

CHAPTER 1

INTRODUCTION

1.1 DODONAEA VISCOSA

Dodonaea viscosa is a species of flowering plant belongs to the family sapindaceae, its common name is hopbush. It is a traditional medicine plant worldwide. It has a cosmopolitan distribution in tropical, sub-tropical and warm temperature regions of the America, Africa, Australia and southern Asia. *Dodoneae* belongs to soapberry family. In the south Indian state of Tamil Nadu, this plant is called as virali. In Australia it has many common names include: Hopbush, candlewood, soapwood, sticky hopbush, broadleaf hopbush etc., The wood is extremely tough and durable. It is used for tool handles, tools, brooms, spears, clubs and poles. It is used in reforestration. In ecological studies, researchers have explored its role in different ecosystems, including its ability to thrive in arid and semi-arid regions, its interactions with other plant species, and its contribution to soil stabilization and biodiversity conservation. Additionally, investigations into its reproductive biology, seed dispersal mechanisms, and response to environmental stressors have provided valuable insights into its adaptability and resilience in various habitats.

The pharmacological properties of *Dodonaea viscosa* have been a subject of growing interest. Studies have identified bioactive compounds present in different parts of the plant, such as flavonoids, alkaloids, and terpenoids, and have investigated their potential medicinal properties. Research has focused on its traditional uses in indigenous medicine, including its anti-inflammatory, antimicrobial, and antioxidant effects, as well as its potential in treating various ailments such as skin disorders, gastrointestinal problems, and respiratory infections. (Pérez-Narváez, et al., 2023)

1.2 CASE OF DODONAEA VISCOSA

Growth habit and size: *Dodonaea viscosa* is an evergreen shrub or small tree, reaching a maximum height of 20 feet (6 meters).

Botanical classification: It belongs to the Sapindaceae family, which includes other plants like lychee and rambutan.

Leaf morphology: The leaves are narrow and lance-shaped, with a glossy green coloration.

Flower characteristics: Flowers are small and inconspicuous, typically greenish-yellow.

Fruit: Fruits are small capsules containing seeds.

Habitat: The plant thrives in diverse environments like coastal areas, woodlands, scrublands, and disturbed locations.

Distribution: Native to a wide range, encompassing Africa, Australia, Asia, and parts of the Americas.

Climate preferences: Specifying the temperature and rainfall conditions suitable for *Dodonaea viscosa* growth (Yaqub et al. 2023).

1.3 REASON BEHIND THE CHOICE OF THE PLANT DODONAEA VISCOSA

Feature	Description
Traditional Uses	Documented history of use in treating skin infections, gastrointestinal disorders, and respiratory conditions.
Ethnopharmacological Relevance	Aligns with the approach of exploring medicinal plants based on indigenous knowledge.
Distribution and Accessibility	Widely distributed and readily available in native or cultivated regions.
Sourcing Potential	Convenient source of plant material for bioactive compound extraction.
Applications	Pharmaceuticals, cosmeceuticals, and nutraceuticals.

Table 5.1: Ethnopharmacological Significance and Accessibility

Feature	Description
Ongoing Research	Scientific studies may have identified specific bioactive compounds with potential therapeutic or commercial value.
Extraction and Characterization	Isolation, purification, and identification of bioactive compounds using techniques like chromatography and spectroscopy.
Synergistic Effects	Potential for combined bioactive compounds to exhibit enhanced therapeutic efficacy compared to individual compounds.
Extraction Benefit	Enables investigation of potential synergies and therapeutic applications.

Table 5.2: Bioactive Compound Identification and Synergistic Effects

1.4 MOLECULAR DOCKING

Molecular docking is a computational technique used in the field of structural biology and drug discovery to predict how small molecules, such as drug candidates or ligands, interact with a target protein or receptor at the molecular level. The goal of molecular docking is to determine the most energetically favorable orientation and conformation of the ligand within the binding site of the protein, which can provide insights into the binding affinity and potential biological activity of the ligand (Elbasuni et al. 2024)

- Preparation of Target Protein and Ligand
- Binding Site Identification
- Docking Algorithm
- Scoring and Ranking
- Analysis and Validation

1.5 Natural compounds are often considered better leads in drug discovery for several reasons

Natural compounds offer a vast array of chemical structures, providing a rich source of chemical diversity that can be explored for potential therapeutic activities. This diversity increases the likelihood of finding compounds with unique biological properties. Natural compounds often exhibit lower toxicity compared to synthetic compounds. This can be attributed to their evolutionary adaptation within biological systems, making them more compatible with human physiology. Natural compounds are derived from living organisms and are thus more likely to interact favorably with biological targets and pathways. This can result in higher efficacy and fewer adverse effects. Many natural products contain multiple bioactive compounds that can act synergistically to enhance therapeutic effects. This synergism can improve efficacy and reduce the risk of resistance development. Plants and other natural sources have been used for centuries in traditional medicine systems around the world. This empirical knowledge can guide the selection of natural compounds with known therapeutic properties, facilitating drug discovery efforts. Natural compounds are often sourced from renewable resources, reducing environmental impact compared to the synthesis of synthetic compounds, which may involve complex chemical processes and generate waste. There is often a perception among consumers that natural compounds are safer and more desirable than synthetic alternatives. This can lead to greater acceptance and compliance with natural-based therapies (Ntwasa and Dlamini 2024).

CHAPTER 2

REVIEW OF LITERATURE

Several *Dodonaea* species have been used widely and frequently by society as well as traditional practitioners for different ailments. The leaves, stem, and sometimes the fruits are used in the formulation of traditional medicine. The most frequently investigated *dodonaea* species are *d.viscosa* and *d. angustifolia*. *Dodonaea viscosa* is a flowering plant commonly found in tropical, subtropical and temperate areas of Africa, America, southern Asia and Australia.

This species of *dodonaea* is known to occur from southern Africa to Arabia and in Australia and New Zealand (Orwa *et al.*, 2009). All parts of the plant are hairless. The common therapeutic uses include stem, leaf and root infusions to treat sore throats and cold. It is used in Ethiopian traditional medicine to treat malaria (Melaku *et al.*, 2017; Mengiste *et al.*, 2012). Activities such as antidiabetic (Shanmugavasan and Ramachandran, 2011), antibacterial (Gemeda *et al.*, 2011), antifungal (Gemeda *et al.*, 2011), anti-inflammatory (Revathi and Dhanaraj, 2019a) and antidiarrheal (Anode *et al.*, 2018) properties have been also noticed. *Dodonaea* genus has been also used in agriculture sectors, for instance as weedicide, pest control, on plant growth promotion, used for its anti-insect activity and have shown the allelopathic effect (Al-Jobori and Ali, 2014a, Al-Jobori and Ali, 2014b; Mogahed and Gesraha, 2005; Xiao-Ping 2008; Barkatullah *et al.*, 2010; Diaz *et al.*, 2015; Afzal *et al.*, 2017). Various biological responses of *Dodonaea* genus revealing an extensive range of plant-derived compounds in various classes of chemical groups.

Hossain (2019) reported that extract obtained from *d. viscosa* has shown significant antidiabetic, antimicrobial, insecticidal, antioxidant, cytotoxic, antifertility, anti-inflammatory, analgesic, anti-ulcer, antispasmodic, antidiarrheal and detoxification effects (Khurram *et al.* 2015).

The rise in antibiotic-resistant dermatological pathogens has spurred interest in natural products with antimicrobial properties. This study evaluated the antibacterial activity of ethanolic extracts from *Dodonaea viscosa* aerial parts and *Mammea americana* leaves and seeds against resistant *Staphylococcus* strains isolated from skin lesions and *S. aureus* ATCC 25923. *Mammea americana* seed extract

exhibited the highest antibacterial activity, with minimum bactericidal concentrations ranging from 2.3 µg/mL to 19.5 µg/mL, comparable to gentamicin. Phytochemical screening revealed coumarins and lactone compounds in active PTLC-fractions, suggesting a synergistic effect of secondary metabolites. The study highlights the potential of natural products, particularly *M. americana* seed extract, as alternatives for combating antibiotic-resistant dermatological pathogens. (Pérez-Narváez, et al., 2023)

In the quest for effective anticancer agents with minimal side effects, natural products offer promising leads due to their structural diversity and lower toxicity compared to synthetic compounds. *Dodonaea viscosa*, an evergreen shrub rich in bioactive compounds like terpenoids and flavonoids, presents potential as a source of anticancer agents. Its traditional uses in treating various ailments underscore its medicinal significance (Priya et al. 2021)

Studies have reported the anticancer activity of *Dodonaea viscosa* extracts, highlighting its potential in cancer therapy. The plant's diverse phytochemical profile, including terpenoids and flavonoids, contributes to its pharmacological activities, which encompass antibacterial, anti-inflammatory, antioxidant, antidiabetic, and antiviral effects. Further research is warranted to elucidate the mechanisms underlying its anticancer properties and to explore its therapeutic potential in combating cancer, addressing the urgent need for novel anticancer agents. (Alghamdi, Nazreen, Ali, & Amna, 2022)

Overall, this study suggests that *D. viscosa* extract holds promise as a natural therapeutic agent for managing diabetes and its associated complications, offering potential benefits in regulating glucose metabolism, reducing oxidative tissue injury, and alleviating inflammation. (Alanazi, Al-Rejaie, Ahmed, & Alhazzani, 2023).

This study investigated the potential anti-diabetic effects of *Dodonaea viscosa* (*D. viscosa*) herbal extract in rats with streptozotocin (STZ)-induced diabetes. Daily administration of *D. viscosa* extract demonstrated promising outcomes in controlling hyperglycemia and mitigating diabetes-related complications in vital organs such as the liver and kidneys. The bioactive constituents of *D. viscosa*, including phenolic compounds, flavonoids, terpenoids, steroids, and tannins, are believed to contribute to its pharmacological activities.

In diabetic rats, *D. viscosa* treatment significantly improved liver and kidney functions, as evidenced by reduced levels of liver enzymes (GPT, GOT) and renal markers (creatinine, urea). Moreover, *D. viscosa* extract countered STZ-induced dyslipidemia by restoring lipid profile parameters, including cholesterol, triglycerides, LDL, and HDL levels. Additionally, *D. viscosa* demonstrated renoprotective effects by improving renal functions and histopathological changes.

Furthermore, *D. viscosa* treatment attenuated inflammation and oxidative stress associated with diabetes, as indicated by reduced levels of pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6) and increased activity of antioxidant enzymes (GPx, CAT, SOD, GR, GST). The anti-inflammatory and antioxidant properties of *D. viscosa* may contribute to its protective effects against diabetic complications(Pullaiah 2022).

CHAPTER 3

AIM AND OBJECTIVE OF THE PROPOSED STUDY

3.1 AIM:

The aim of this study is to comprehensively investigate the therapeutic properties of *Dodonaea viscosa*, a plant species with a rich history of traditional medicinal use. Through a multidisciplinary approach encompassing pharmacology, phytochemistry, and molecular biology, this research seeks to elucidate the pharmacological activities and mechanisms of action of *Dodonaea viscosa* extracts and bioactive compounds. The primary objective is to evaluate the potential therapeutic applications of *Dodonaea viscosa* in various health conditions, including but not limited to antibacterial activity, antifungal activity, anticancer potential, and modulation of metabolic disorders such as diabetes. By systematically examining its biological effects, this study aims to contribute to the understanding of *Dodonaea viscosa* as a valuable source of natural remedies and pave the way for its development as a novel therapeutic agent.

3.2 OBJECTIVE:

The scope of this research encompasses a comprehensive exploration of the therapeutic properties of *Dodonaea viscosa* at both preclinical and clinical levels. Experimental investigations will involve in vitro and in vivo studies to assess its pharmacological activities, including but not limited to antimicrobial, anti-inflammatory, antioxidant, anticancer, antidiabetic, and immunomodulatory effects. Phytochemical analysis will be conducted to identify and characterize the bioactive compounds present in *Dodonaea viscosa* extracts. Molecular studies will be employed to elucidate the underlying mechanisms of action responsible for its therapeutic effects. Additionally, this research will explore the potential synergistic interactions between *Dodonaea viscosa* and existing therapeutic agents. Clinical studies may be considered to evaluate the safety, efficacy, and therapeutic potential of *Dodonaea viscosa*-based interventions in human subjects. The findings of this study aim to contribute to the development of novel natural products and therapies for the prevention and treatment of various diseases, ultimately promoting health and well-being.

