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Therapeutic Insights into Cucumber Peel: Phytochemical Profiling and Docking Against Key Inflammatory Enzymes

Lubna Kanwal*
Department of Zoology, University of Okara, Okara, Pakistan
Phone: +92 (0) 3052999575, Email: lubna.kanwal@uo.edu.pk

Amina Nasrullah
Department of Zoology, University of Okara, Okara, Pakistan

Habiba Anum
Department of Chemistry, Lahore College for Women University, Lahore, Pakistan

Maqsood Ahmad
Department of Statistics, University of Okara, Okara, Pakistan

Author Details

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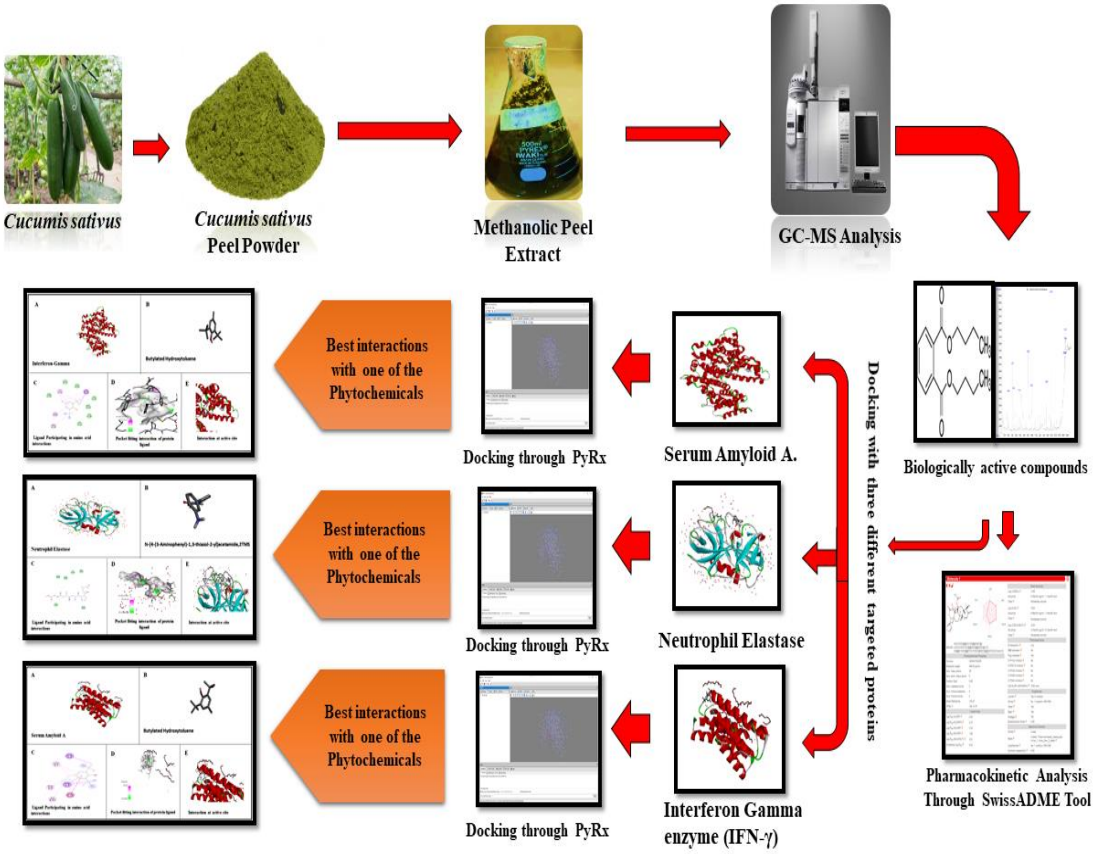
Corresponding E-mail & Author*:

Lubna Kanwal*
Department of Zoology, University of Okara, Okara, Pakistan
Phone: +92 (0) 3052999575, Email: lubna.kanwal@uo.edu.pk

Abstract

Cucumis sativus L, a widely consumed vegetable has been traditionally used for its medicinal properties. Despite its medical promise, little is known about this plant's phytochemicals. C. sativus exhibits anti-inflammatory, antioxidant and anti-bacterial characteristics, demonstrating potential for the treatment of various inflammatory disorders. Therefore, present research aimed to investigate the metabolite profile of the methanolic peel extract of C. sativus using gas chromatography-mass spectrometry (GC-MS), and to evaluate its therapeutic potential through in-silico molecular docking analysis. The GC-MS analysis showed the diverse phytochemicals exhibited notable biological potentials. Pharmacokinetic evaluation using SwissADME revealed favorable drug-like properties for the identified compounds. Furthermore, to evaluate the inhibitory potential of these compounds from C. sativus, all of the compounds were docked against the active sites of the target enzyme. Twelve bioactive compounds were identified from this peel extract, six of which exhibited great binding affinity to suppress the upregulation of three different enzymes. Notably, these phytocompounds showed inhibitory potential against the enzymes Serum Amyloid A, Neutrophil Elastase, and Interferon Gamma, which are linked with the pathogenesis of infections and inflammatory diseases including Pneumonia, Cystic Fibrosis, and Tuberculosis respectively. The results suggest that Cucumis sativus extract may be a valuable source of bioactive compounds for the prevention and treatment of different ailments including infectious and inflammatory disorders. This study provides a comprehensive understanding of the therapeutic potential of this plant, making it possible for future drug discovery and development.

Graphical abstract



Introduction

Plants are vital for human survival, providing food and medicinal benefits. Traditional medicine systems use herbs to heal and balance body chemistry [1]. Herbal medicine utilizes plants and plant extract to treat various ailments, applicable topically or consumed orally. Civilizations have used herbal remedies for centuries to address diseases like malaria and digestive issues [2]. Ethno-pharmacological surveys reveal rural and ethnic herbal medicine use [3]. The WHO says 80% of the globe uses medicinal plants for health. Despite more than 70,000 plants being used, only 15% have been studied medically. Ethno-pharmacology fuels drug discovery [4].

Cucumis sativus L (Cucumber), versatile plant in the Cucurbitaceae family, used as a vegetable and in traditional medicine for its antimicrobial and antioxidant characteristics. It grows up to 2 meters annually, with distinctive leaves and fruits up to 60 cm long [5].

Cucumbers are 90-95% water, alkaline-rich and contain cancer fighting compounds. They are vulnerable to anthracnose, Fusarium wilt and downy mildew [6]. C. sativus shows multiple pharmacological effects, including antibacterial, antioxidant and hepatoprotective properties due to its diverse chemical constituents [7]. Cucumis sativus Linn (Kheera), contains valuable phytoconstituents including tannins, alkaloids, saponins, flavonoids, and phenolic chemicals. Its low calorie, high water content makes it a nutritious option [8].

Phytochemicals are biologically active plant compounds with phyto derived from the Greek word for plant [9]. Phytochemical found in all plant parts, comprise around 4,000 classified compounds including carotenoids, polyphenols and flavonoids with potential medicinal applications [10]. Phytochemicals are not needed for human survival, but they can help prevent or treat many common illnesses [11].

C. sativus seeds may include phytochemicals, terpenoids, tannins, and flavonoids [12]. The Chromatography-Mass Spectrometry (GC-MS) study of cucumber peel's

methanolic extract showed the presence of diverse phytochemicals including, Thymine, 1,3,5-Triazine-2,4,6-triamine, 4H-Pyran-4-one,2,3-dihydro-3,5- **dihydroxy-6-methyl,** Glyceraldehyde, N-Methoxy-N-methylacetamide, 1,2,3-Propanetriol,1-acetate, Glycerol 1,2-diacetate, Butanoic acid, 3-oxo-, hexyl ester, Butylated Hydroxytoluene, Butanoic acid,2-oxo-,.alpha.-D-Digitoxopyranose, D-erythro-Pentose,2-deoxy-, n-Hexadecanoic acid [13].

Serum Amyloid A (SAA) binds High-Density Lipoproteins (HDLs) in the blood [14]. SAA proteins have been found to help with metalloproteinase-mediated tissue remodeling, atherosclerosis-related local tissue alterations, cancer metastasis, lung inflammation, fetal and maternal health, and intestinal physiology [15]. Acute Phase response (ARP) produces SAA, a major acute-phase protein. During the acute phase reaction, blood SAA levels rise, indicating active inflammation [16].

Researchers discovered Neopterin (NP) and SAA as biomarkers for detecting pneumonia and other infections in stroke patients, offering potential for improved diagnosis. SAA is sensitive and helpful for evaluating mycoplasma and viruses in community-acquired pneumonia patients. Dynamic SAA monitoring can assess patient growth, prognosis, and therapy efficacy [6]. Pneumonia commonly caused by bacterial, viral, fungal and parasitic infections [17]. Pneumonia a global health threat caused 50,000 US deaths and 1 million hospitalizations annually pre COVID-19 [18].

Neutrophil elastase (NE) fights germs, but its release in airways paradoxically contributes to lung disease, highlighting a delicate balance between its protective and destructive roles [19]. Neutrophil bridge innate and adaptive immunity, protecting against respiratory illnesses by clearing cellular waste and pathogens [20]. NE levels in sputum predict clinical outcomes for cystic fibrosis and bronchiectasis patients, balancing infection control and inflammation [21]. Cystic fibrosis affects 60,000 worldwide, with Pseudomonas aeruginosa infecting nearly half of patients and over 80% of adults [22].

Interferon-gamma (IFN-γ) is essential for immune defense, controlling responses to infections and cancer but excessive levels can lead to tissue damage and inflammation. IFN-γ strengthens innate and adaptive immunity, fighting cancer and other threats [23]. Tuberculosis is a global health issue. The immunological response to tuberculosis is mediated by the interferon system, specifically interferon-gamma [24].

Molecular docking has become a key activity in computer-assisted drug creation due to its ability to boost efficiency and lower research expenses [25]. A computational modelling technique called molecular docking can determine the preferred binding orientation of a ligand and a receptor when they form a stable complex [26]. If in-silico models can replicate or surpass in-vitro or ex-vivo trials in reflecting relevant clinical circumstances, these methods can be replaced [27].

Materials and Methods

Gathering and determining plant material

Cucumis sativus (Cucumbers) were purchased from a nearby market and their peels were removed using a peeler.

