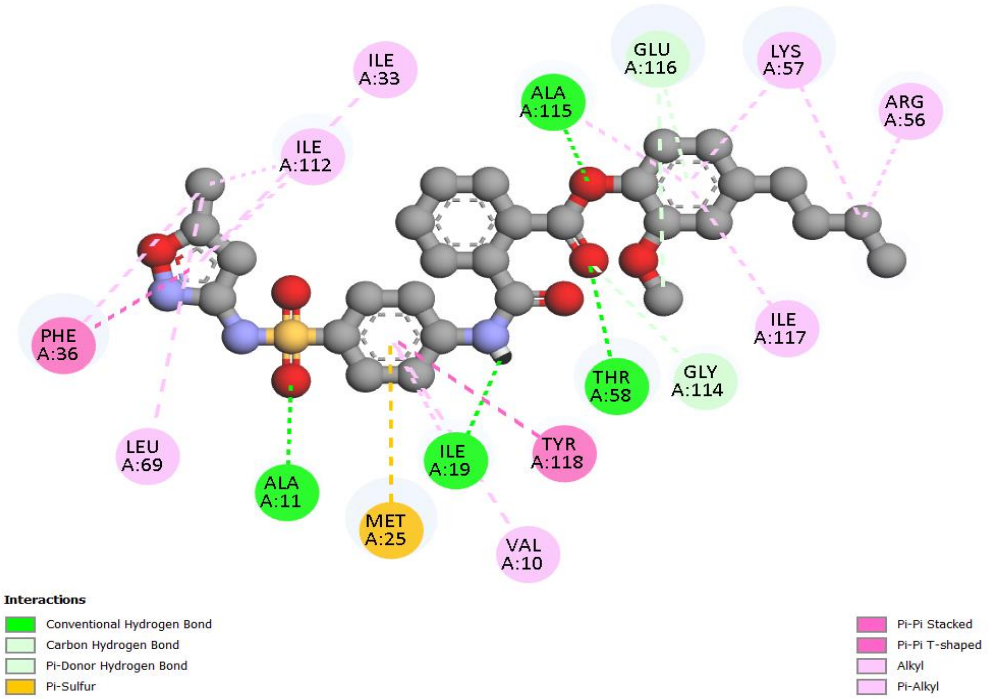
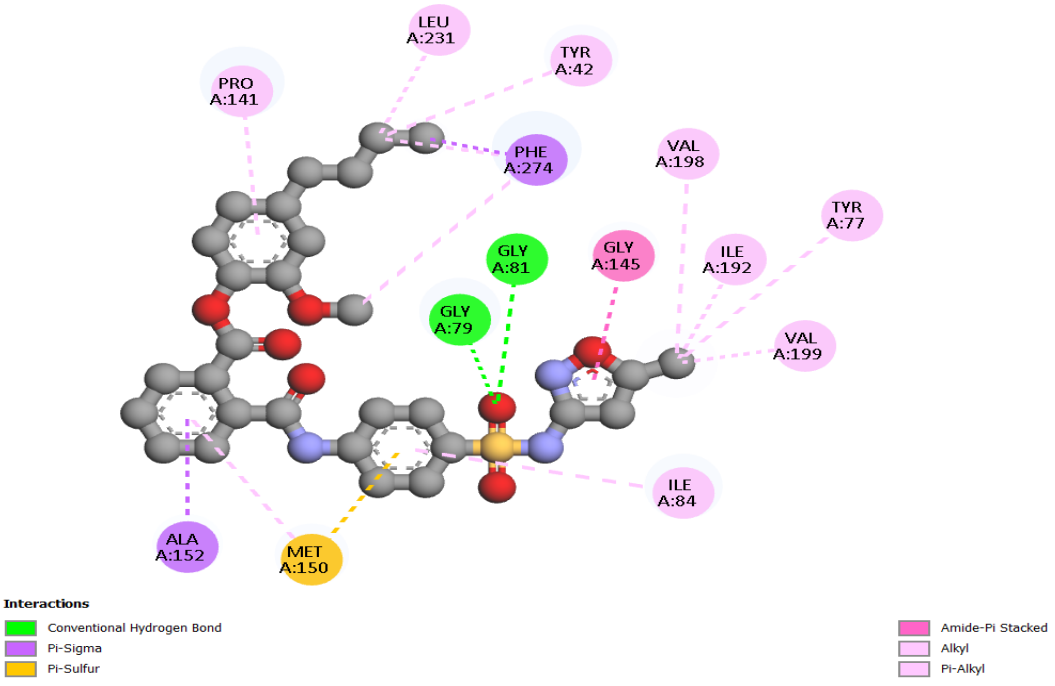


Figure 10. Molecular docking of DIHYDROFOLATE REDUCTASE PROTEIN Binding Domain Complexed with H3 shows 2D



model of the interactions.

Figure 11. Molecular docking of UDP-N-ACETYLENOLPYRUVOYLGLUCOSAMINE REDUCTASE PROTEIN Binding Domain Complexed with H3 shows 2D model of the interactions.