CHAPTER 4

METHODOLOGY

4.1 INDIAN MEDICINAL PLANTS, PHYTOCHEMISTRY AND THERAPEUTIC (IMPPAT)

A comprehensive database that offers details on the phytochemicals, therapeutic benefits, and therapeutic uses of Indian medicinal plants is known as Indian Medicinal Plants, Phytochemistry and Therapeutics 2.0 (IMPPAT 2.0). The first IMPPAT database was introduced in 2011, and this is an updated version of it. Information on more than 3,000 Indian medicinal plants, including their phytochemical makeup, can be found in the IMPPAT 2.0 database. Along with information on their pharmacological characteristics and potential therapeutic uses, it also provides information in the conventional uses of these plants in Ayurveda, Unani, and Siddha medicine.

A group of scientists from the Indian Institute of Integrative Medicine, CSIR, Jammu, and the Central Council for Research in Ayurveda Science, New Delhi, created the database. The data in the database was gathered from a variety of sources, including academic research, classic books, and professional opinions.

It is the goal of the IMPPAT 2.0 database to serve as a helpful tool for academics, medicinal professionals, and the general public. It can be used to locate possible sources of herbal treatments for a variety of illnesses and to direct additional investigation into the pharmacological characteristics of Indian medicinal plants. (Singh VK *et al.*, 2019).

4.2 PUBCHEM

The National Centre for Biotechnology Information (NCBI), a division of the United States National Library of Medicine (NLM), is responsible for maintaining PubChem, a database of chemical compounds that is open to the public. Since the launch in 2004, PubChem has become a key chemical information resource for scientists, students, and the general public.

A variety of data on chemical compounds, including their chemical composition, physical characteristics, bioactivity, and pharmacological characteristics, can be

found in the PubChem database. It can be searched for using several criteria, including chemical name, molecular formula, and chemical structure. PubChem offers a variety of tools and resources for academics in addition to its modelling tools, and data visualization tools. Users can contribute their own data to the database, such as bioassay results and chemical structures, to help it become more accurate and comprehensive.

4.3 PROTEIN DATA BANK

The Protein Data Bank (PDB) is a database that provides 3D structural information of proteins, nucleic acids, and complex assemblies. It contains information on the atomic coordinates of these macromolecules, as well as their experimental data and related information.

The PDB is a vital resource for researches in various fields, including biochemistry, biophysics, structural biology, and drug discovery. It allows researchers to analyse the structures of biological molecules and understand their functions, interaction, and mechanisms of action. The PDB has contributed significantly to various fields, including drug discovery and design, structural genomics and protein engineering. It has led to the development of new drugs, improved our understanding of disease mechanisms, and facilitated the design of novel proteins and enzymes for industrial applications(Burley et al. 2024)

4.4 SWISS ADME

SwissADME is a free online tool for predicting the physicochemical and pharmacokinetic characteristics of small molecules. It offers users a variety of tools for drug research and discovery and is maintained by the Swiss Institute of Bioinformatics (SIB). Based on the small molecule's molecular structure, SwissADME forecasts a variety of pharmacokinetic characteristics like absorption, distribution, metabolism and excretion (ADME). It offers details on physical and chemical characteristics such as molecular weight, lipophilicity, solubility, and pKa values. SwissADME also forecasts a compound's probable toxicity based on its structural makeup. To assure accuracy of its forecasts and to incorporate new prediction algorithms, the tool is frequently updated. As of 2017, researches in the

pharmaceutical sector and academia frequently employed SwissADME, which had been mentioned in more than 50 papers. (Daina A *et al.*, 2017)

4.5 DISCOVERY STUDIO

Dassault Systemes BIOVIA created and maintains Discovery Studio, a comprehensive software suite for molecular modelling, simulations, and visualization. It is extensively utilized for drug development and discovery in both the pharmaceutical sector and academia. Virtual screening, molecular docking, and pharmacophore modelling are just a few of tools that Discovery Studio offers for ligand-based drug creation. It also has an intuitive user interface. It also has resources for forecasting a compound's ADME and toxicity. It offers other research fields in addition to drug creation, such as protein modelling, chemical biology, and materials science. It has sophisticated molecular dynamics simulation techniques as well as tools for simulating protein-ligand interactions. Discovery Studio makes it possible to visualize molecular structures and their interaction with proteins, which aids in understanding how drugs work. It also makes it possible to identify important binding residues and analyses protein-ligand interaction. (Chen, J. *et al.*, 2019)

4.6 TARGET IDENTIFICATION

The process of identifying the biological molecule or pathway that a medicine or chemical substance affects is known as target identification. It is a crucial stage in the discovery and development of new therapeutics since it enables researchers to comprehend how a drug function and spot any negative effects or interactions with other medications. In order to discover possible targets, this includes employing computational tools to analyze and interpret data from diverse sources. The target will be obtained from PDB and the heteroatoms are removed.

4.7 LIGAND IDENTIFICATION

It involves the identification of small molecules that can bind to the specific target protein and modulate its activity. Virtual screening is a computational method that involves the screening of large chemical libraries to identify potential ligands that can bind to a target protein. This process is typically performed using various computational methods, including virtual screening, molecular docking, and molecular dynamics simulation. Identified phytochemicals present in the plant (of

dodonea viscosa) using IMPPAT database and pubchem. And the SDF file for these compounds has been downloaded to visualize the compounds in Discovery studio.

4.8 PHARMACOKINETICS PROPERTIES

Pharmacokinetics analysis can be performed to evaluate the drug-likeness and ADME (absorption, distribution, metabolism, and excretion) properties. This analysis can be done using in silico tool such as SwissADME.

The tool uses a variety of machine learning models to predict properties such as bioavailability, blood-brain barrier penetration and toxicity. Steps involved in using Swiss ADME PREDICTION:

Import the compounds into Swiss ADME by uploading the smiles notation for each compound.

Prediction of physicochemical properties: Once the input model is uploaded, SWISSADME will predict various physicochemical properties such as molecular weight, logP, polar surface area, and number of hydrogen bond donors and acceptors. These properties are important in determining the drug-likeness of the natural compound(Xu et al. 2024).

The molecules will be screened based on Lipinsk's rule of five, which is a set of rules utilized in medication discovery and development.

- Lipinsk's guidelines: Molecular weight [≤ 500 Daltons]
- LogP (partition coefficient) [≤ 5]
- Number of hydrogen bond donor [≤ 5]
- TPSA [<140]

4.9 MOLECULAR DOCKING

Molecular docking is a computational method used to predict the binding of a small molecule (ligand) to a target protein. It is a powerful tool in drug discovery and design, as it can help identify potential drug candidates and guide optimization efforts.

Ligandfit is a tool in Discovery studio, which is a software suite for molecular docking and drug discovery.

Steps involved in using the Ligandfit tool in Discovery studio:

Import or generate the 3D structure of the receptor (usually a protein) you want to dock the ligand into.

Preparation of ligand molecule: Import the 3D structure of the ligand molecule you want to dock into the receptor, remove water molecules and add the missing atoms.

Identify and define the active sites of the receptor where the ligand is expected to bind:

- Docking parameters: Set up the docking parameters like docking algorithms, search space, the scoring function, and the number of docking runs to perform.
- Perform docking simulation: Run the docking simulation using the defined parameters. The Ligandfit tool will generate multiple docking process (conformation) of the ligand within the active site of the receptor.
- Analyze the Docking result: The docked poses and scores can be used to evaluate the potential binding affinity of the ligand to the protein, interaction energy, hydrogen bonding, and other factors that contribute to ligand-receptor interactions.

4.10 PHARMACOPHORE AND DISTANCE ANALYSIS USING DISCOVERY STUDIO

Ligand-based Pharmacophore Analysis: Ligand-based pharmacophore analysis involves identifying the common features of a set of ligands that are responsible for their biological activity. These features can include hydrogen bond acceptors, hydrogen bond donors, aromatic rings, and hydrophobic regions. A pharmacophore model is then generated based on these common features, which can be used to identify new compounds with similar pharmacophore properties (Pullaiah 2022; Langer and Hoffmann 2006)

Distance Analysis: Distance analysis is another important technique used in drug discovery. This technique involves measuring the distance between atoms or functional groups in a ligand or protein, and using this information guide the design of new compounds with improved binding affinity. Discovery studio includes several tools for distance analysis, including the Distance measurements tool.

CHAPTER 5

RESULT AND DISCUSSION

5.1 TARGET IDENTIFICATION

5.1.1 SHIKIMATE KINASE(4Y0A)

The structure of the target protein was retrieved from the PDB database. The target name is 4y0a shikimate kinase from *Acinetobacter baumannii*.

Acinetobacter baumannii is a gram-negative bacterium known for its ability to cause infections, particularly in healthcare settings. It is a significant concern due to its ability to develop resistance to multiple antibiotics, leading to difficult-to-treat infections.

The structure with PDB ID 4Y0A represents the shikimate kinase from *Acinetobacter baumannii*. Determining the structure of this enzyme provides insights into its molecular architecture, including active sites and potential binding sites for inhibitors.

Shikimate kinase is an important enzyme for the survival and growth of bacteria like *Acinetobacter baumannii*. Targeting this enzyme with specific inhibitors could potentially disrupt bacterial growth and offer avenues for the development of new antibiotics.

The structure of shikimate kinase from *Acinetobacter baumannii* (4y0a) may serve as a valuable resource for structure-based drug design efforts aimed at developing novel antibiotics or antimicrobial agents to combat infections caused by this pathogen. Studying the structure and function of shikimate kinase from *Acinetobacter baumannii* can contribute to our understanding of bacterial metabolism, antibiotic resistance mechanisms, and potential strategies for combating bacterial infections.

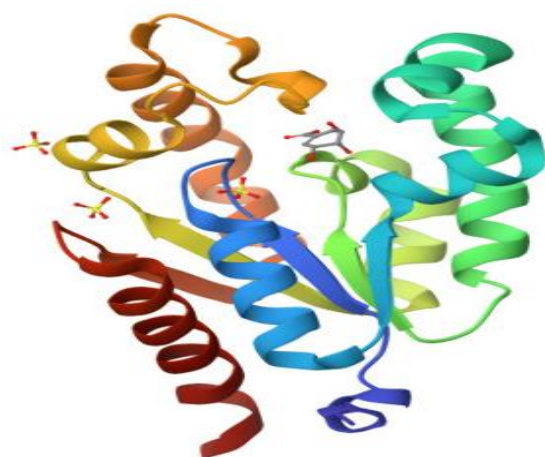


FIG 5.1 SHIKIMATE KINASE(4Y0A)

5.1.2 LIPID KINASE PI3K ALPHA (4JPS)

The co-crystal structures represented by PDB entry 4jps involve the lipid kinase PI3K alpha, which is a key player in cellular signaling pathways implicated in cancer progression. While the specific context of 4jps might not directly denote an "anticancer" compound or activity, understanding the structure of PI3K alpha and its interactions with potential inhibitors or modulators is highly relevant to anticancer drug discovery and development.

PI3K alpha is a well-known oncogenic kinase that is frequently dysregulated in various cancers. Its aberrant activation contributes to tumor growth, survival, and resistance to therapy. Therefore, targeting PI3K alpha with specific inhibitors is a promising strategy for anticancer therapy.

The co-crystal structures in 4jps provide detailed insights into the three-dimensional arrangement of PI3K alpha and its binding pockets when bound to different ligands or inhibitors. Understanding the structural basis of PI3K alpha inhibition helps in the rational design of more potent and selective anticancer agents.

The information gleaned from 4jps aids in the development of novel anticancer drugs targeting PI3K alpha. By studying the interactions between PI3K alpha and small molecules within the active site, researchers can optimize compound design to enhance efficacy and minimize off-target effects.

Compounds that inhibit PI3K alpha activity have shown promise in preclinical and clinical studies for the treatment of various cancers. Understanding the structural nuances of PI3K alpha inhibition, as depicted in 4jps, helps in predicting drug efficacy and guiding clinical development.