Preparation of methanolic extract of Cucumis sativus peel

After washing with tap water, fresh Cucumis sativus peels were dried in the shade at room temperature before use. The dried peels were ground into a coarse powder with an electric grinder, sieved to remove larger particles, and stored in a zip-lock plastic bag for later use. For extraction, 50 g of powdered peel was dissolved in 75% methanol at a ratio of 1 g:10 mL. The mixture was subjected to shaking at 24 °C and 250 rpm in an orbital shaker for 72 h. After extraction, the solution was filtered through Whatman No. 1 filter paper and dried at 40°C. It was kept at 4°C for later use.

Analysis of gas chromatography-mass spectrometry (GC-MS)

The bioactive components of C. sativus methanolic extract were examined using GC-MS. At various concentrations, these components comprised flavonoids, alkaloids, phenols, saponins, reducing sugars, steroids, tannins, and glycosides. Agilent's GC 7890B and MS 5977A gas chromatography-mass spectrometry (GC-MS) system used a capillary standard and DB 5MS nonpolar column. It measured 30 millimeters long, 0.25 millimeters wide, and 0.25 micrometers thick. Helium was the carrier gas, and the mobile phase flowed one milliliter per minute. The temperature of the oven went from 50 to 250 °C at 10 °C/min for 5 min and then it went up to 300 °C for 10 min. Injection volumes were set at one microliter (μL). For GC-MS, a 70 eV electron ionization energy system was used. The total running time was 49 minutes. The methanol was used to dissolve the extract and analyzed with a 10-850 m/z mass spectrometer. We identified the extract's active components by comparing retention indices, peak area percentages, and mass spectra fragmentation patterns to the NIST database [28].

Pharmacokinetic Analysis

The Phytocompounds derived after GC-MS analysis from C. sativus were further analyzed for pharmacokinetic profiles using SwissADME by entering the SMILES formula of each substance. Lipinski Rule of Five analyses were carried out to determine the pharmaco-kinetic ability of the compound.

Ligand-Protein Docking Study

Three proteins docked with Phytocompounds from C. sativus. NE, SAA, and interferon-gamma were these proteins. Molecular docking studies using PyRx 0.8 revealed ligand-protein binding mechanisms. RCSB-PDB provided the receptor protein's 3D structure in PDB format. The PubChem database included SDF chemical structures of active phytoconstituents. After integrating polar hydrogen atoms, eliminating water molecules, and releasing protein ligands, the desired protein structure was created. Then, we utilized the BIOVIA Discovery Studio Visualizer (version 21.1.0.20298) to create and visualize Phytocompounds-target protein interactions and maps [29].

Results

Identification of bioactive compounds of C. sativus peel extract by GC-MS

GCMS analysis of C. sativus methanolic peel extract evident in Figure. 2, showed the presence of 12 bioactive compounds. The molecular formula, peak area, and retention length of phytochemicals assisted in determining them. Retention time and mass spectra are compared to databases or standards to locate peaks. This method helps in the identification of compounds present in the extract of the plant. The compound with a high peak area shows more concentration of that compound in the extract. All of these compounds with their class name, peak area, retention time, and structure are given in Table 1. A compound Dibutyl phthalate showed the highest peak of 22.10 % with RT of 14.879 minutes while N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl]acetamide, 2TMS showed the lowest peak of 3.67 % with RT of 18.402 minutes.

The GC-MS chromatogram of C. sativus peel extract is shown in Fig. 1.

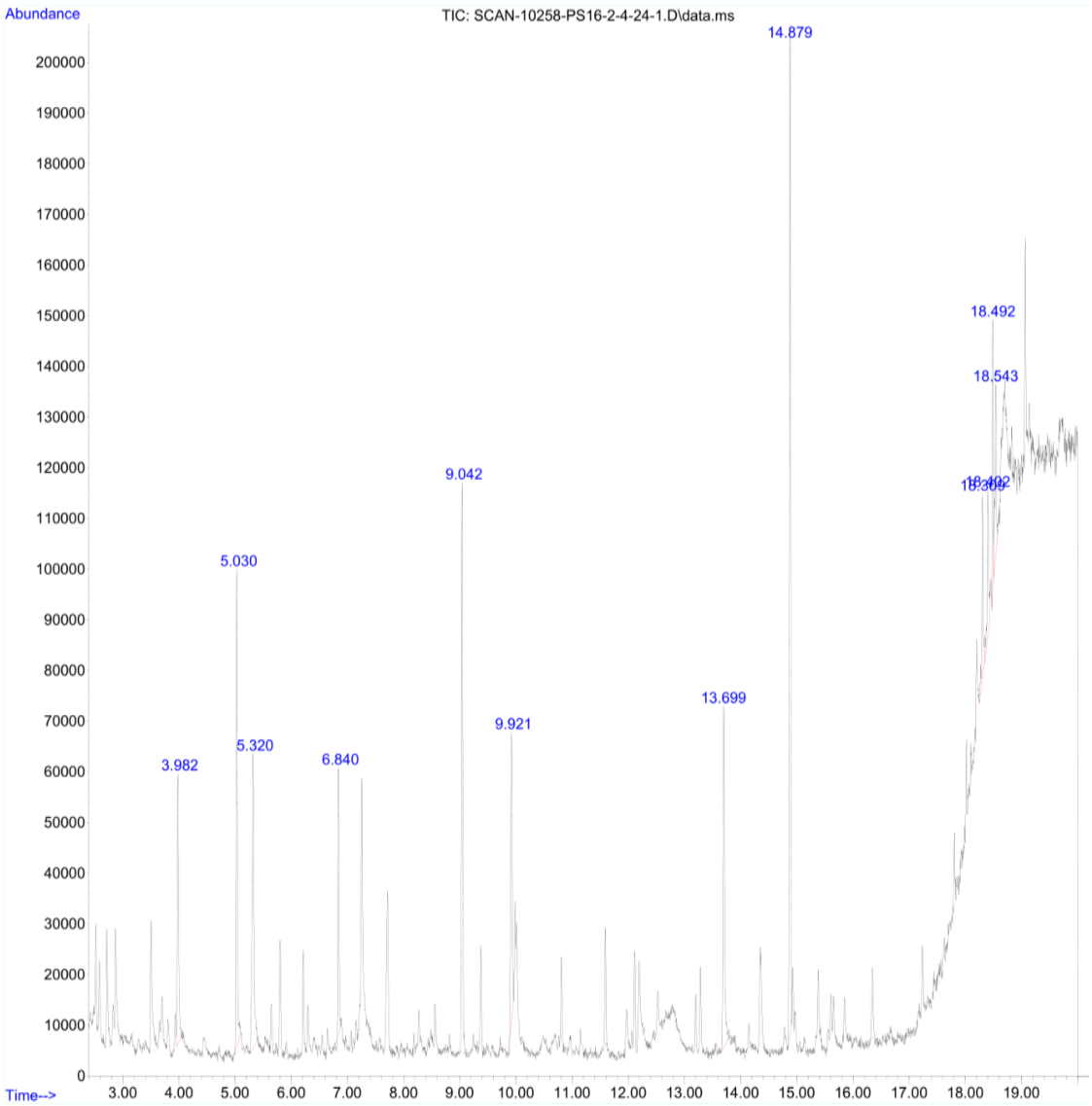


Fig. 1 GC-MS chromatogram of methanolic peel extract of *Cucumis sativus*

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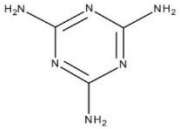
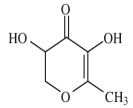
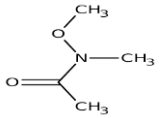
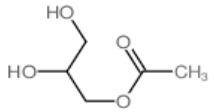
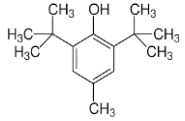
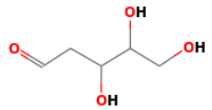
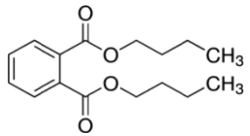
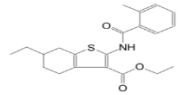
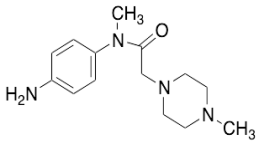
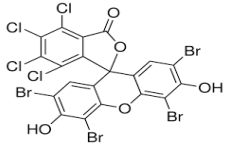
Table 1. GC-MS extracted bioactive compounds from the C. sativus methanolic peel extract.

Sr. No.	Compound name	Class name	Peak area (%)	RT	Structure
1.	1,3,5-Triazine-2,4,6-triamine	Triazines	6.92	3.982	
2.	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	Pyranones	10.66	5.030	
3.	N-Methoxy-N-methylacetamide	Amides	9.63	5.320	
4.	1,2,3-Propanetriol,1-acetate	Polyols	5.05	6.840	
5.	Butylated Hydroxytoluene	Hydroxytoluenes	12.47	9.042	

6.	D-erythro-Pentos, 2-deoxy	Deoxysugars	8.02	9.921	
7.	n-Hexadecanoic acid	Fatty acids	9.43	13.699	
8.	Dibutyl phthalate	Phphalates	22.10	14.879	
9.	Benzothiophene-3-carboxylic acid,4,5,6,7-trtrahydro-2-amino-6-ethyl-,ethyl ester	Benzothiophenes	3.81	18.309	
10.	N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl]acetamide,2TMS	Phenylthiazoles	3.67	18.402	
11.	Stannane, tetraethyl	Alkylstannanes	4.13	18.492	
12.	Ethyl 5'-amino-2,3' -bithiophene-4'-carboxylate	Thiophenes	4.10	18.543	

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Pharmacokinetic Analysis of Cucumis sativus Phytoconstituents

The Phytocompounds derived after the GCMS analysis of C. sativus were analyzed for pharmacokinetic profiles using SwissADME by entering the SMILES notation of each active compound. Lipinski Rule of Five (LR5) was used to assess the pharmacokinetic ability of the compound. The compounds meeting the LR5 criteria were categorized as drug like. Furthermore, we identified the physicochemical features such as hydrogen bond donors and acceptors, lipophilicity (LogP), molecular weight and drug-likeness were analyzed. We also analyzed the medicinal chemistry of the compounds as shown in Table 2.