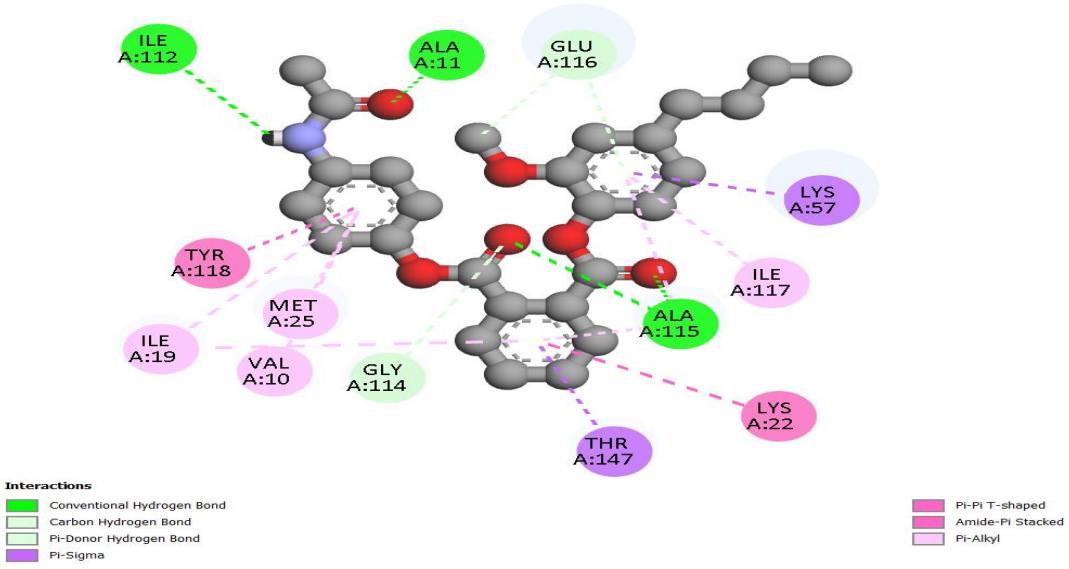


Figure 12. Molecular docking of DIHYDROFOLATE REDUCTASE PROTEIN Binding Domain Complexed with H2 shows 2D model of the interactions.

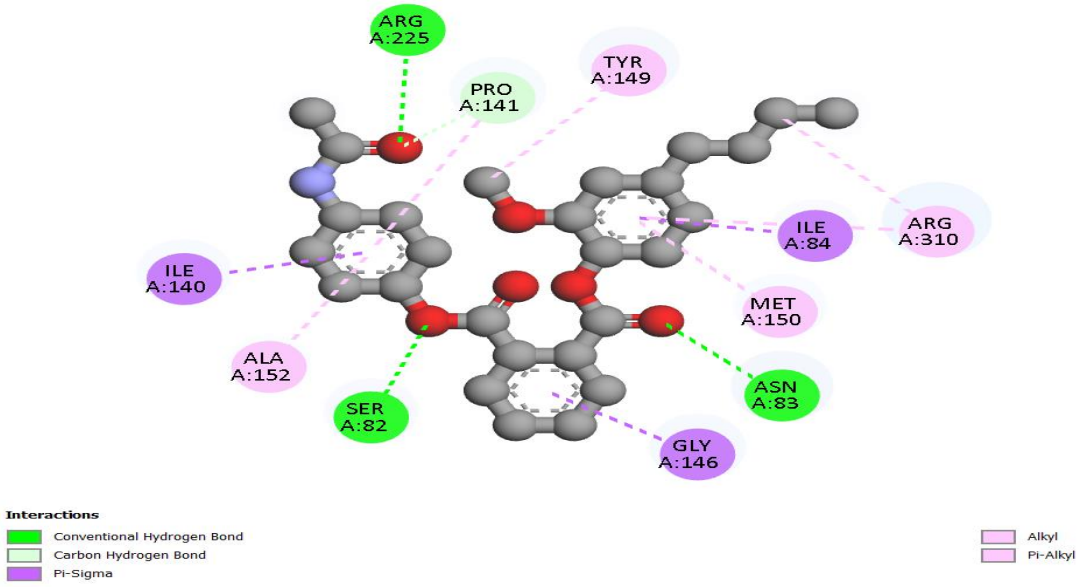


Figure 13. Molecular docking of UDP-N-ACETYLENOLPYRUVOYLGLUCOSAMINE REDUCTASE PROTEIN Binding Domain Complexed with H2 shows 2D model of the interactions.

4. Conclusion

Eugenol and phthalic anhydride were combined in the research effort to create molecules, which were then integrated with pharmaceuticals like paracetamol, sulfamethoxazole, and phenylephrine. Compound H3 is the primary inhibitor of both DHFR and MurB enzymes due to its high PLP fitness score. The proper structure and degree of purity of all synthesized derivatives were established by the combination of FTIR and 1H-NMR spectroscopy.

The analytical tests demonstrated successful controlled chemical changes and demonstrated that functional groups were appropriately integrated. According to the biological testing, when it comes to

common pathogenic microbes like Candida albicans, Escherichia coli, and Staphylococcus aureus, the generated complexes show strong antibacterial and antifungal properties. These structural elements combine nitrogen functional groups with aromatic rings to increase biological activity. adding sulfamethoxazole and phenylephrine structures to the derivatives improved their antibacterial qualities beyond those of paracetamol derivatives.

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Conflicts of Interest

There are no conflicts of interest, according to the authors.

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Ethics Statements

The study does not require ethical authorization.

Author Contribution

The authors attest to their involvement in the work. Each author examined the findings and gave their approval to the completed work.

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