Given the heterogeneity of cancer, personalized medicine approaches that consider the molecular profile of individual tumors are gaining importance. Targeting PI3K alpha with tailored inhibitors, informed by structural data from 4jps, may offer more effective and precise treatment options for cancer patients.

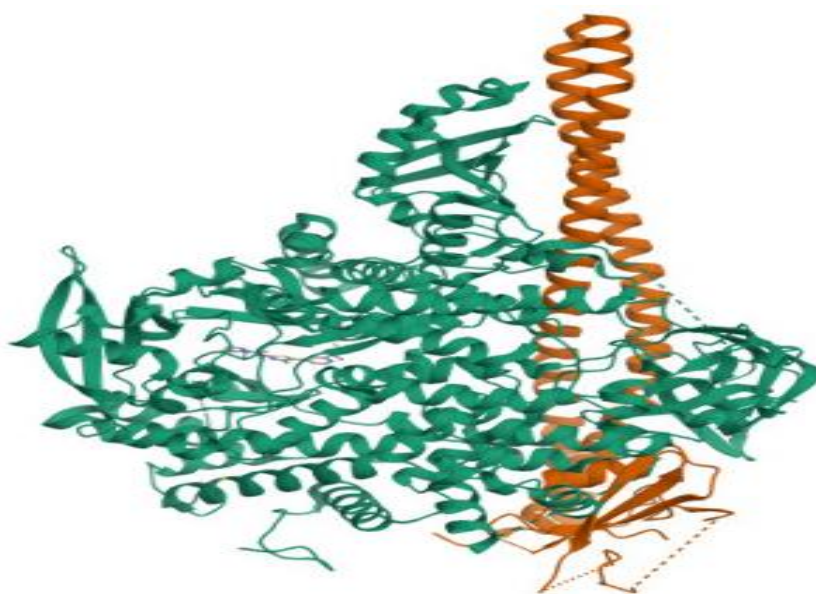


FIG 5.2 Lipid kinase PI3K ALPHA

5.1.3 HUMAN COX-2(5KIR)

5KIR represents the crystal structure of the anti-inflammatory drug Vioxx (rofecoxib) bound to human cyclooxygenase-2 (COX-2). Cyclooxygenase-2 (COX-2) is an enzyme involved in the production of prostaglandins, which are lipid mediators implicated in inflammation and pain. Drugs like Vioxx are selective inhibitors of COX-2 and are used as nonsteroidal anti-inflammatory drugs (NSAIDs) to relieve pain and inflammation. The crystal structure captured in PDB entry 5KIR reveals the three-dimensional arrangement of atoms in the complex formed between Vioxx and human COX-2. This structure provides insights into the binding mode and interactions between the drug and its target enzyme. The structure elucidates how Vioxx interacts with specific amino acid residues within the active site of COX-2, thereby inhibiting its enzymatic activity. Understanding the structural basis of COX-2 inhibition by Vioxx is crucial for optimizing drug design and developing safer and more effective NSAIDs.

Vioxx was once widely prescribed for the treatment of pain and inflammation due to its selective inhibition of COX-2, which was expected to reduce the risk of gastrointestinal side effects associated with non-selective NSAIDs. However, concerns arose regarding cardiovascular risks associated with long-term Vioxx use, leading to its withdrawal from the market in 2004. Despite the withdrawal of Vioxx, the structural insights gained from its interaction with COX-2, as depicted in 5KIR, continue to inform drug development efforts targeting inflammation and pain. Researchers aim to design new COX-2 inhibitors with improved safety profiles while retaining therapeutic efficacy.

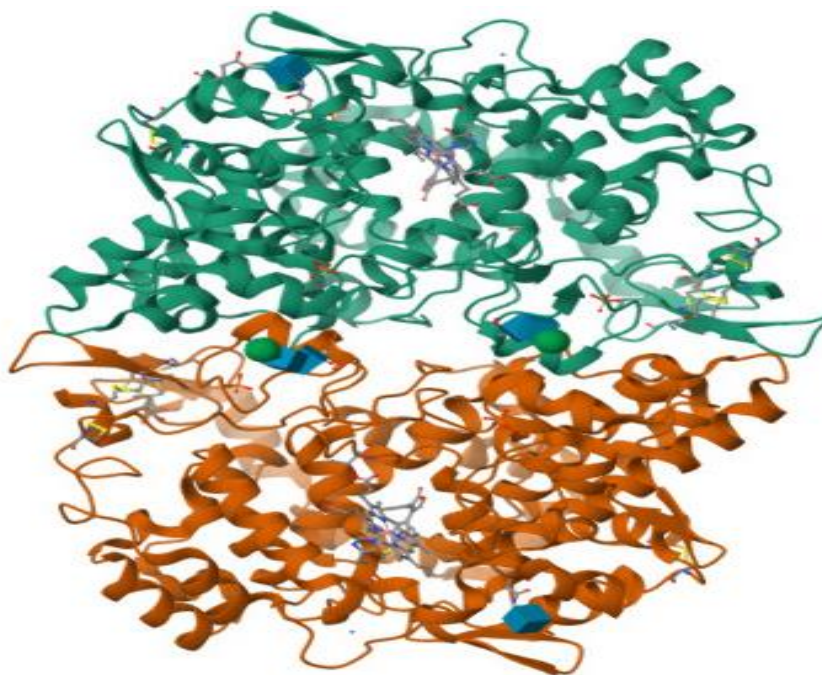


FIG 5.3 2D HUMAN COX-2(5KIR)

5.1.4 HUMAN DIPEPTIDYL PEPTIDASE IV/CD26 IN COMPLEX(4PNZ)

4PNZ represents the crystal structure of human dipeptidyl peptidase IV (DPP-4), also known as CD26.

Dipeptidyl Peptidase IV (DPP-4): DPP-4 is a membrane-bound serine protease involved in various physiological processes, including glucose homeostasis, immune regulation, and cell signaling. It is best known for its role in the regulation of blood glucose levels through the degradation of incretin hormones, such as glucagon-like peptide 1 (GLP-1) and glucose-dependent insulintropic peptide (GIP). The crystal structure captured in PDB entry 4PNZ provides detailed information about the three-dimensional arrangement of atoms in the DPP-4 protein. Understanding the structure of DPP-4 is crucial for elucidating its catalytic mechanism, substrate specificity, and interactions with inhibitors or ligands. DPP-4 inhibitors are a class of drugs used in the treatment of type 2 diabetes mellitus. By inhibiting DPP-4 activity, these drugs prolong the half-life of endogenous incretin hormones, leading to enhanced glucose-dependent insulin secretion and suppression of glucagon secretion, ultimately lowering blood glucose levels.

The structural insights provided by 4PNZ aid in the rational design and optimization of DPP-4 inhibitors for the treatment of diabetes. By understanding how inhibitors interact with the active site and other regions of DPP-4, researchers can develop more potent and selective drugs with improved pharmacokinetic properties and reduced side effects. DPP-4 inhibitors have become an important class of antidiabetic drugs, offering an alternative treatment option for patients with type 2 diabetes who may not tolerate or respond well to other medications. Understanding the structural basis of DPP-4 inhibition guides the development of safer and more effective therapeutics for managing diabetes and related metabolic disorders.

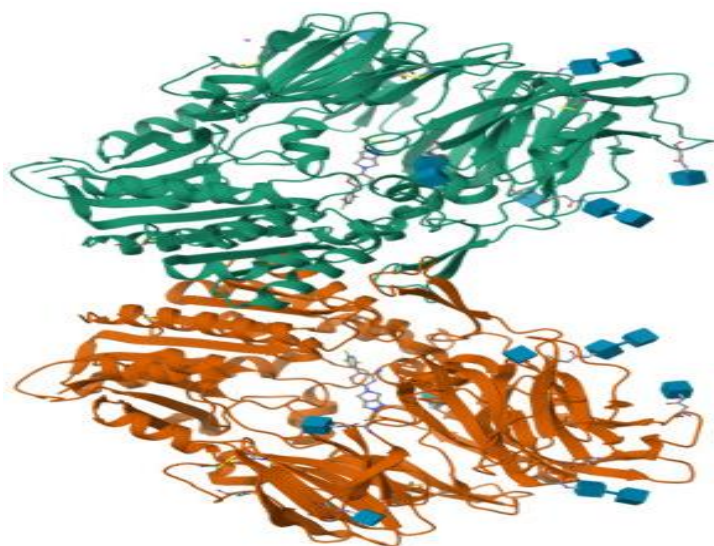


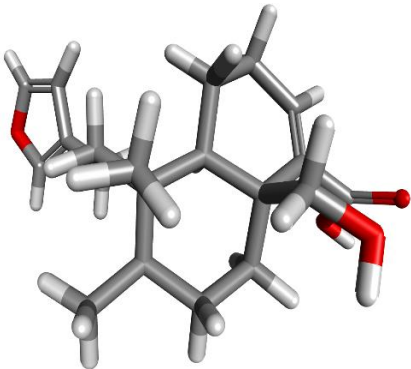
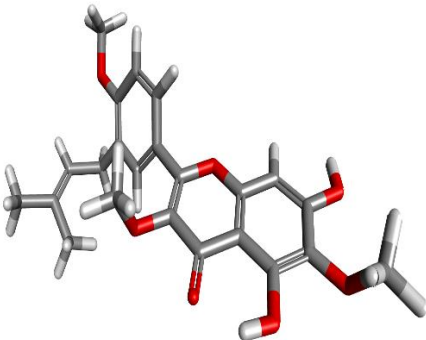
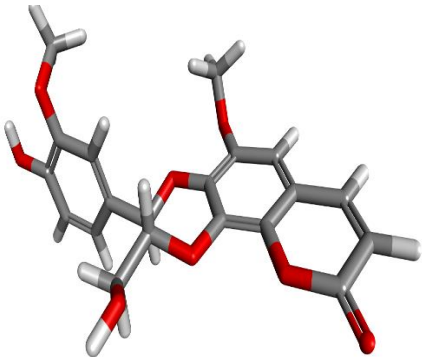
FIG 5.4 HUMAN DIPEPTIDYL PEPTIDASE IV/CD26 IN COMPLEX(4PNZ)

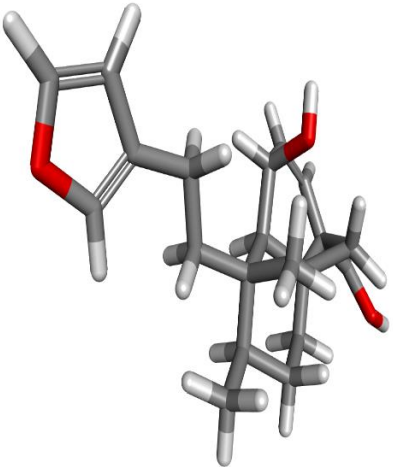
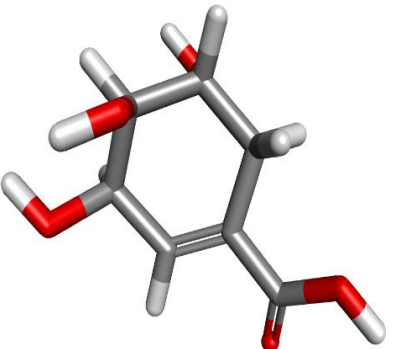
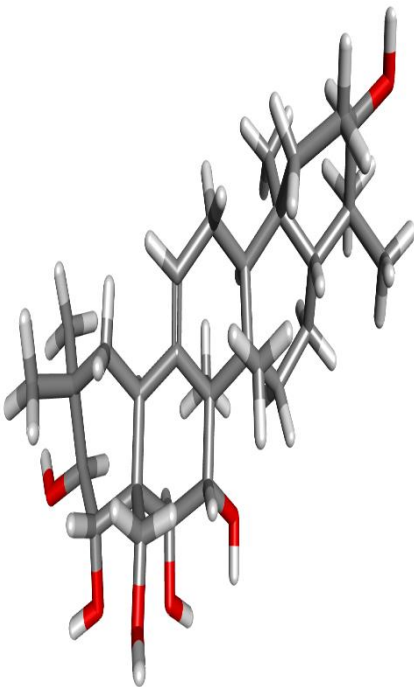
5.2 LIGAND IDENTIFICATION