Table 2. Pharmacokinetic Analysis of C. sativus Constituents

Sr. No.	Compound	Molecular Mass(g/mol)	Acceptor H	Donor H	LogP	Lipinski
1.	1,3,5-Triazine-2,4,6-triamine	126.12	3	3	-1.27	Yes
2.	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	144.13	4	2	-0.22	Yes
3.	N-Methoxy-N-methylacetamide	103.12	2	0	0.08	Yes
4.	1,2,3-Propanetriol,1-acetate	134.13	4	2	-0.46	Yes
5.	D-erythro-Pentos, 2-deoxy	134.13	4	3	-1.16	Yes
6.	n-Hexadecanoic acid	256.42	2	1	5.20	Yes
7.	Dibutyl phthalate	278.34	4	0	3.69	Yes
8.	Benzothiophene-3-carboxylic acid,4,5,6,7-trtrahydro-2-amino-6-ethyl-,ethyl ester	176.12	6	4	-1.28	Yes
9.	N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl] acetamide,2TMS	233.29	2	2	1.65	Yes
10.	Stannane,tetraethyl	384.48	4	0	4.07	Yes
11.	Ethyl 5'-amino-2,3'-bithiophene-4'-carboxylate	253.34	2	1	2.93	Yes

In-Silico Molecular Docking of Cucumis sativus **Peel Extract Phytocompounds Against Key Inflammatory Targets**

To evaluate the therapeutic potential of Cucumis sativus, molecular docking of its bioactive compounds (identified from the methanolic peel extract) was carried out against three key inflammatory enzymes: Serum Amyloid A (SAA), Neutrophil Elastase (NE), and Interferon Gamma (IFN-γ). The docking simulations were performed using the PyRx software, and binding affinities were recorded in terms of docking scores (kcal/mol). Compounds with higher binding affinity (i.e., more negative scores) were considered more promising as potential inhibitors. The results, along with PubChem IDs and reported biological activities of the ligands, are presented in Table 3.

Table 3. Molecular docking score of Bioactive Compounds from C. sativus Peel Extract against SAA, NE, and IFN-γ

Sr. No.	Ligand	PubChem ID	Docking Score			Reported Biological Activity
			SAA	NE	IFN-γ	
1.	1,3,5-Triazine-2,4,6-triamine	7955	-4.7	-4.8	-5.4	Antibacterial and antifungal activity [30].
2.	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-4.5	-4.3	-5.6	Antimicrobial, anti-inflammatory activity [31].
3.	N-Methoxy-N-methylacetamide	537505	-3.3	-3.1	-3.8	Anticancer activity and anti-proliferative activity against cell lines in breast cancer [32].
4.	1,2,3-Propanetriol,1-acetate	33510	-3.8	-3.3	-4.1	Antibacterial activity [33].
5.	Butylated Hydroxytoluene	31404	-6.2	-4.8	-6.6	Antioxidant [34].
6.	D-erythro-Pentos, 2-deoxy	5460005	-4	-4.1	-4.1	Antimicrobial [35].
7.	n-Hexadecanoic acid	985	-4.7	-4.2	-3.9	Antioxidant, antibacterial anti-inflammatory activities [36].
8.	Dibutyl phthalate	3026	-5.4	-4.7	-5.5	Antimicrobial and antifungal activity [37].
9.	Benzothiophene-3-carboxylic acid,4,5,6,7-trtrahydro-2-amino-6-ethyl-,ethyl ester	54670067	-4.9	-4.4	-5.4	Antimicrobial activity [38].
10.	N-[4-(3-Aminophenyl)-1,3-	6471763	-5.5	-5.3	-5.8	Anti-tumoractivity [39].

	thiazol-2-yl] acetamide,2TMS					
11.	Stannane,tetraethyl	3286	-3.9	-3.6	-3.8	Antimicrobial and antibacterial activity [40].
12.	Ethyl 5'-amino-2,3'-bithiophene-4'-carboxylate	718227	-4.4	-4.7	-4.5	Antimicrobial activity [41].

Molecular Docking of Phytocompounds with Serum Amyloid A.

Bioactive compounds in C. sativus extract were identified using molecular docking against Serum Amyloid A (SAA) protein using the PyRx docking tool. A total of 12 bioactive compounds, obtained through GC-MS analysis, were docked with SAA to evaluate their binding affinities. Among these, four compounds exhibited good binding energies. The molecular docking study revealed that Butylated Hydroxytoluene demonstrated the highest binding affinity with the protein, indicating a strong interaction and potential biological significance with the binding score of -6.2 (Fig. 2), N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl] acetamide, 2TMS with a binding score of -5.5 (Fig. 3), Dibutyl phthalate with a binding score of -5.4 (Fig. 4) and Benzothiophene-3-carboxylic acid,4,5,6,7-trtrahydro-2-amino-6-ethyl-, ethyl ester with docking score of-4.9 (Fig. 5). The molecular interactions between these compounds and the active site of SAA were visualized using the Discovery Studio software. Table 4 shows specific amino acid residues have binding interactions for each compound.

Table 4. Binding interaction residues of Phytochemicals with Serum Amyloid A (SAA)

Sr. No.	Ligand	PubChem ID	Docking Score (Kcal/mol)	Interaction Residues of (SAA)
1.	Butylated Hydroxytoluene	31404	-6.2	PHE A:4, LEU A:7, PHE A:6, ILE B:65, PHE B:69, PHE A:3
2.	N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl] acetamide, 2TMS	6471763	-5.5	ALA A:14, TRP A:18, ARG A:15, P A:4C203, PHE A:11
3.	Dibutyl phthalate	3026	-5.4	PHE A:3, PHE A:69, ILE B:65, PHE A:4, LEU A:7, GLN B:66
4.	Benzothiophene-3-carboxylic acid,4,5,6,7-trtrahydro-2-amino-6-ethyl-, ethyl ester	54670067	-4.9	TRP A:53, PRO A:49 GLU A:56, ASN B:64, ARG B:67, ILE B:65, PHE A:6, VAL A:52, PHE B:68

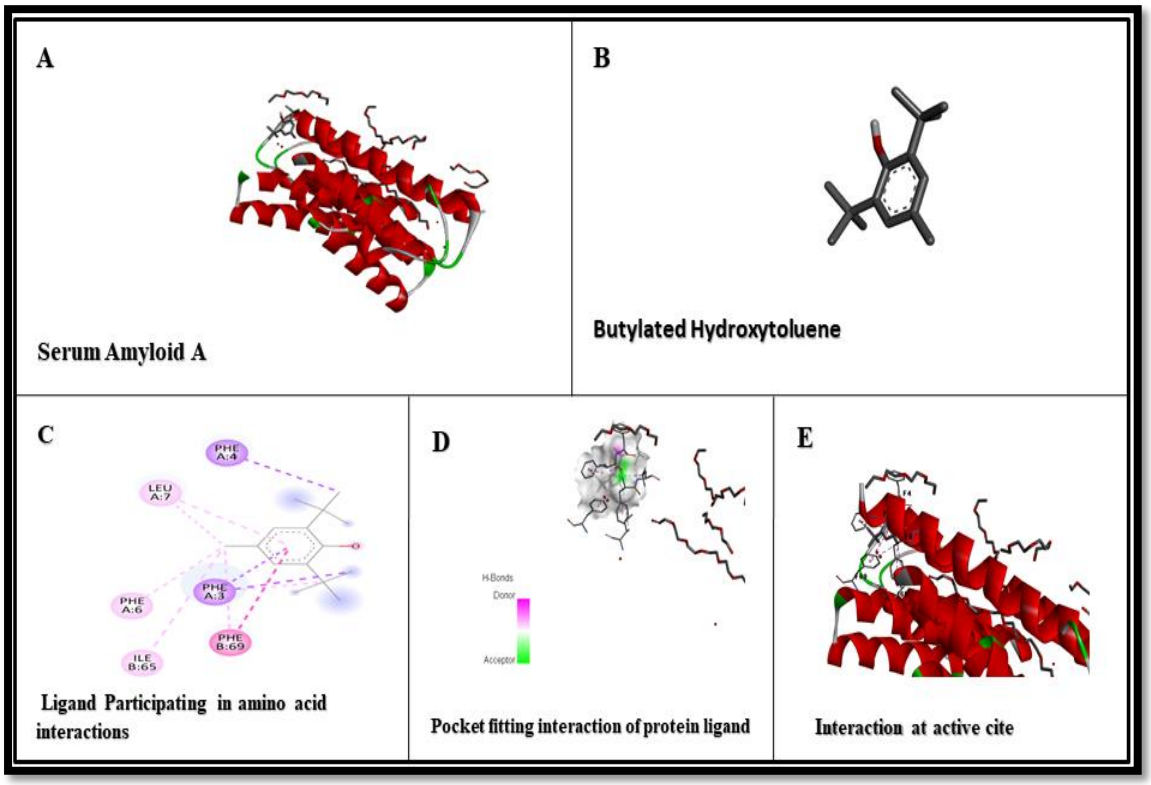

Fig. 2 Molecular interaction of Butylated Hydroxytoluene with Serum Amyloid A (SAA)

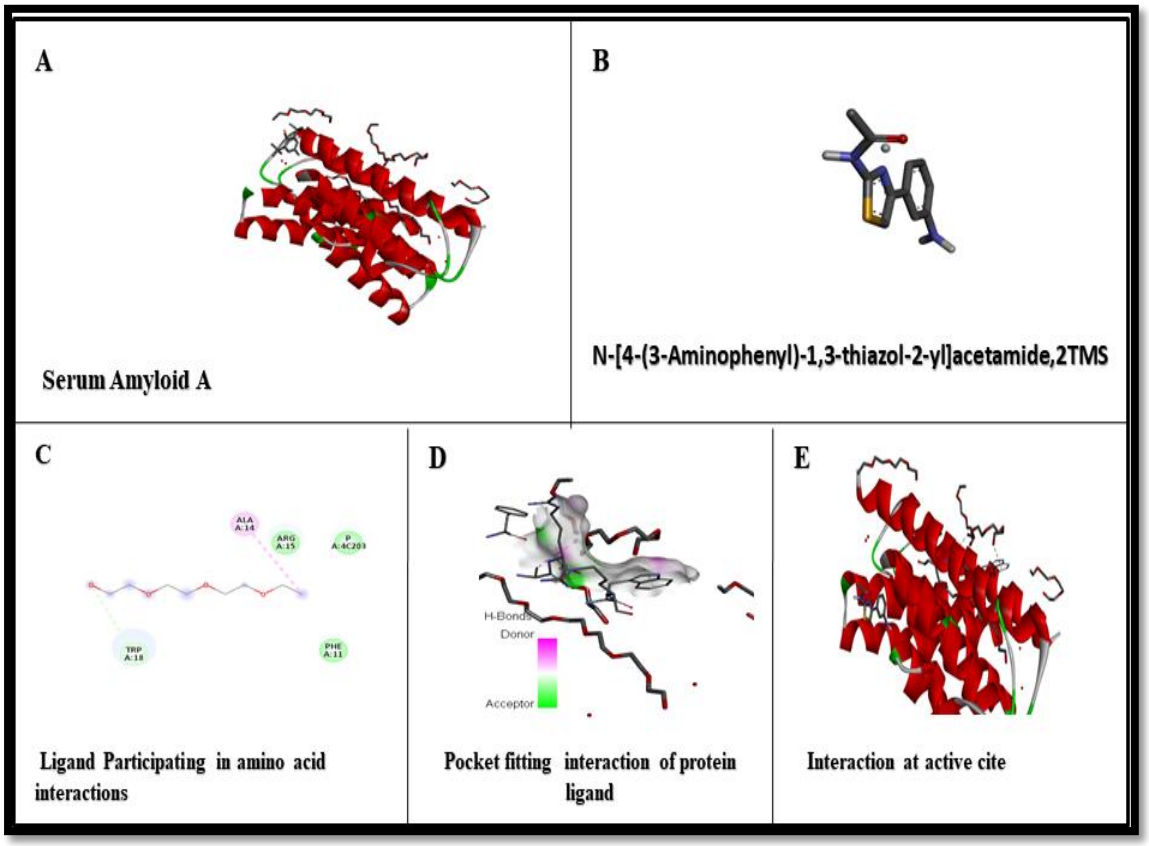

Fig. 3 Molecular interaction of N-[4-(3-Aminophenyl)-1,3-thiazol-2yl] acetamide, 2TMS with Serum Amyloid (SAA)