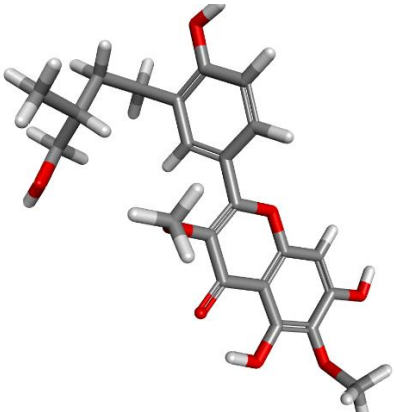
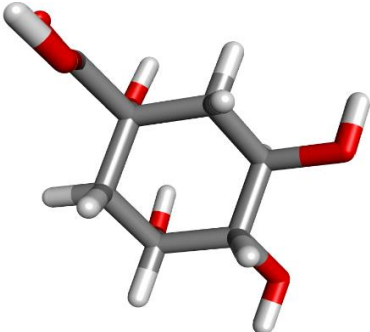
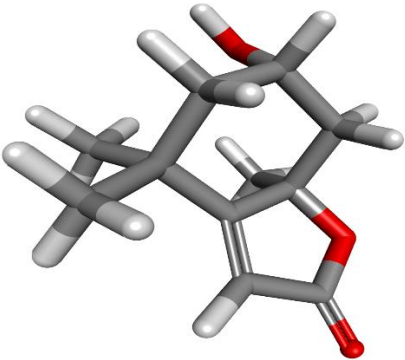
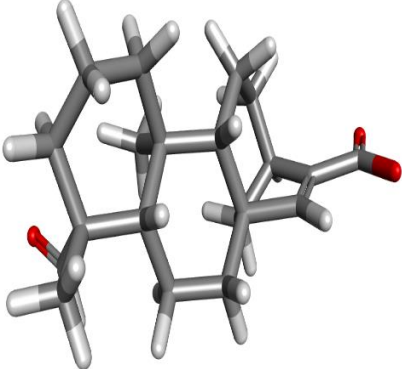
Phytochemicals from the plant *Dodonaea viscosa* were identified and their SDF file was downloaded from IMPPAT.

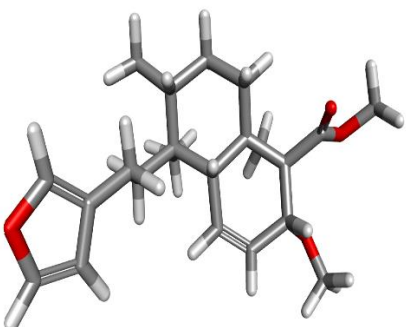
Total 1000 phytochemicals were subjected for therapeutic properties. ADME prediction was done, where the compounds got filtered to 11 compounds with respect to the drug absorption, distribution, metabolism, excretion and toxicity values. The 11 compounds were further considered for docking, among which only 2 compounds got docked and showed affinity towards the protein.

TABLE 5.1 DETAIL ON OF IDENTIFIED COMPOUNDS

Plant specis	Molecule name/id	Molecule structure
	Hautriwaic acid IMPHY009398	
	Viscosal IMPHY002903	
	Cleomiscosin A IMPHY011335	

	(1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[<i>j</i>]naphthalene-1a-carboxylic acid IMPHY005688	
	Shikimic acid IMPHY006945	
	R1-Barrigenol IMPHY008974	

	<u>Aliarin</u> IMPHY002405	
	Quinic acid 6508	
	Loliolide 100332	
	Kauralexin B3 90658844	

	Dodovisnoid 132495251	
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5.3 PHARMACOKINETICS PROPERTIES OF IDENTIFIED COMPOUNDS

The pharmacokinetic properties of the identified compounds from *Dodonaea viscosa* play a crucial role in determining their efficacy and safety as potential therapeutic agents. These properties include absorption, distribution, metabolism, and excretion (ADME), which collectively influence the bioavailability and systemic exposure of the compounds in the body.

Absorption refers to the process by which the compounds are taken up into the bloodstream after administration. Factors such as molecular size, lipophilicity, and solubility influence the absorption of the compounds from the gastrointestinal tract or other routes of administration.

Excretion refers to the elimination of the compounds and their metabolites from the body, primarily through renal or hepatic routes. Factors such as renal clearance, hepatic clearance, and half-life influence the rate and extent of excretion, thereby impacting the overall pharmacokinetic profile of the compounds.

Evaluation of these pharmacokinetic properties is essential for predicting the ADME profile of the identified compounds and optimizing their pharmacological efficacy while minimizing potential adverse effects. Computational tools and in vitro experiments can be employed to assess these properties and guide the further development of *Dodonaea viscosa* compounds as therapeutic agents.

Table 5.2: Pharmacokinetics properties of proposed compounds

COMPOUND PROPERTIES	(iLOGP)	XLOGP3	WLOGP	MLOGP	Silicons - IT Log P	Consensus Log P
HAUTRIWAIC ACID	2.53	4.22	4.05	2.67	3.73	3.44
VISCOSOL	4.04	5.07	4.41	1.22	4.91	3.93
CLEOMISCOSIN A	2.79	2.12	2.06	0.66	2.74	2.07
(1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[<i>h</i>]naphthalene-1a-carboxylic acid	2.77	3.7	3.66	2.67	3.19	3.2
SHIKIMIC ACID	2.77	3.7	3.66	2.67	3.19	3.2
R1- BARRIGENOL	2.94	3.66	3.02	2.62	27061	3
ALIARIN	3.05	3.55	3.16	0.29	3.92	2.79
QUINIC ACID	-0.12	-2.37	-2.32	-2.14	-1.82	-1.75
LOLIOLIDE	1.88	1	1.41	1.49	1.86	1.53
KAURALEXIN B3	2.5	4.68	2.88	3.66	3.74	3.49
MKAPWANIN	2.95	4.25	3.57	3.53	4.12	3.68

COMPOUND PROPERTIES	Silicos-IT Solubility (mol/l)	ESOL class	Ali class	Silicos-IT LogSw
HAUTRIWAIC ACID	1.28e-02mg/ml; 3.85-05 mol/l	MODERATELY SOLUBLE	MODERATELY SOLUBLE	-4.41
VISCOSOL	1.18e-04 mg/ml ;2.87e-07 mol/l	MODERATELY SOLUBLE	POORLY, SOLUBLE	-6.54
CLEOMISCOSIN A	2.78e-03 mg/ml ; 7.19e-06 mol/l	0	SOLUBLE, MODERATELY SOLUBLE	-5.14
(1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-	4.99e-02 mg/ml ;	1.51e-04 mol/l	MODERATELY SOLUBLE,	-3.82

hexahydrocyclopropa[1,2-b]naphthalene-1a-carboxylic acid			MODERATELY SOLUBLE	
SHIKIMIC ACID	4.99e-02 mg/ml ; 1.51e-04 mol/l	MODERATELY SOLUBLE	SOLUBLE, MODERATELY SOLUBLE	-3.82
R1- BARRIGENOL	2.53e-01 mg/ml ; 4.99e-04 mol/l	MODERATELY SOLUBLE, MODERATELY SOLUBLE	0	-3.3
ALIARIN	9.50e-04 mg/ml ; 2.28e-06 mol/l	MODERATELY SOLUBLE	MODERATELY SOLUBLE	-5.64
QUINIC ACID	2.30e+02 mg/ml ; 1.20e+02 mol/l	HIGHLY SOLUBLE	HIGHLY SOLUBLE	2.08
LOLIOLIDE	3.00e+00 mg/ml ; 1.53e-02 mol/l	VERY SOLUBLE	VERY SOLUBLE	-1.82
KAURALEXIN B3	1.2e-01 mg/ml ; 3.81e-04 mol/l	MODERATELY SOLUBLE	MODERATELY SOLUBLE	-3.42
MKAPWANIN	2.34e-02 mg/ml ; 7.08e-05 mol/l	MODERATLY	SOLUBLE, MODERATELY SOLUBLE	-4.15

COMPOUND PROPERTIES	GI absorption	Pgp substrate	CYP1 A2 inhibitor	CYP2 C19 inhibitor	CYP2 C9 inhibitor	CYP2 D6 inhibitor	CYP3 A4 inhibitor	log Kp (cm/s)
HAUTRIWAIC ACID	HIGH	YES	NO	NO	NO	NO	NO	-5.33 cm/s
VISCOSOL	HIGH	YES	NO	NO	NO	NO	NO	-5.22 cm/s

CLEOMISCOSIN A	HIGH	YES	NO	NO	YES	YES	YES	-7.15 cm/s
(1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[j]naphthalene-1a-carboxylic acid	HIGH	YES	NO	NO	NO	YES	NO	- 5.69c m/s
SHIKIMIC ACID	HIGH	YES	NO	NO	NO	YES	NO	- 5.69c m/s
R1- BARRIGENOL	HIGH	YES	NO	NO	NO	NO	NO	-6.79 cm/s
ALIARIN	HIGH	NO	NO	NO	YES	YES	YES	-6.32 cm/s
QUINIC ACID	LOW	NO	YES	NO	NO	NO	NO	-9.15 cm/s
LOLIOLIDE	HIGH	YES	NO	NO	NO	NO	NO	-6.79 cm/s
KAURALEXIN B3	HIGH	YES	NO	YES	YES	NO	NO	- 4.90c m/s
MKAPWANIN	HIGH	NO	NO	YES	YES	NO	YES	-5.30 cm/s

COMPOUND PROPERTIES	Ghose #violations	Egan #violations	Muegge #violations	Bioavailability Score	Lipinski #violations
HAUTRIWAIC ACID	YES	YES	YES	0.85	YES; 0 violation
VISCOSOL	YES	YES	YES	0.55	YES; 0 VIOLATION
CLEOMISCOSIN A	YES	YES	YES	0.55	YES; 0 VIOLATION
(1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-	YES	YES	YES	0.85	YES; 0 VIOLATION

hexahydrocyclopropa[<i>h</i>]naphthalene-1a-carboxylic acid					
SHIKIMIC ACID	YES	YES	NO	0.85	YES; 0 violation
R1- BARRIGENOL	No; 3 violation:MW>480, MR>130 #atoms>70	YES	No; 1 violation: H-don>5	0.17	No;2 violation; MW>500 , NHorOH >5
ALIARIN	YES	YES	YES	0.55	YES; 0 violation
QUINIC ACID	No; 1 violation; WLOGP<-0.4	YES	YES	0.56	YES; 0 VIOLATION
LOLIOLIDE	YES	YES	NO; 1 violation: MW<200	0.55	YES; 0 violation
KAURALEXIN B3	YES	YES	YES	0.85	YES; 0 violation
MKAPWANIN	YES	YES	YES	0.55	YES; 0 violation

COMPOUND PROPERTIES	PAINS #alerts	Brenk #alerts	Leadlikeness #violations
HAUTRIWAIC ACID	0 ALERT	0 ALERT	NO; 1 Violation; XLOGP3>3.5
VISCOSOL	0 ALERT	1 alert:isolated -alkene	NO;2 violation:MW>350, XLOGP3>3.5
CLEOMISCOSIN A	0 ALERT	1 ALERT: CUMARINE	NO ; 1 VIOLATION : MW>350
(1a <i>S</i> ,4 <i>S</i> ,4a <i>R</i> ,5 <i>S</i> ,6 <i>R</i> ,8a <i>S</i>)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[<i>h</i>]naphthalene-1a-carboxylic acid	0 ALERT	1 ALERT: isolated-alkene	No; 1 violation: XLOGP3>3.5
SHIKIMIC ACID	0 ALERT	1 ALERT: isolated-alkene	NO; 1 violation :XLOGP3>3.5
R1- BARRIGENOL	0 ALERT	1 ALERT: isolated -alkene	NO; 2 violations: MW>350, XLOGP3>3.5S
ALIARIN	0 ALERT	0 ALERT	NO; 2 violation: MW>350, XLOGP3>3.5
QUINIC ACID	0 ALERT	0 ALERT	NO; 1 violation:MW<250
LOLIOLIDE	0 ALERT	0 ALERT	NO; 1 violation: MW<250
KAURALEXIN B3	0 ALERT	1 ALERT	NO; 1 violation: XLOGP3>3.5
MKAPWANIN	0 ALERT	1 ALERT: more than 2 esters	NO; 1 violation: XLOGP3>3.5

5.4 PHARMACOPHORE ANALYSIS

The pharmacophore analysis of compounds has been done.

The output of pharmacophore analysis includes a 3d model of the pharmacophore, which displays the key features such as hydrogen bond acceptors and donors and hydrophobic regions. The analysis also provides information on the quality of the pharmacophore model, such as the degree of fit to the active compounds and the statistical significance of the pharmacophore features.

Pharmacophore features include:

- **Hydrogen Bond Acceptor (HBA):**

A chemical group capable of accepting hydrogen bonds from hydrogen donors. Hydrogen bond acceptors can form hydrogen bonds with hydrogen atoms attached to electronegative atoms (e.g., nitrogen or oxygen) in proteins, such as the amide backbone or side chains of amino acids like serine or threonine.

- **Hydrogen Bond Donor (HBD):**

A chemical group capable of donating hydrogen bonds to hydrogen acceptors. Hydrogen bond donors can form hydrogen bonds with electronegative atoms (such as oxygen or nitrogen) in proteins, such as those found in the side chains of amino acids like asparagine or glutamine. A flat, cyclic arrangement of atoms with alternating double bonds. Aromatic rings can engage in π - π stacking interactions with other aromatic rings in proteins, such as those present in the side chains of amino acids like phenylalanine, tyrosine, and tryptophan. These interactions are important for stabilizing protein-ligand complexes.

- **Aliphatic Group:**

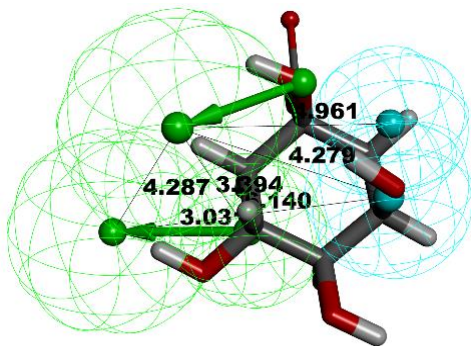
A linear or branched hydrocarbon chain. Aliphatic groups can interact with hydrophobic regions in proteins through hydrophobic interactions. These interactions contribute to the overall binding affinity of a ligand to its target protein.

- **Positive Ionizable Group:**

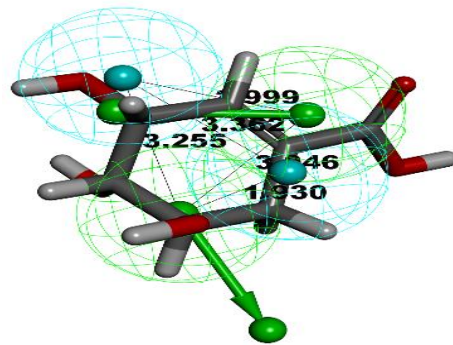
A chemical group that can be protonated to form a positive charge. Positive ionizable groups can interact with negatively charged residues in proteins, such as aspartate or glutamate, through electrostatic interactions. These interactions are important for ligand binding and recognition in proteins.

- Negative Ionizable Group:

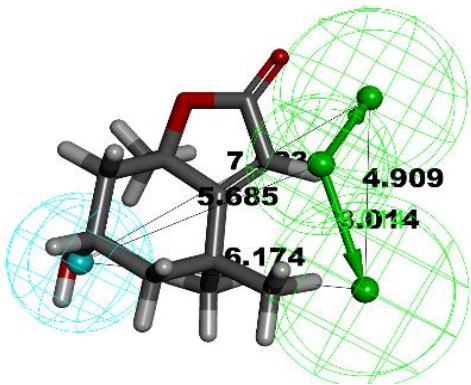
A chemical group that can be deprotonated to form a negative charge. Negative ionizable groups can interact with positively charged residues in proteins, such as lysine or arginine, through electrostatic interactions. Similar to positive ionizable groups, these interactions contribute to ligand binding and recognition in proteins.



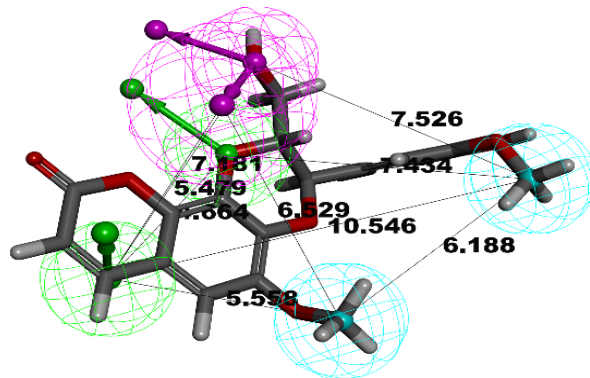
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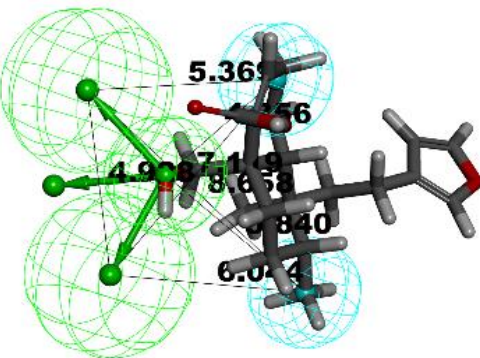
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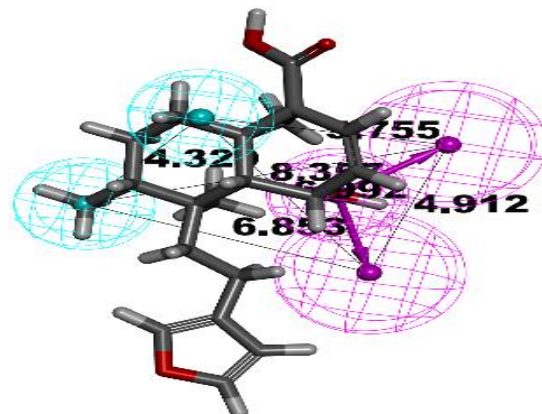
c)



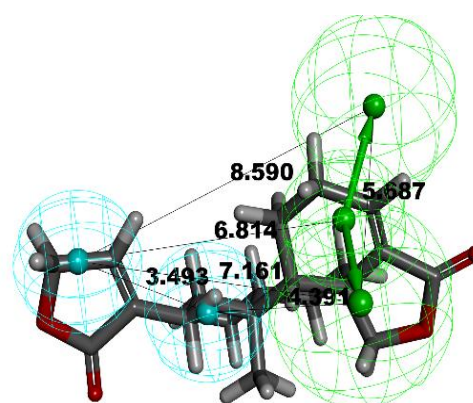
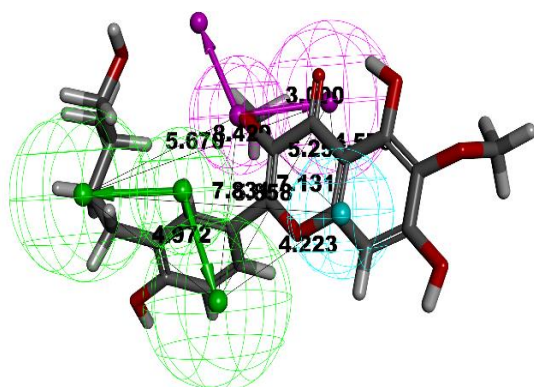
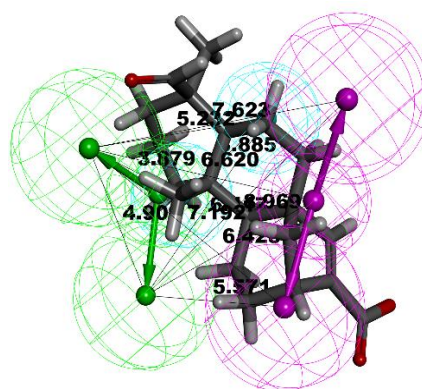
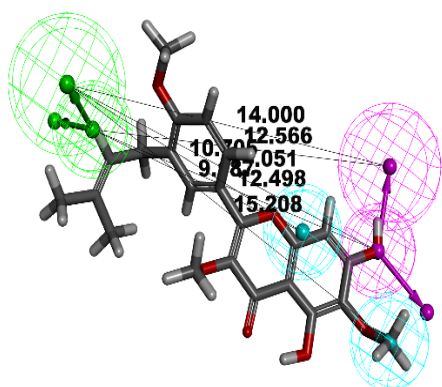
d)



e)

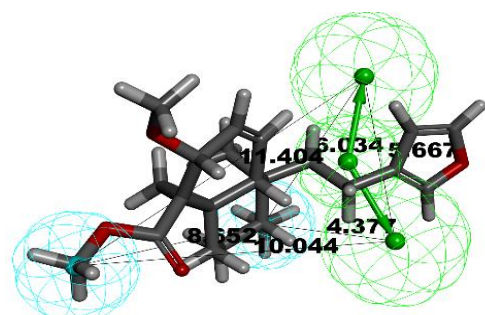


f)



i)

j)



k)



Acceptor



Donor



Hydrophobic

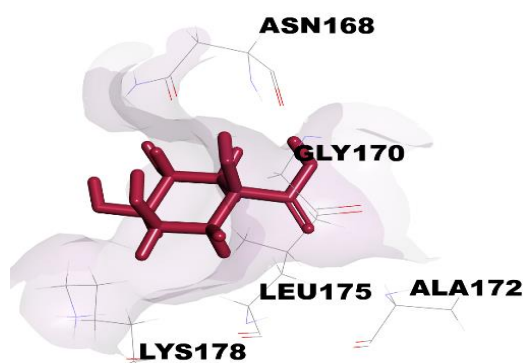
FIG 5.5: Pharmacophore proposed plant compounds

(A) Quinic acid, (B) Shikimic acid, (C) Loliolide, (D) Cleomiscosin A, (E) Hautriwaic acid, (F) (1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl) ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[j]naphthalene-1a-carboxylic acid, (G) Viscosal, (H) Kauralexin, (I) Aliarin, (J) Mkapwanin, (K) methyl (1aR,2R,4aR,5S,6R,8aS)-5-[2(furan3yl)ethyl]2methoxy5,6dimethyl1,2,4a,6,7,8hexahydrocyclopropa[j]naphthalene-1a-carboxylate.

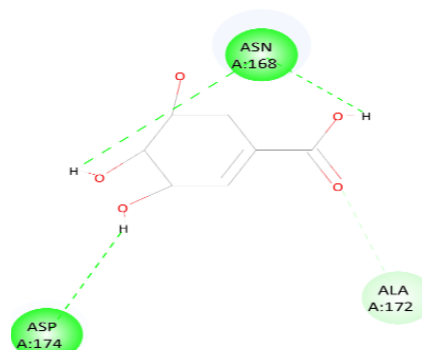
5.5 INTERACTION STUDIES OF DOCKED COMPOUNDS

The 2D and 3D image shows the various types of interactions that occur between the ligand and protein, such as hydrogen bonds, van der Waals interactions, and electrostatic interactions. It also displays the information about the binding affinity between the ligand and protein, as well as the specific amino acids or residues involved in the interaction.