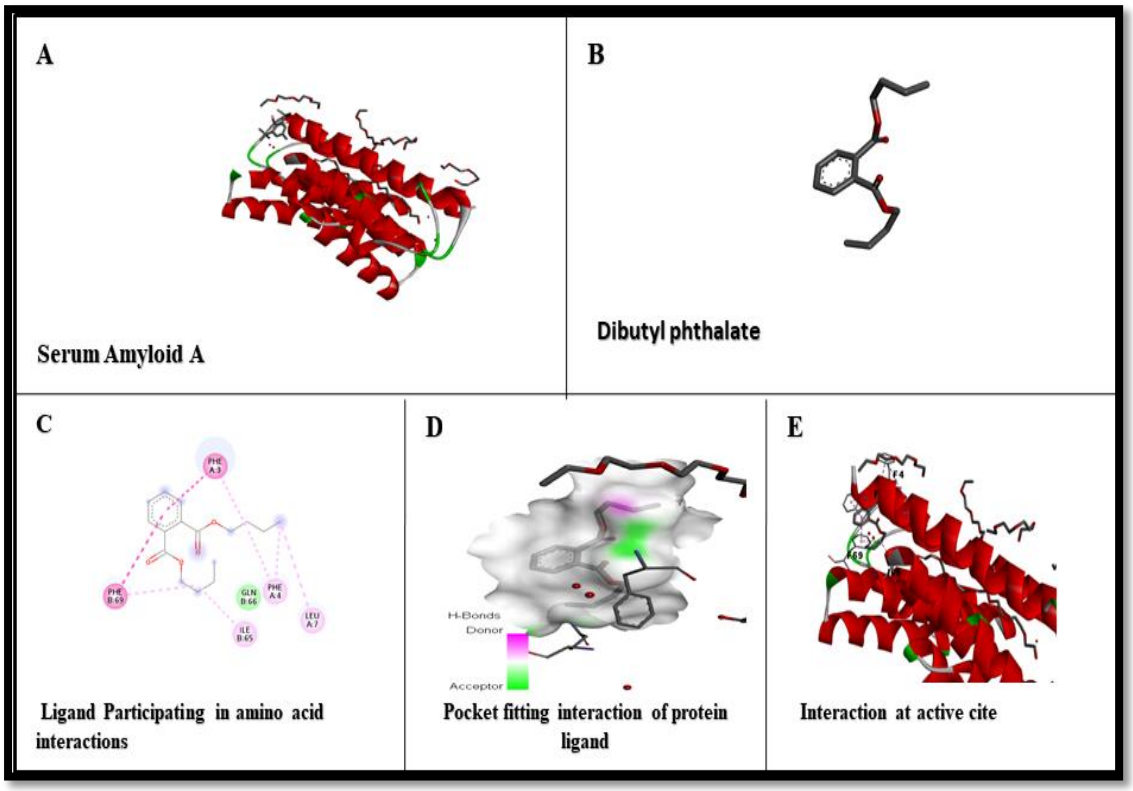

Fig. 4 Molecular interaction of Dibutyl Phthalate with Serum Amyloid A (SAA)

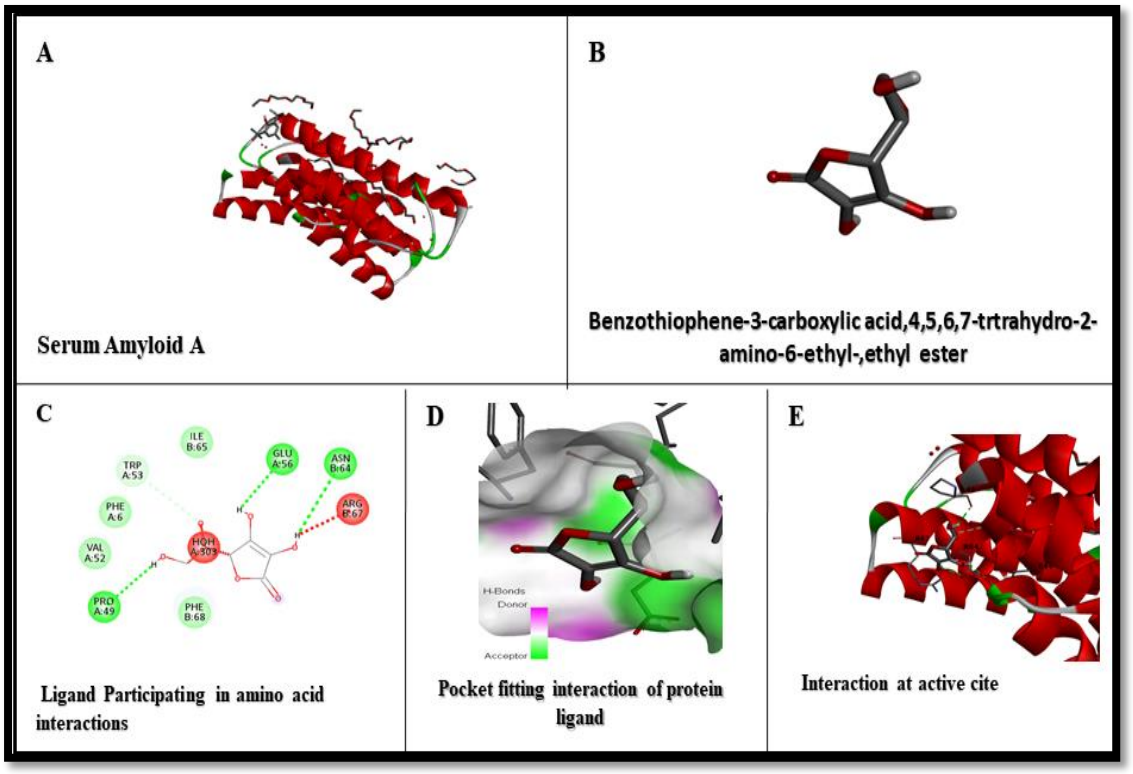

Fig. 5 Molecular interaction of Benzothiophene-3-carboxylic acid,4,5,6,7-trtrahydro 2-amino-6-ethyl-,ethyl ester with Serum Amyloid A (SAA)

Molecular Docking of Phytocompounds with Neutrophil Elastase

Four phytocompounds derived from Cucumis sativus exhibited notable binding affinities with Neutrophil Elastase. These compounds interacted with the target protein's active site by generating conventional hydrogen bonds and Van der Waals forces, exhibiting strong binding affinity. The top four docking complexes were, N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl] acetamide, 2TMS with binding score of -5.3 (Fig. 6), 1,3,5-Triazine-2,4,6-triamine with binding score of -4.8 (Fig. 7), Butylated Hydroxytoluene with docking score of -4.8 (Fig. 8), Ethyl 5'-amino-2,3'-bithiophene-4'-carboxylate with binding score of -4.7 (Fig. 9) respectively. Table 5 lists Discovery Studio-examined amino acid residues implicated in ligand-protein interactions.

Table 5. Binding interaction residues of the Phytochemicals with Neutrophil Elastase (NE)

Sr No.	Ligand	PubChem ID	Docking Score (Kcal/mol)	Interaction Residues of (NE)
1.	N-[4-(3-Aminophenyl)-1,3-thiazol-2yl]acetamide, 2TMS	6471763	-5.3	ASP E:194, CYS E:191, HOH E:457, HOH E:314, GLY E:218, HOH E:424
2.	1,3,5-Triazine-2,4,6-triamine	7955	-4.8	HOH E:457, CYC E:191, ASP E:194, GLY E:218, HOH E:424
3.	Butylated Hydroxytoluene	31404	-4.8	HOH E:417, HOH E:418, GLY E:205, VAL E:200, GLN E:122, ALA E:121, VAL E:120, ARG E:23, ALA E:26, HOH E:349, HOH E:446, PHE E:29, HOH E:360, TRP E:120, TRP E:27, HOH E:425, HOH E:332, HOH E:334, HOH E:388, PRO E:28, GLN E:119
4.	Ethyl 5'-amino-2,3'-bithiophene-4'-carboxylate	718227	-4.7	HIS E:57, MOH I:422, CYS E:58, MOH E:379, ILE E:151, MOH I:108, PRO I:4, ALV I:5, GLY C:193, I:OQ6, MOH I:148, CYS E:42, PHE E:41