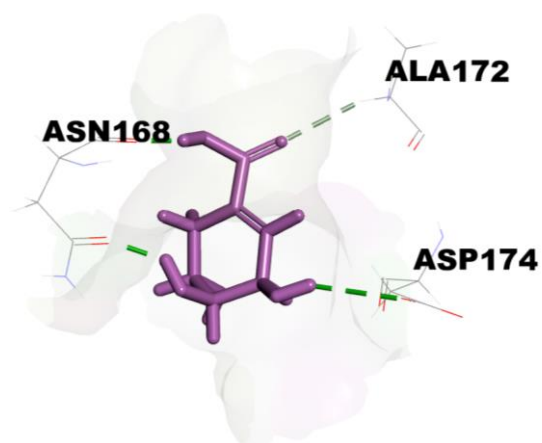
5.5.1 PICTORIAL REPRESENTATION OF DOCKED COMPOUNDS



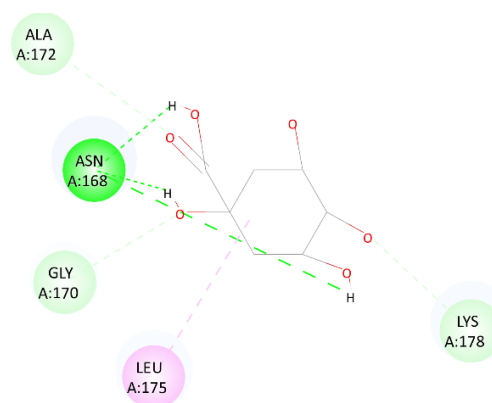
a)



b)

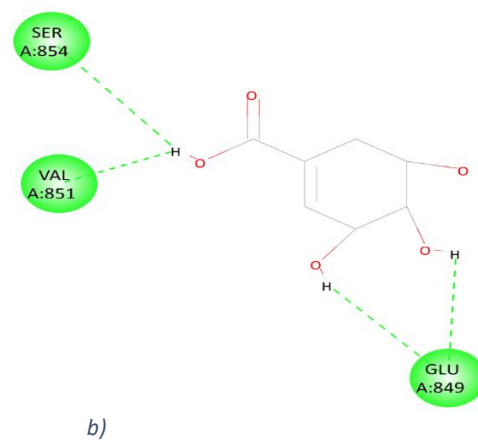
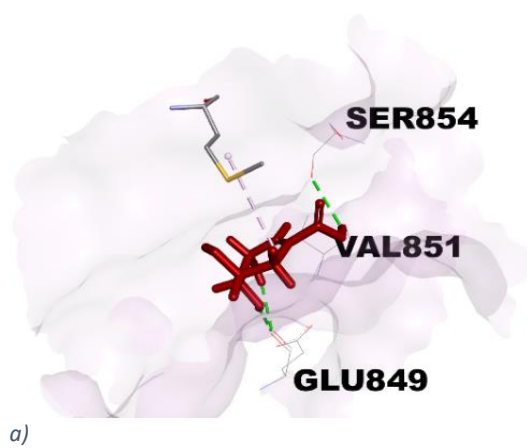


c)



d)

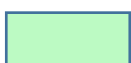
(A) Quinic acid, (B) Shikimic acid



Shikimic acid



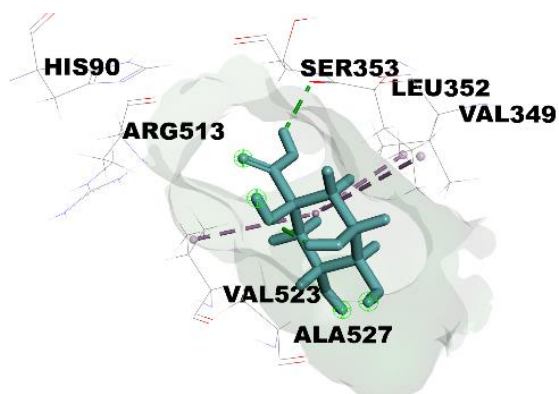
Hydrogen bond



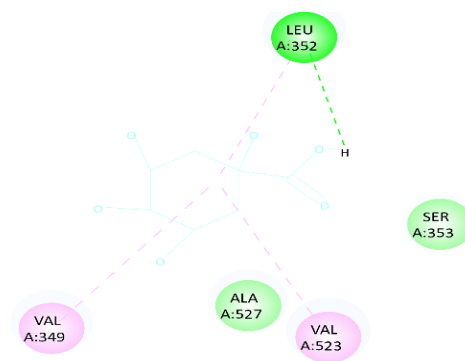
Carbon-hydrogen interaction



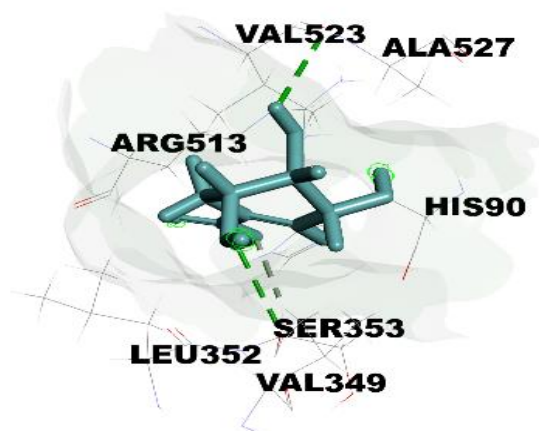
Alkyl Interaction



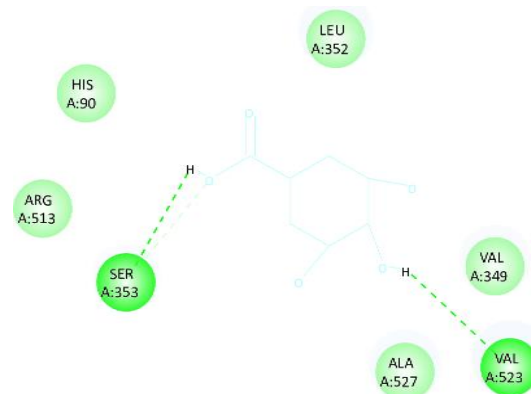
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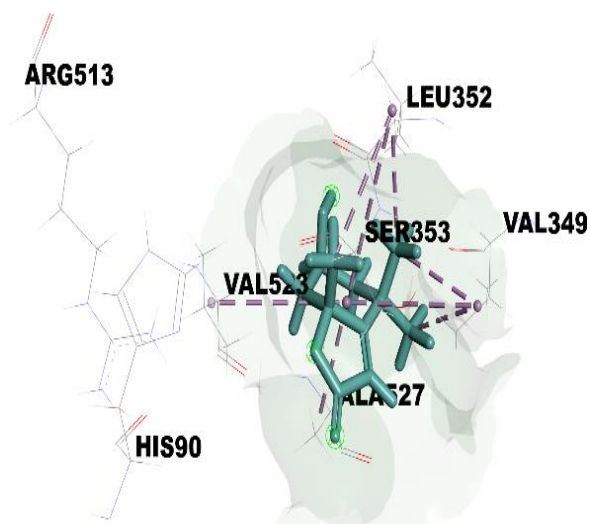
b)



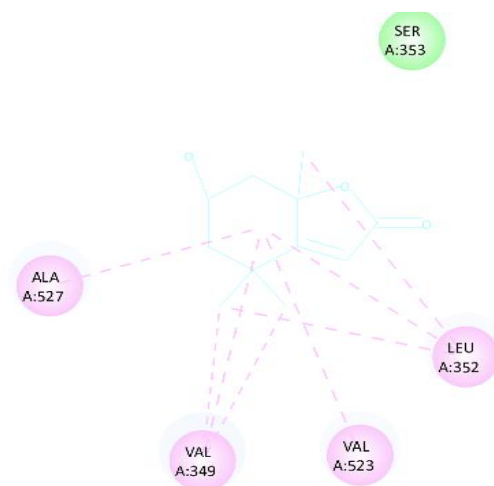
c)



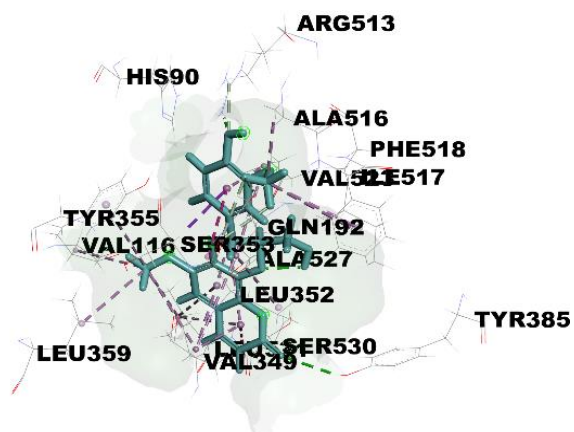
d)



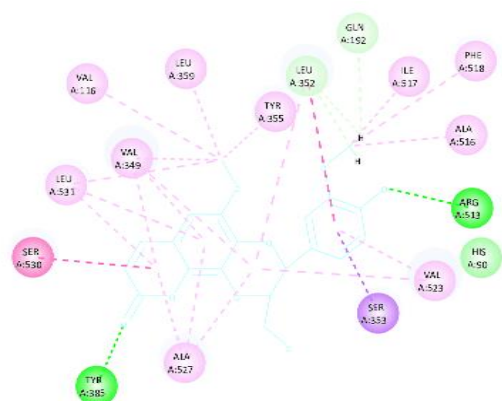
e)



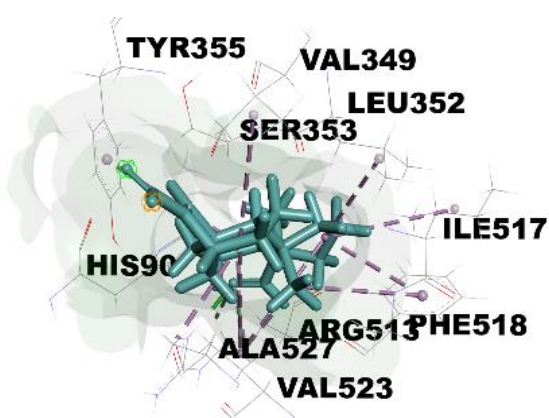
f)



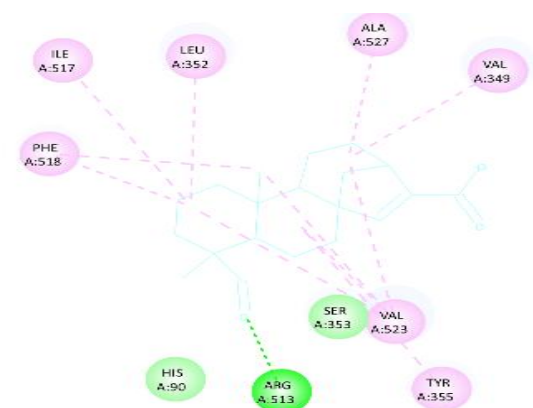
g)



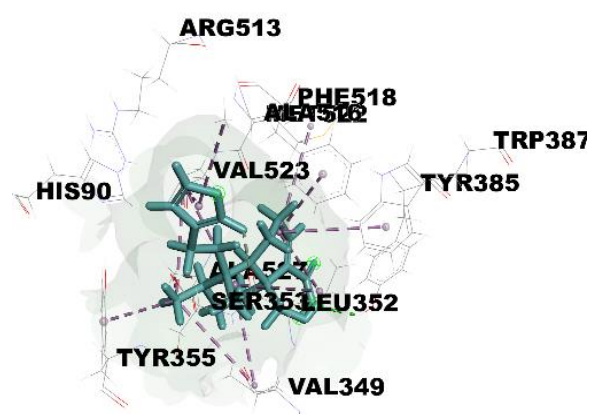
h)



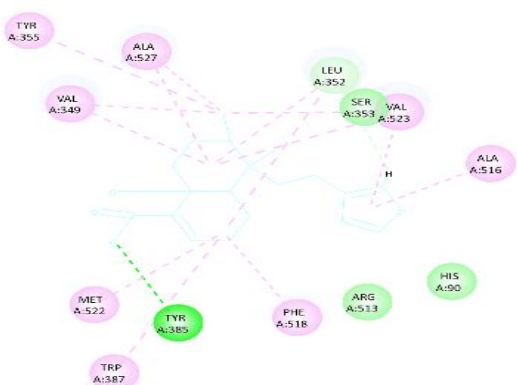
i)



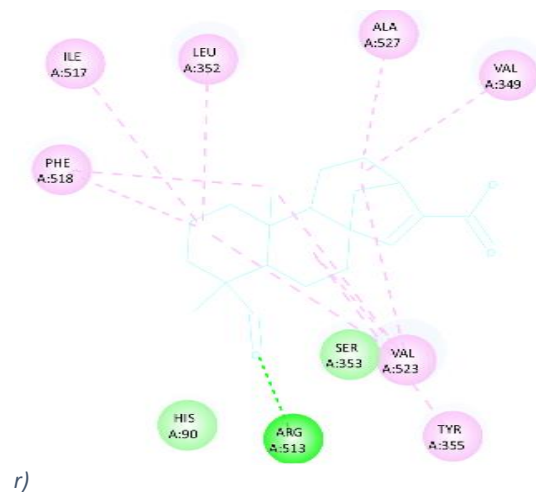
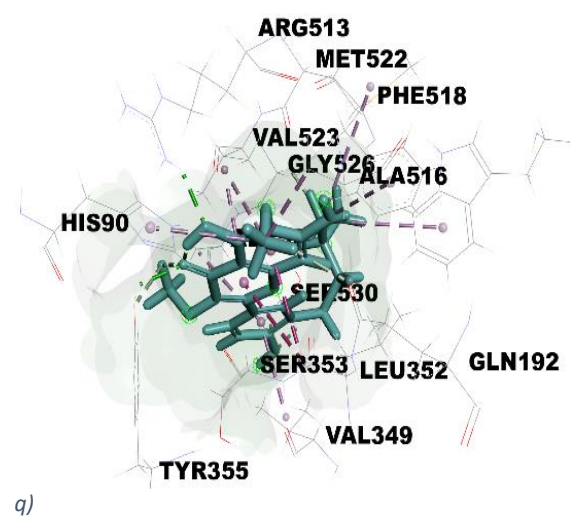
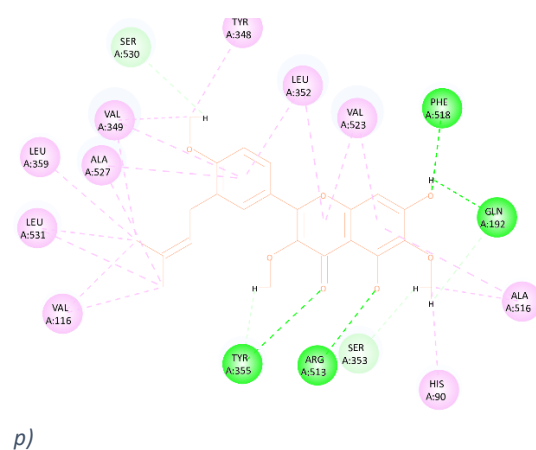
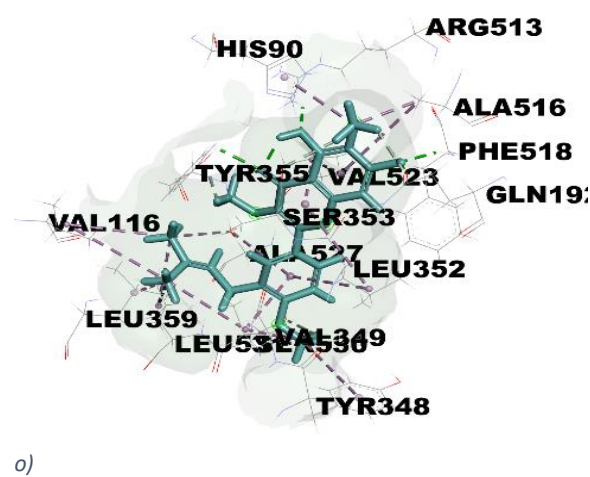
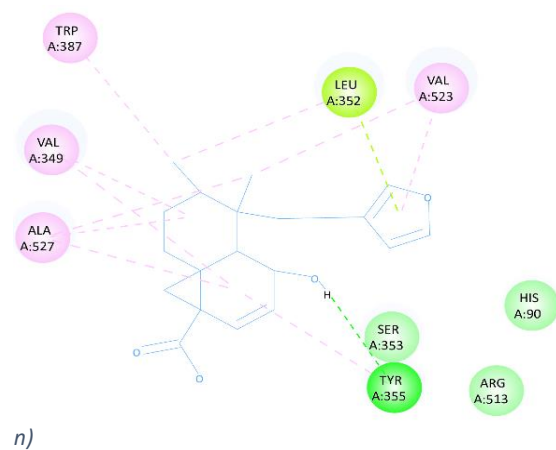
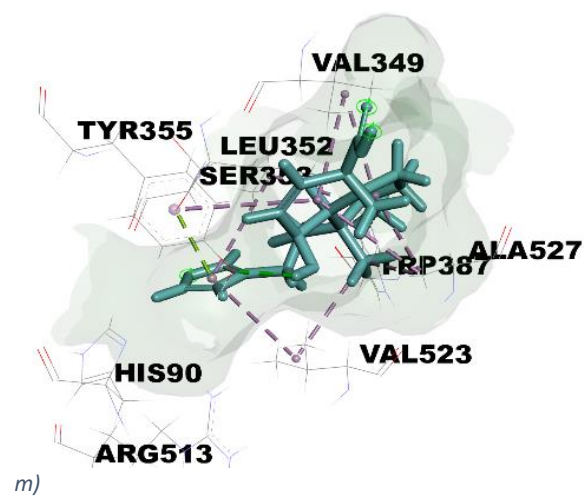
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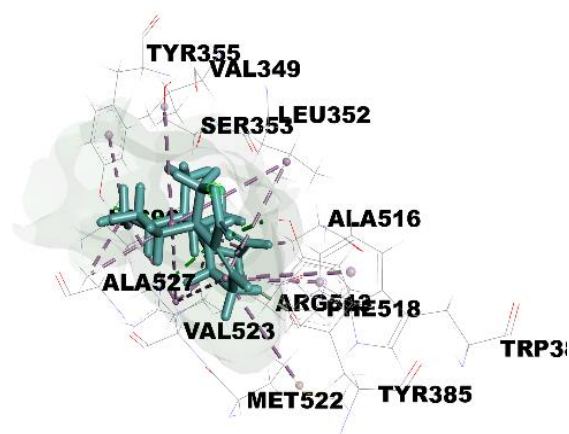


k)

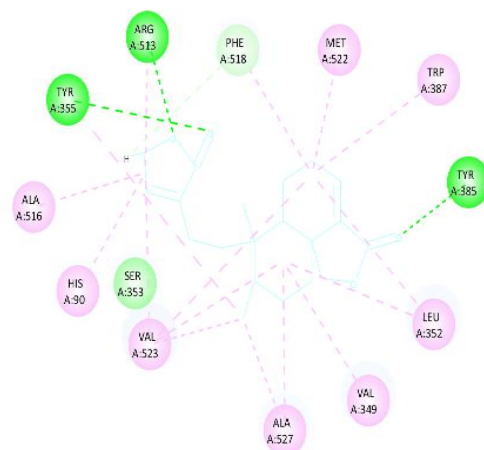


l)





s)

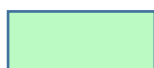


t)

(A) Quinic acid, (B) Shikimic acid, (C) Loliolide, (D) Cleomiscosin A, (E) Hautriwaic acid, (F) (1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl) ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[j]naphthalene-1a-carboxylic acid, (G) Viscosal, (H) Kauralexin, (I) Aliarin, (J) Mkapwanin,



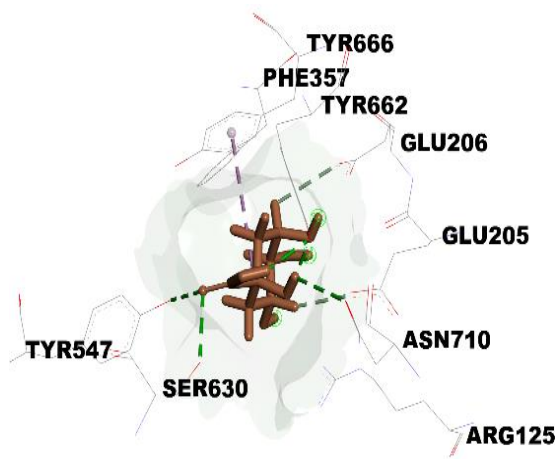
Hydrogen bond



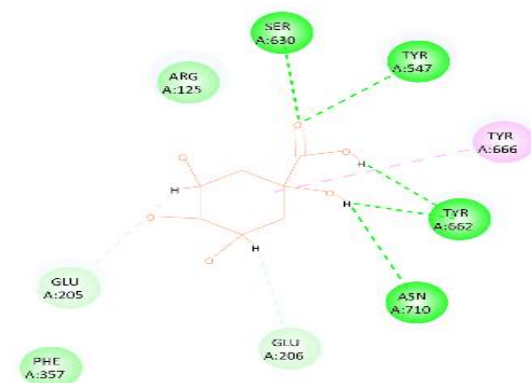
Carbon-hydrogen interaction



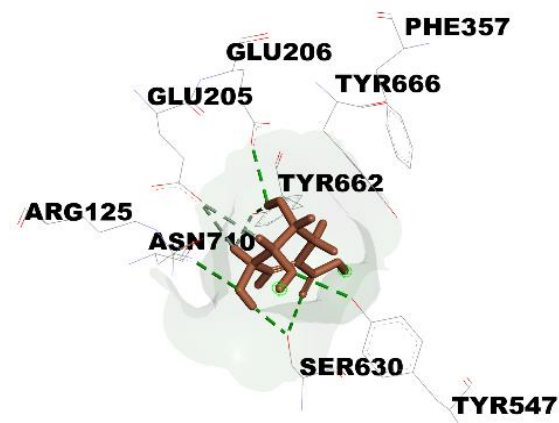
Alkyl Interaction



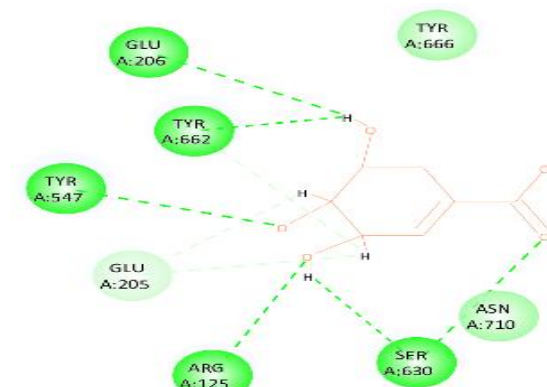
a)



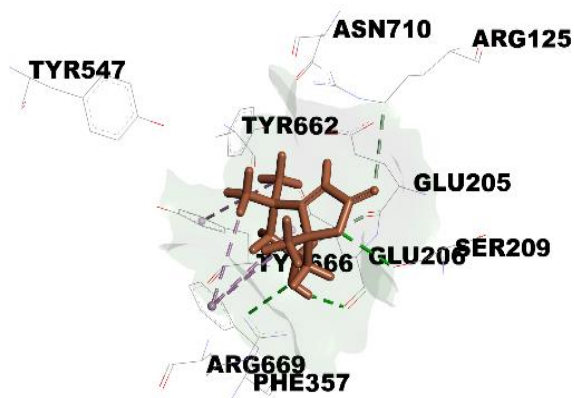
b)



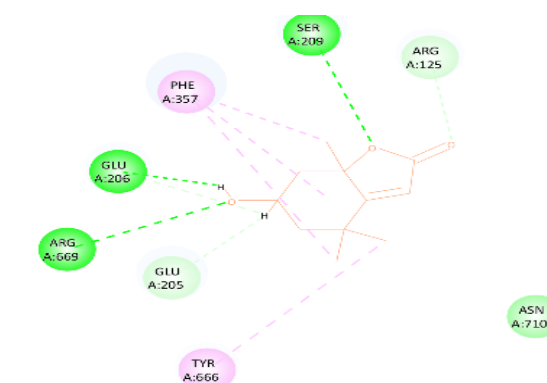
c)



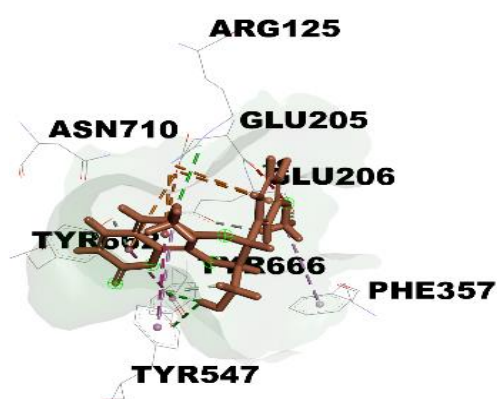
d)