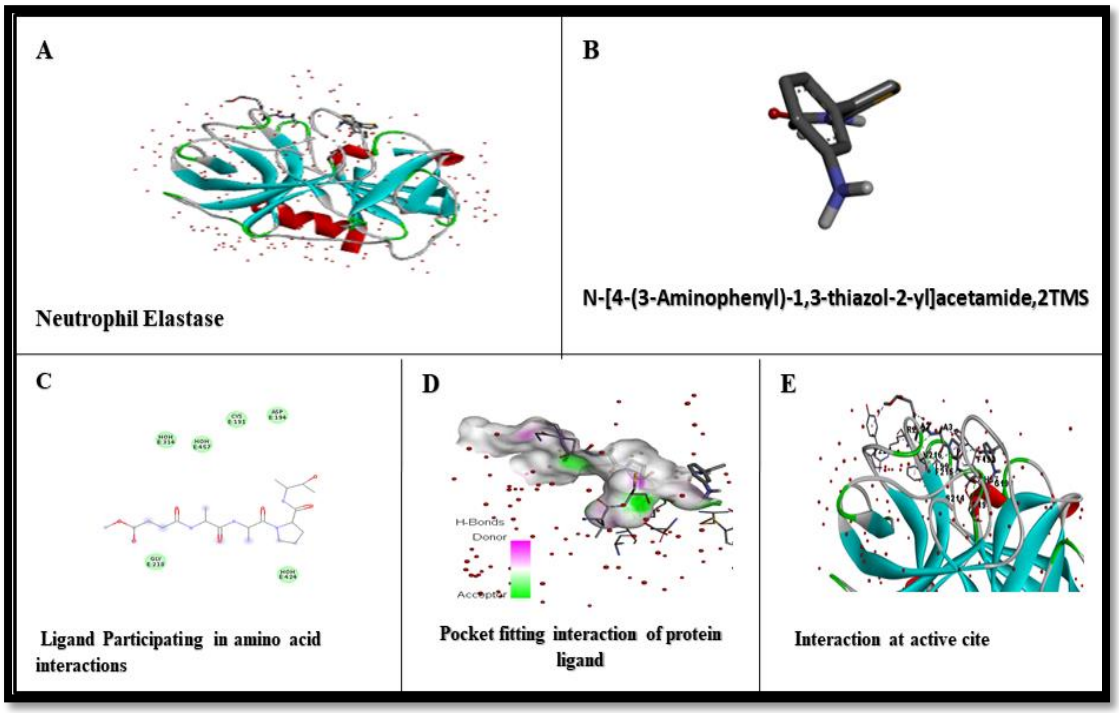

Fig. 6 Molecular interaction of N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl] acetamide, 2TMS with Neutrophil Elastase (NE)

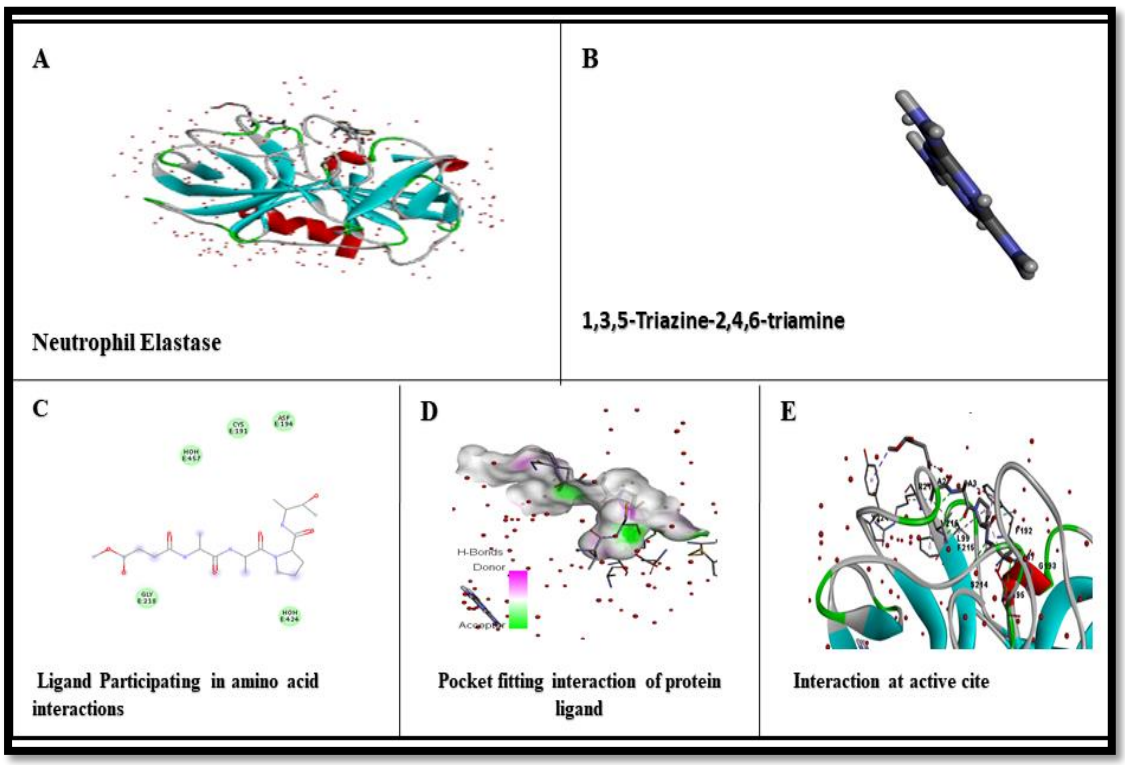

Fig. 7 Molecular interaction of ,3,5-Triazine-2,4,6-triamine with Neutrophil Elastase (NE)

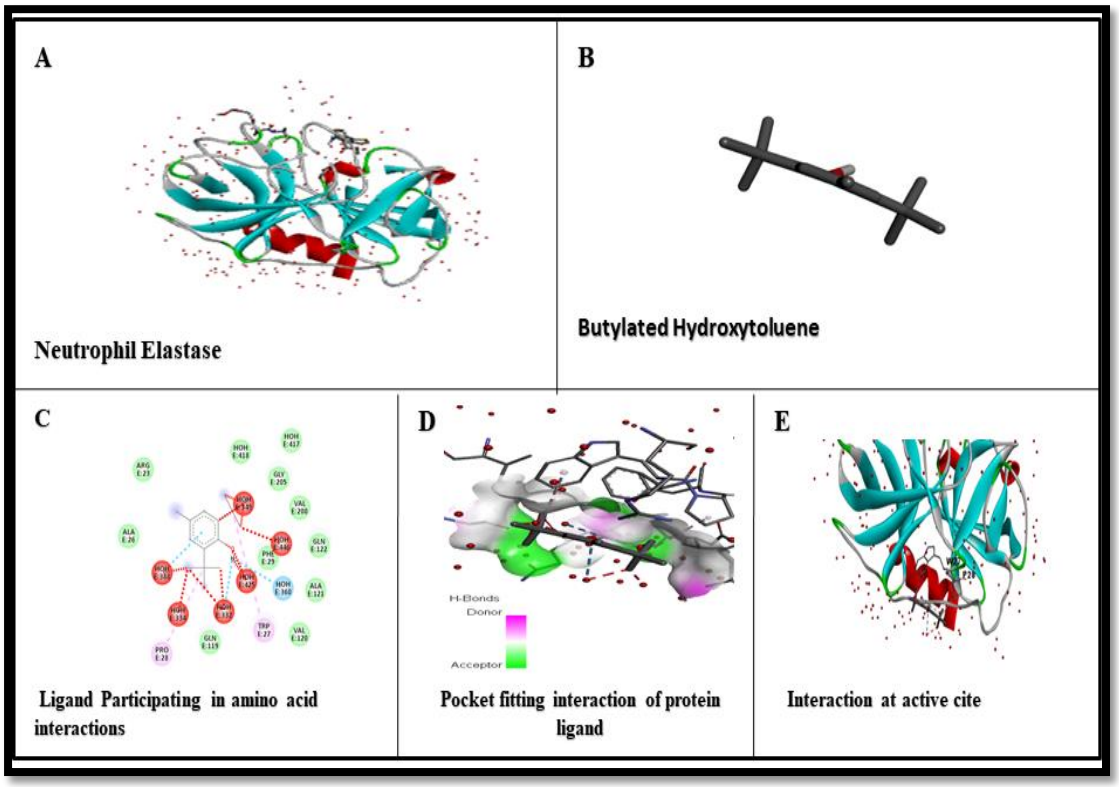

Fig. 8 Molecular interaction of Butylated Hydroxytoluene with Neutrophil Elastase (NE)

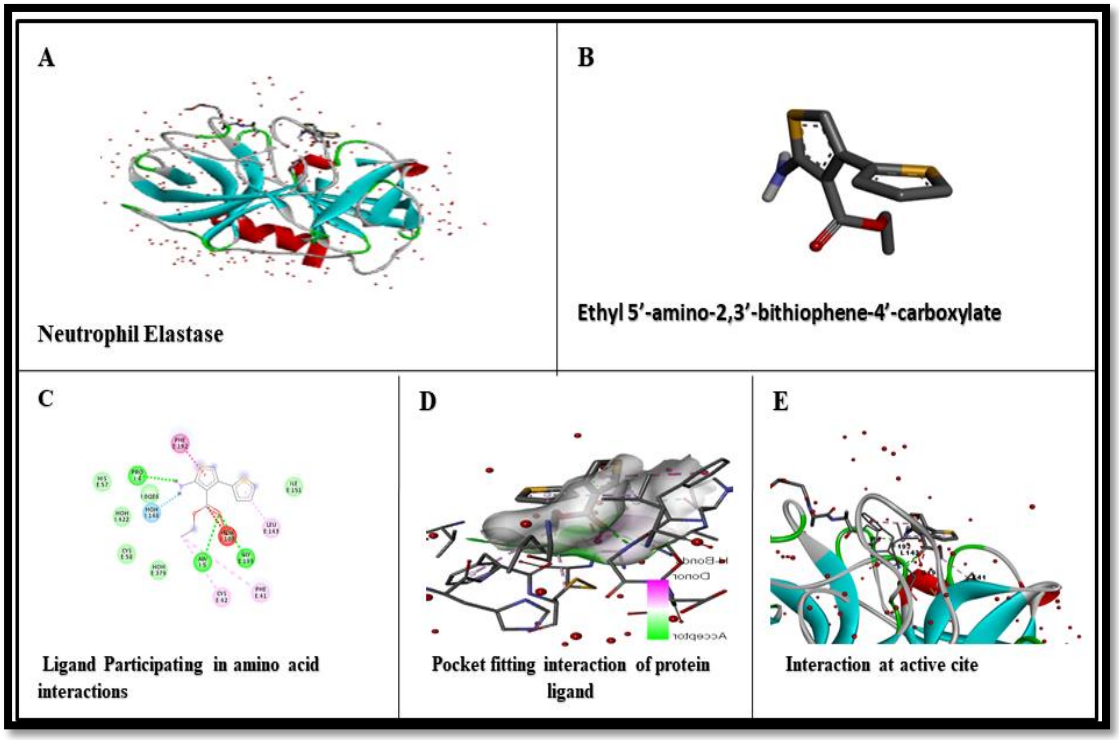

Fig. 9 Molecular interaction of Ethyl 5'-amino-2,3'-bithiophene-4'-carboxylate with Neutrophil Elastase (NE)

Molecular Docking of Bioactive compound with Interferon Gamma

The molecular docking study identified four phytocompounds from Cucumis sativus with favorable binding properties with Interferon Gamma. These compounds established stable interactions within the protein's active site through conventional hydrogen bonds and van der Waals forces, indicating strong binding potential. Protein Interaction with compounds were visualized using Discovery Studio. The docking complexes of the top four compounds were Butylated Hydroxytoluene with binding affinity of -6.6 in (Fig. 10), N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl] acetamide, 2TMS with binding score of -5.8 in (Fig. 11), 4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl with binding score of -5.6 in (Fig. 12) and Dibutyl phthalate with binding score of -5.5 in (Fig. 13). The participating amino acid residues at the proteins binding pockets are summarized in the Table 6.

Table 6. Binding interactions residues of the Phytochemicals with Interferon Gamma enzyme (IFN-γ)

Sr. No.	Ligand	PubChem ID	Docking Score (Kcal/mol)	Interaction Residues of (IFN-γ)
1.	Butylated Hydroxytoluene	31404	-6.6	LEU A:115, GLU A:141, TYR A:161, MET A123, TYR A:138, VAL A:122, THR A:133, LYS A:137, ALA A:126, PRO A:118, PHE A:134
2.	N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl]acetamide,2TMS	6471763	-5.8	PHE A:228, VAL A:325, SER A:232, ASP A:324, ALA A:350
3.	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-5.6	GLU A:292, GLU A:153, ALA A291, DKA A:1003, CIT A:2001, LYS A199, HIS A:242, TYR A:150, GIN A:196, LYS A:195
4.	Dibutyl phthalate	3026	-5.5	APG A:117, GLU A:141, TYR A:138, VRL A:116

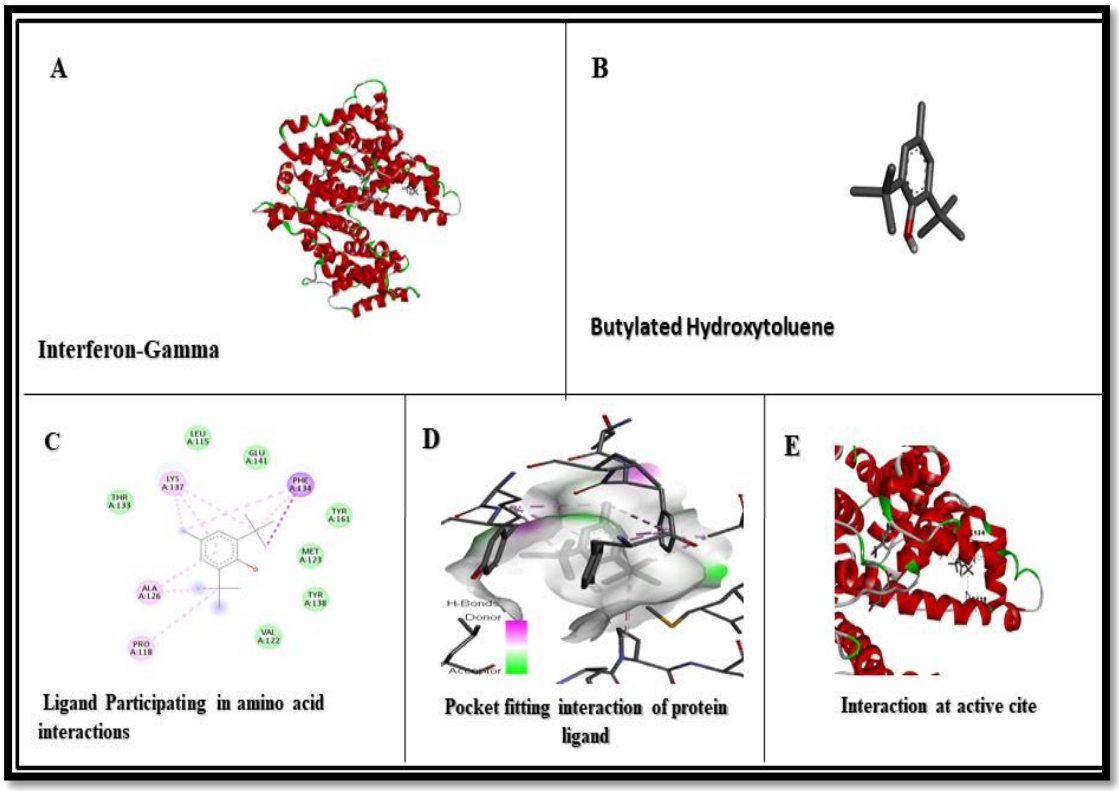

Fig. 10 Molecular interaction of Butylated Hydroxytoluene with Interferon Gamma (IFN-γ)

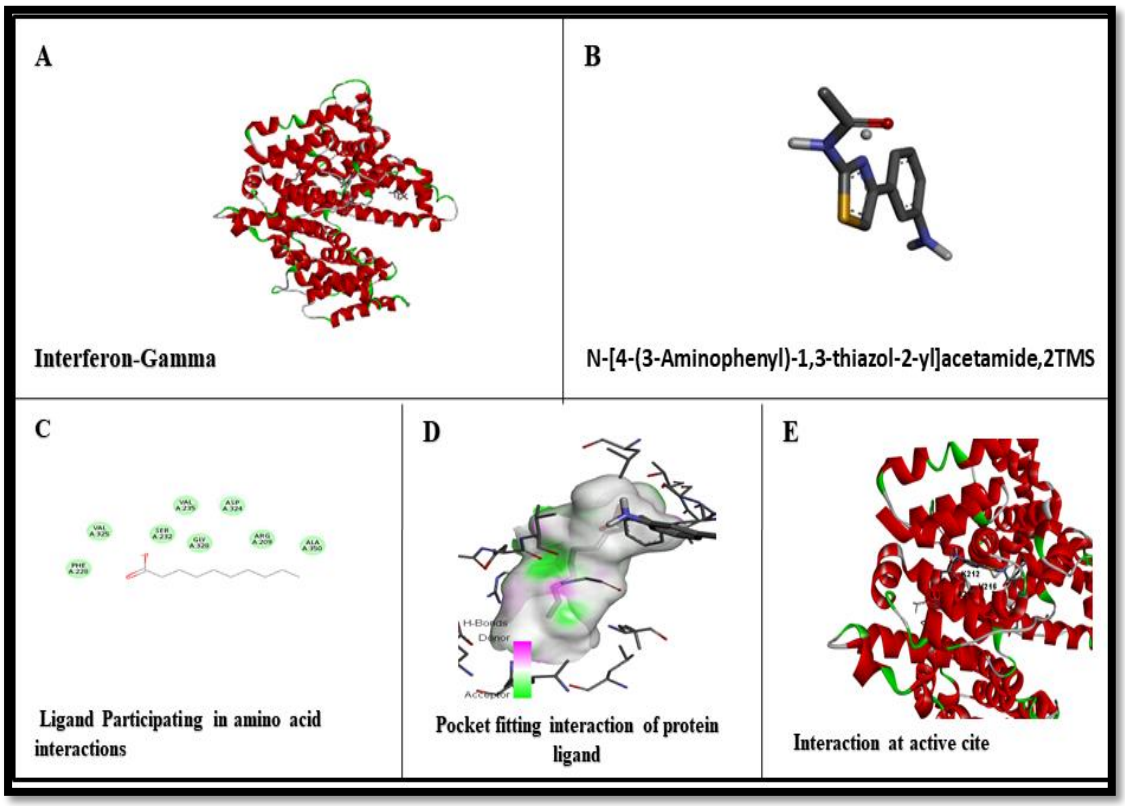

Fig. 11 Molecular interaction of N-[4-(3-Aminophenyl)-1,3-thiazol-2-yl]acetamide, 2TMS with Interferon Gamma (IFN-γ)

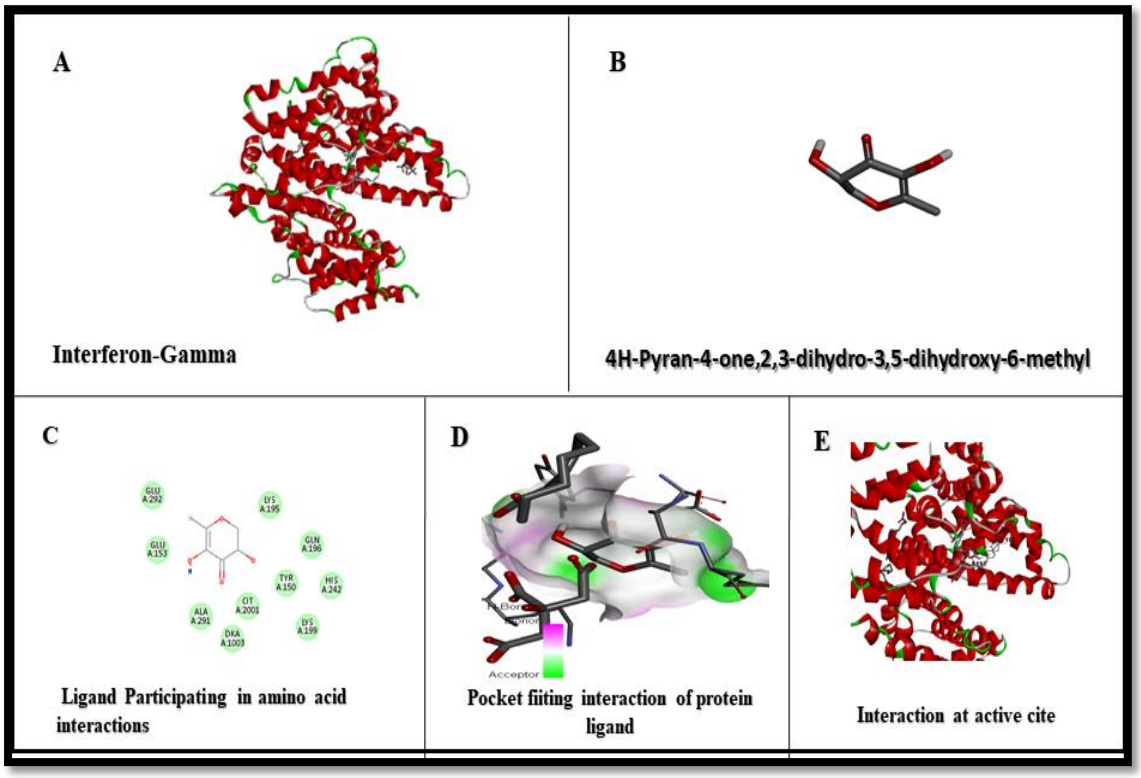

Fig. 12 Molecular interaction of 4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl with Interferon Gamma (IFN-γ)

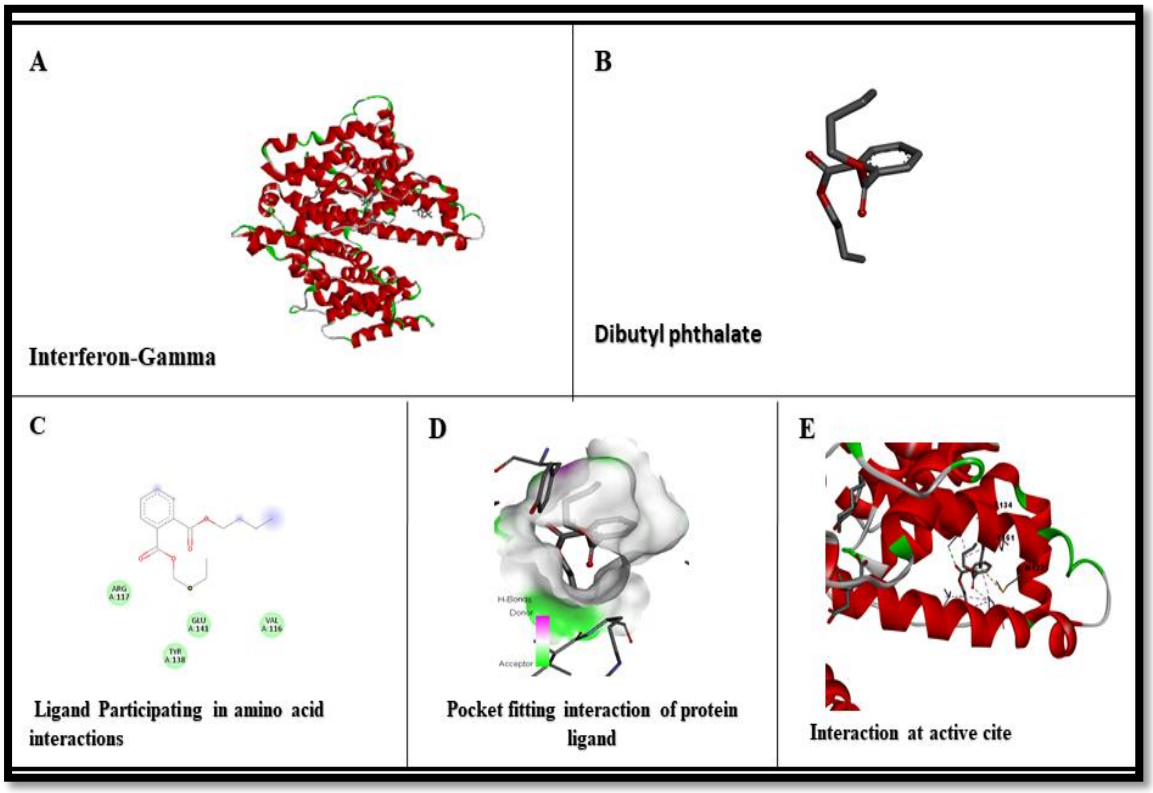

Fig. 13 Molecular interaction of Dibutyl Phthalate with Interferon Gamma (IFN-γ)

Discussion

Herbal remedies, the key component of traditional medicine, have shown significant global pharmacological and economic value. The study highlights their importance, as an estimated 80 % of pharmaceutical components derived from medicinal plants [42]. Herbal treatments offer temporary and permanent relief for cardiovascular illness, prostate issues, depression, inflammation, and immune system damage, without significant side effects. Herbal medicine has gained acceptance, supplementing modern allopathic medicines. Scientific studies including [43], validate herbal medicines efficacy in treating medical conditions driving demand for natural health products.

Our study validates that Cucumis sativus derived phytochemicals have diseases preventing and treating properties, aligning with previous findings [44]. Although non-essential for human survival, phytochemicals demonstrate significant health benefits, warranting further research into their preventive and therapeutic potential.

Phytochemicals possess significant anti-inflammatory and antioxidant activities consistent with previous research [45]. In vitro and in vivo research demonstrates phytochemicals antioxidant effects with Curcumin, resveratrol, and anthocyanins reducing inflammation by modulating cytokine production, enzyme inhibition and prostaglandin nuclear factor-κB activity.

Enzyme inhibitors found in nature and drugs regulate metabolism by binding to enzymes. Our research on herbal remedies, enzyme inhibiting properties, focusing on C. sativus phytochemicals builds on existing knowledge [46]. These compounds bind to enzymes, inhibiting biochemical reactions with potential therapeutic applications.

C. sativus possesses numerous phytoconstituents containing vitamins, minerals, amino acids, phytosterols, phenolic acids, fatty acids, and cucurbitacin, exhibiting antifungal, antacid, cytotoxic, hypoglycemic, carminative, hypolipidemic, hepatoprotective, anti-bacterial, wound healing, and anti-ulcerative properties [47]. GC-MS and pharmacokinetic analysis of C. sativus confirm its pharmacological potential aligning with previous research.

Acute inflammation results from increased blood vessel permeability, leading to edema and fluid accumulation. Research shows citrus fruits and C. sativus may be anti-inflammatory and antioxidant [48]. Our study identified biochemicals like n-hexadecanoic acid in C. sativus, demonstrating anti-inflammatory, antibacterial, and antioxidant activities.

Serum Amyloid A (SAA) cytokine recruits immune cells to protect tissues from pathogens. Our study supporting [49] findings, highlighting SAA role in inflammatory responses and its diagnostic value in assessing inflammation and treatment efficacy.

Mycoplasma pneumoniae (MP), causes community-acquired pneumonia in children, potentially leading to respiratory inflammation, immune disorders and multiple organ failure. SAA and C-reactive protein (CRP) levels significantly rise in response to MP and other infections [50].

Neutrophil secreted elastase contributes to inflammatory diseases like cystic fibrosis, rheumatoid arthritis and pulmonary fibrosis. Our findings relate with previous study [51], Emphasizing respiratory infections role in exacerbating elastase related conditions.

Globally, tuberculosis (TB) is the most significant infectious disease fatality. Interferon-gamma (IFN-γ) is a cytokine that helps the immune system in fighting infections. Interferon-gamma is an infectious disease biomarker. Our research findings, in line with earlier studies [52], indicate that several phytochemicals that may reduce interferon gamma overexpression, suggesting a therapeutic approach to managing tuberculosis.

GC-MS analysis identified 12 bioactive compounds in C. sativus, supporting its traditional use in treating various ailments. Consistent with our findings, GC-MS study can detect phytocompounds in plant extract [53].

Virtual molecular screening identified lead compounds with desired biological functions through protein-ligand docking. Our in-silico analysis using PyRx confirmed

previous research [54], demonstrating virtual screening's value in drug development and optimization.

Advances in computing power have popularized in-silico methods like network pharmacology and screening for understanding plant pharmacology. Consistent with recent research [55], predicting pharmacokinetics and bioactive properties, we used the web-based Swiss ADME method to predict the pharmacokinetics of bioactive chemicals found in cucumber extracts by GC-MS.

Conclusion

The present study focused on phytochemical analysis and in-silico study of methanolic peel extract of Cucumis sativus, provide important information on the safety and therapeutics of this plant. We uncovered the bioactive compounds present in Cucumis sativus peel extract through GC-MS analysis.12 biologically active compounds were found in the peel extract of this plant and few of them were found with good binding energies. Our pharmacokinetic analysis and molecular docking analysis further demonstrated the drug like properties of these compounds. This screening identified the methanolic peel extract of C. sativus as a possible inhibitor of three different enzymes including Serum Amyloid A, Neutrophil Elastase, and Interferon Gamma respectively. GC-MS has revealed several compounds with therapeutic purposes. This study shows that a new viewpoint on pharmacological research can lead to novel and more effective drugs for many diseases.

References

Aslam, M. S., & Ahmad, M. S. (2016). Worldwide importance of medicinal plants: Current and historical perspectives. Recent Adv Biol Med, 2(2016), 909.

Sam, S. (2019). Importance and effectiveness of herbal medicines. Journal of pharmacognosy and phytochemistry, 8(2), 354-357.

Ahmad, M., Zafar, M., Shahzadi, N., Yaseen, G., Murphey, T. M., & Sultana, S. (2018). Ethnobotanical importance of medicinal plants traded in Herbal markets of Rawalpindi-Pakistan. Journal of Herbal Medicine, 11, 78-89.

Süntar, I. (2020). Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. Phytochemistry Reviews, 19(5), 1199-1209.

Sharma, V., Sharma, L., & Sandhu, K. S. (2020). Cucumber (Cucumis sativus L.). Antioxidants in vegetables and nuts-Properties and health benefits, 333-340.

Mallick, P. K. (2022). Evaluating potential importance of cucumber (Cucumis sativus L.-Cucurbitaceae): a brief review.

Sahu, T., & Sahu, J. (2015). Cucumis sativus (cucumber): A review on its pharmacological activity. Journal of Applied Pharmaceutical Research, 3(1), 04-09.

Khan, A., Mishra, A., Hasan, S. M., Usmani, A., Ubaid, M., Khan, N., & Saidurrahman, M. (2022). Biological and medicinal application of Cucumis sativus Linn.–review of current status with future possibilities. Journal of Complementary and Integrative Medicine, 19(4), 843-854.

Velavan, S. (2015). Phytochemical techniques-a review. World Journal of Science and Research, 1(2), 80-91.

Balamurugan, V., Fatima, S., & Velurajan, S. (2019). A guide to phytochemical analysis. International Journal of Advance Research and Innovative Ideas in Education, 5(1), 236-245.

Nyamai, D. W., Arika, W., Ogola, P. E., Njagi, E. N., & Ngugi, M. P. (2016). Medicinally important phytochemicals: an untapped research avenue. Journal of pharmacognosy and phytochemistry, 4(4), 2321-6182.

Agatemor, U. M. M., Nwodo, O. F. C., & Anosike, C. A. (2018). Phytochemical and proximate composition of cucumber (Cucumis sativus) fruit from Nsukka, Nigeria. African Journal of Biotechnology, 17(38), 1215-1219.

Šeregelj, V., Šovljanski, O., Tumbas Šaponjac, V., Vulić, J., Ćetković, G., Markov, S., & Čanadanović-Brunet, J. (2022). Horned melon (Cucumis metuliferus E. Meyer Ex. Naudin)—Current knowledge on its phytochemicals, biological benefits, and potential applications. Processes, 10(1), 94.

Yao, X., Kaler, M., Qu, X., Kalidhindi, R. S. R., Sviridov, D., Dasseux, A., ... & Levine, S. J. (2024). Asthmatic patients with high serum amyloid A have proinflammatory HDL: Implicationsfor augmented systemic and airway inflammation. Journal of Allergy and Clinical Immunology, 153(4), 1010-1024.

Sack, G. H. (2020). Serum amyloid A (SAA) proteins. Vertebrate and Invertebrate Respiratory Proteins, Lipoproteins and Other Body Fluid Proteins, 421-436.

Ye, R. D., & Sun, L. (2015). Emerging functions of serum amyloid A in inflammation. Journal of Leucocyte Biology, 98(6), 923-929.

Sattar, S. B. A., Sharma, S., & Headley, A. (2023). Bacterial pneumonia (nursing). In StatPearls [Internet]. StatPearls Publishing.

Stotts, C., Corrales-Medina, V. F., & Rayner, K. J. (2023). Pneumonia-induced inflammation, resolution and cardiovascular disease: causes, consequences and clinical opportunities. Circulation research, 132(6), 751-774.

Voynow, J. A., & Shinbashi, M. (2021). Neutrophil elastase and chronic lung disease. Biomolecules, 11(8), 1065.

Karampoor, S., Hesamizadeh, K., Maleki, F., Farahmand, M., Zahednasab, H., Mirzaei, R., ... & Keyvani, H. (2021). A possible pathogenic correlation between neutrophil elastase (NE) enzyme and inflammation in the pathogenesis of coronavirus disease 2019 (COVID-19). International Immunopharmacology, 100, 108137.

Oriano, M., Terranova, L., Sotgiu, G., Saderi, L., Bellofiore, A., Retucci, M., ... & Blasi, F. (2019). Evaluation of active neutrophil elastase in sputum of bronchiectasis and cystic fibrosis patients: a comparison among different techniques. Pulmonary Pharmacology & Therapeutics, 59, 101856.

Chiappini, E., Taccetti, G., & de Martino, M. (2014). Bacterial lung infections in cystic fibrosis patients: an update. The Pediatric infectious disease journal, 33(6), 653-654.

Kak, G., Raza, M., & Tiwari, B. K. (2018). Interferon-gamma (IFN-γ): Exploring its implications in infectious diseases. Biomolecular concepts, 9(1), 64-79.

Berns, S. A., Isakova, J. A., & Pekhtereva, P. I. (2022). Therapeutic potential of interferon-gamma in tuberculosis. ADMET and DMPK, 10(1), 63-73.

Fan, J., Fu, A., & Zhang, L. (2019). Progress in molecular docking. Quantitative Biology, 7, 83-89.

Agarwal, S., & Mehrotra, R. J. J. C. (2016). An overview of molecular docking. JSM chem, 4(2), 1024-1028.

Viceconti, M., Emili, L., Afshari, P., Courcelles, E., Curreli, C., Famaey, N., ... & Pappalardo, F. (2021). Possible contexts of use for in silico trials methodologies: a consensus-based review. IEEE Journal of Biomedical and Health Informatics, 25(10), 3977-3982.

Saravanan, R., Raja, K., & Shanthi, D. (2022). GC–MS Analysis, molecular docking and pharmacokinetic properties of phytocompounds from Solanum torvum unripe fruits and its effect on breast cancer target protein. Applied biochemistry and biotechnology, 194(1), 529-555.

Arif, R., Bukhari, S. A., Mustafa, G., Ahmed, S., &Albeshr, M. F. (2024). Network Pharmacology and Experimental Validation to Explore the Potential Mechanism of Nigella sativa for the Treatment of Breast Cancer. Pharmaceuticals, 17(5), 617.

Chadotra, S. N., & Baldaniya, B. B. (2016). Synthesis and Characterizations of Some New 1, 3, 5-Triazine-2, 4, 6-Triamine Based Derivatives as Potent Antimicrobial and Antiinfective Agents. Int. J. Sci. Res. Chem.(IJSRCH), 1, 39-43.

Ramalakshmi, S., & Muthuchelian, K. (2012). Studies on cytotoxicity, phytotoxicity and volatile profile of flower extract of Tabebuia rosea (Bertol.) DC. Medicinal Plants-International Journal of Phytomedicines and Related Industries, 4(3), 154-161.

Musini, A., Rao, J. P., & Giri, A. (2015). Phytochemicals of Salacia oblonga responsible for free radical scavenging and antiproliferative activity against breast cancer cell lines (MDA-MB-231). Physiology and Molecular Biology of Plants, 21, 583-590.

Saeed, H. M., Ferdosi, M. F., Khan, I. H., Javaid, A., & Sultan, M. W. (2023). Antibacterial activity and GCMS analysis of white flowers extract of Nerium oleander L. International Journal of Biology and Biotechnology, 20(1), 163-168.

Yehye, W. A., Rahman, N. A., Ariffin, A., Abd Hamid, S. B., Alhadi, A. A., Kadir, F. A., & Yaeghoobi, M. (2015). Understanding the chemistry behind the antioxidant activities of butylated hydroxytoluene (BHT): A review. European journal of medicinal chemistry, 101, 295-312.

Robina, I., Carmona, A. T., Moreno-Vargas, A. J., & Moreno-Clavijo, E. (2011). Total asymmetric synthesis of monosaccharides and analogues. Chimia, 65(1-2), 85-85.

Ganesan, T., Subban, M., Christopher Leslee, D. B., Kuppannan, S. B., & Seedevi, P. (2024). Structural characterization of n-hexadecanoic acid from the leaves of Ipomoea eriocarpa and its antioxidant and antibacterial activities. Biomass Conversion and Biorefinery, 14(13), 14547-14558.

Shafeian, E., Ghavam Mostafavi, P., Moridi Farimani, M., Mashinchian Moradi, A., & Nazemi, M. (2022). Extraction and investigation of biological activities of dioctyl phthalate and dibutyl phthalate from marine sponge Haliclona (Soestella) caerulea Larak Island, Persian Gulf. Iranian Journal of Fisheries Sciences, 21(5), 1141-1155.

Jafari, A. A., Shohrati, M., Mahmoudi, R., Hoseini, R. H., Nosratpour, S., Pajohi-Alamoti, M., & Latifi, A. M. (2014). Chemical composition and biological activities of Scrophularia striata extracts. Minerva Biotecnologica, 26(3), 183-189.

Ramzan, M. S., Abbasi, M. A., Siddiqui, S. Z., Shah, S. A., Ashraf, M., Lodhi, M.A., ... & Mirza, B. (2018). Synthesis of 2-{[5-(aralkyl/aryl)-1, 3, 4-oxadiazol-2-yl] sulfanyl}-N-(4-methyl-1, 3-thiazol-2-yl) acetamides: Novel bi-heterocycles as potential therapeutic agents. Tropical Journal of Pharmaceutical Research, 17(5), 913-926.

Lingfa, L., & Ankanagari, S. (2023). GC-MS Profiling of reproductive stage Withania somnifera for antimicrobial and anticancer phytochemicals. Biomedical and Pharmacology Journal, 16(1), 197-211.

Amr, A. E. G. E., Ibrahimd, A. A., El-Shehry, M. F., Hosni, H. M., Fayed, A. A., & Elsayed, E. A. (2019). In vitro and in vivo anti-breast cancer activities of some newly synthesized 5-(thiophen-2-yl) thieno-[2, 3-d] pyrimidin-4-one candidates. Molecules, 24(12), 2255.

Sam, S. (2019). Importance and effectiveness of herbal medicines. Journal of pharmacognosy and phytochemistry, 8(2), 354-357.

Varshney, N., Jain, D., Janmeda, P., & Mitra, D. (2021). Role of medicinal plants in pharmaceutical sector: an overview. Glob J Bio-sci Biotechnol, 10(2), 18-24.

Saxena, M., Saxena, J., Nema, R., Singh, D., & Gupta, A. (2013). Phytochemistry of medicinal plants. Journal of pharmacognosy and phytochemistry, 1(6), 168-182.

Zhang, Y. J., Gan, R. Y., Li, S., Zhou, Y., Li, A. N., Xu, D. P., & Li, H. B. (2015).

Antioxidant phytochemicals for the prevention and treatment of chronic diseases. Molecules, 20(12), 21138-21156.
Rauf, A., & Jehan, N. (2017). Natural products as a potential enzyme inhibitors from medicinal plants. Enzyme Inhibitors and Activators, 165, 177.
Amani, T., Surenthar, M., & Shanmugam, R. (2024). Anti-inflammatory and Antioxidant Activity of Cucumis sativus and Citrus macroptera Herbal Formulation: An In-Vitro Study. Cureus, 16(1).
Zhang, Y., Zhang, J., Sheng, H., Li, H., & Wang, R. (2019). Acute phase reactant serum amyloid A in inflammation and other diseases. Advances in clinical chemistry, 90, 25-80.
Jiang, Y., Wang, W., Zhang, Z., Ma, X., Sang, Y., Wang, J., ... & Zhao, S. (2022). Serum amyloid a, C-reactive protein, and procalcitonin levels in children with Mycoplasma pneumoniae infection. Journal of Clinical Laboratory Analysis, 36(3), e24265.
Januarie, K. C., Uhuo, O. V., Iwuoha, E., & Feleni, U. (2022). Recent advances in the detection of interferon-gamma as a TB biomarker. Analytical and Bioanalytical Chemistry, 1-15.
Igwe, K. K., Nwankwo, P. O., Otuokere, I. E., Ijioma, S. N., & Amaku, F. (2015). GCMS analysis of phytocomponents in the methanolic extract of Moringa oleifera leave. Journal of Research in Pharmaceutical science, 2(1).
Dallakyan, S., & Olson, A. J. (2015). Small-molecule library screening by docking with PyRx. Chemical biology: methods and protocols, 243-250.
Kamble, S. A., Barale, S. S., Mohammed, A. A., Paymal, S. B., Naik, N. M., & Sonawane, K. D. (2024). Structural insights into the potential binding sites of Cathepsin D using molecular modelling techniques. Amino Acids, 56(1), 33.