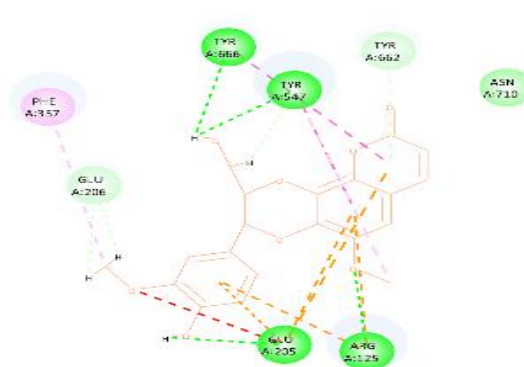
e)



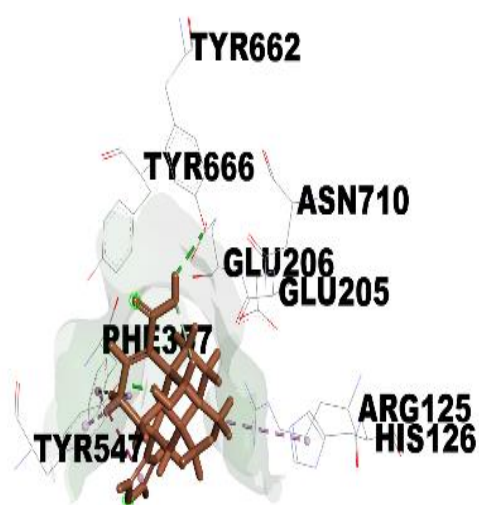
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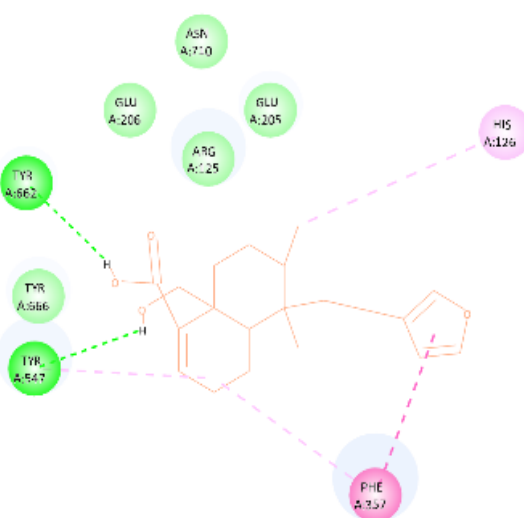
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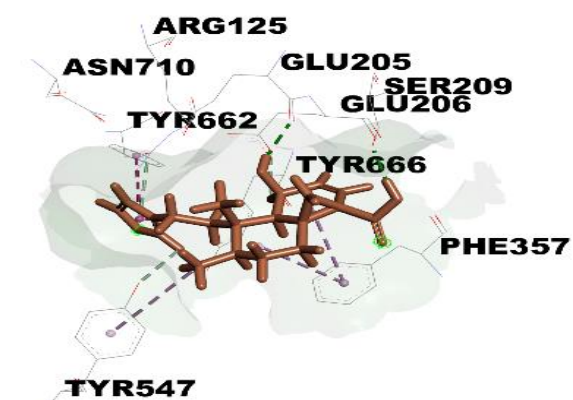
h)



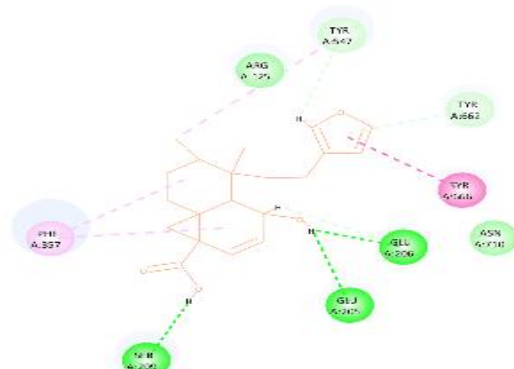
i)



j)



k)



l)

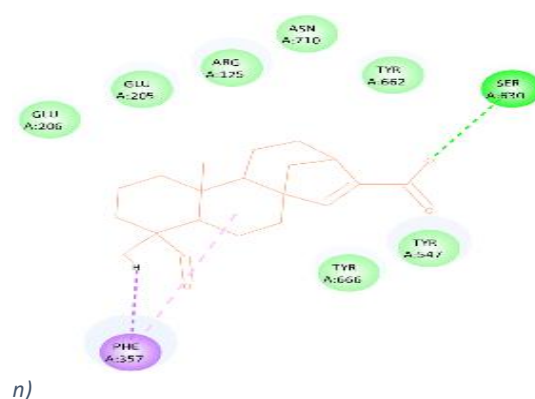
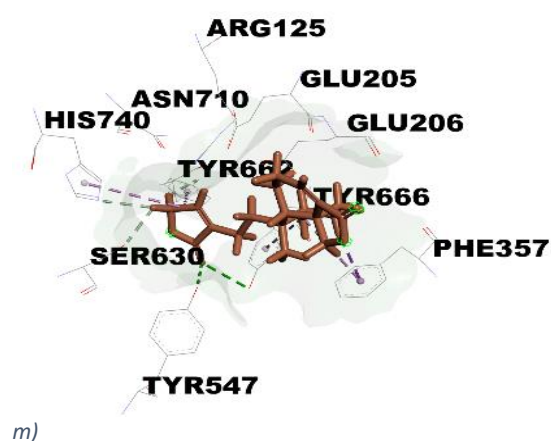
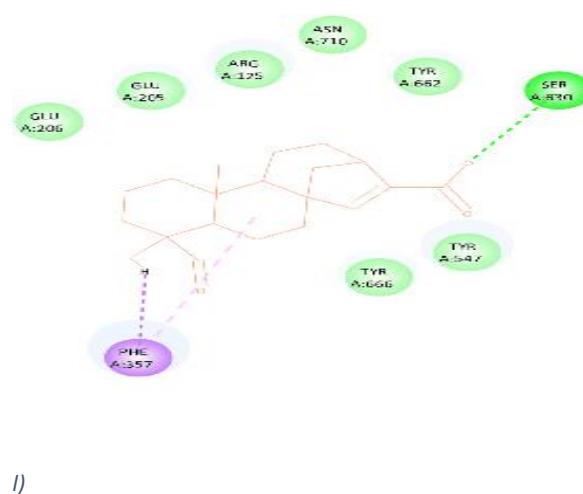
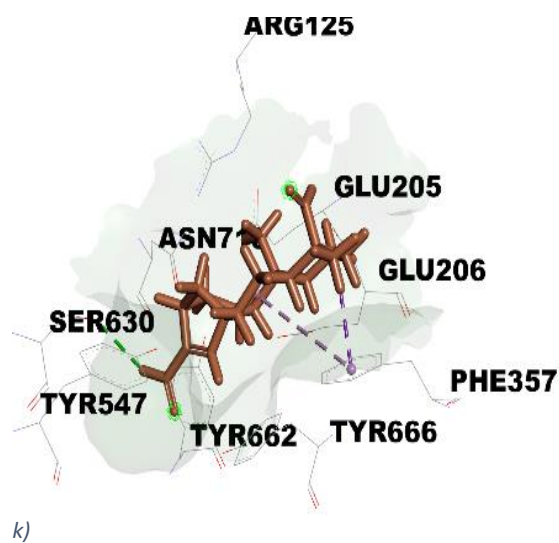
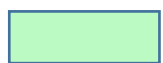


FIG 5.6 PICTORIAL REPRESENTATION OF DOCKED COMPOUNDS

(A) Quinic acid, (B) Shikimic acid, (C) Loliolide, (D) Cleomiscosin A, (E) Hautriwaic acid, (F) (1a*S*,4*S*,4a*R*,5*S*,6*R*,8a*S*)-5-[2-(furan-3-yl) ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[*j*]naphthalene-1a-carboxylic acid, (G) Viscosol, (H) Kauralexin , (I) Aliarin, (J) Mkapwanin.



Hydrogen bond



Carbon-Hydrogen bond
Interaction



Alkyl Interaction

TABLE 5.3 INTERACTION OF KEY AMINO ACID RESIDUES-4Y0A TARGET

COMPOUND IDENTIFIER	HYDROGEN BOND (HB)	PI-SIGMA AND AMIDE	ALKYL INTERACTION	CARBON-HYDROGEN INTERACTION
QUINICACID	ASN163	—	LEY175	ALA172, GLY170, LYS178
SHIKIMIC ACID	ASN168, ASP174	—	—	ALA172

TABLE 5.4 INTERACTION OF KEY AMINO ACID RESIDUES-4JPS TARGET

COMPOUND IDENTIFIER	HYDROGEN BOND (HB) INTERACTION	PI-SIGMA AND AMIDE	ALKYL INTERACTION	CARBON-HYDROGEN INTERACTION
SHIKIMIC ACID	GLU849, VAL851, SER854	—	—	—

TABLE 5.5 INTERACTION OF KEY AMINO ACID RESIDUES-5KIR TARGET

COMPOUND IDENTIFIER	HYDROGEN BOND (HB) INTERACTION	PI-SIGMA AND AMIDE INTERACTION	ALKYL INTERACTION	CARBON-HYDROGEN INTERACTION
QUINIC ACID	LEU352	-	VAL349,V AL532	-
SHIKIMIC ACID	SER353,VA L523			ALA527,V AL349
LOLIOLIDE			ALA527,V AL349,VA L523,LEU3 52	
CLEOMISCOSIN A	TYR385,AR G513	SER353,SER 530	LEU531,V AL116,LE U359,TYR 355,ILE51 7,PHE518, ALA516,	LUE352,G LN192,HI S90
KAURALEXIN B	ARG513		TYR355,V AL349,ILE 517,PHE5 18	
HAUTRIWAIC	TYR385		TRP387,T YR355,VA L349,ALA5 27,PHE51 8,ALA516	LEU352

(1aS,4S,4aR,5S,6R,8aS) -5-[2-(furan-3-yl)ethyl]-4- hydroxy-5,6-dimethyl- 1,4,4a,6,7,8- hexahydrocyclopropa[j]na phthalene-1a-carboxylic acid	TYR355		TRP387,A LA527	
VISCOSOL	TYR355,AR G513,PHE5 18,GLN192		LEU359,L EU531,VA L116,ALA5 27,HIS90, ALA516	SER353,S ER530
ALIARIN	TYR355,AR G513		TRP387,P HE518,VA L523,MET 522,ALA52 7,HIS90,A LA516	SER530,G LY526
MKAPWANIN	TYR385,AR G513,TYR3 55		ALA516,HI S90,VAL5 23,ALA527 ,VAL349,L EU352	PHE518
methyl (1aR,2R,4aR,5S,6R,8aS) -5-[2-(furan-3-yl)ethyl]-2- methoxy-5,6-dimethyl- 1,2,4a,6,7,8- hexahydrocyclopropa[j]na phthalene-1a-carboxylate		LEU531	ARG513,A LA516,VA L523,LEU3 59,VAL116 ,VAL349,A LA527	PHE518,G LN192,SE R353,LEU 352,TYR3 55

TABLE 5.6 INTERACTION OF KEY AMINO ACID RESIDUES-4NPZ TARGET

COMPOUND IDENTIFIER	HYDROGEN BOND (HB) INTERACTION	PI-SIGMA AND AMIDE INTERACTION	ALKYL INTERACTION	CARBON-HYDROGEN INTERACTION
QUINIC ACID	ASN710, TYR662 TYR547, SER630	-	-	GLU205, GLU206
SHIKIMIC ACID	GLU206, TYR662, TYR547, ARG125, SER630	-	-	GLU205
LOLIOLIDE	SER209, GLU206, ARG669	-	-	GLU205, ARG125
CLEOMISCOSIN A	TYR666, TYR547, GLU205, ARG125	-	-	GLU206, TYR662
HAUTRIWAIC ACID	TYR662, TYR547			
(1aS,4S,4aR,5S,6R,8aS)-5-[2-(furan-3-yl)ethyl]-4-hydroxy-5,6-dimethyl-1,4,4a,6,7,8-hexahydrocyclopropa[<i>h</i>]naphthalene-1a-carboxylic acid	SER209, GLU205, GLU206	-	-	TYR547, TYR662
KAWRALEXIN B3	SER630	-	-	
MKAPWANIN	TYR547, TYR666	-	-	TYR662, HIS740, SER630

CHAPTER 6

SUMMARY AND CONCLUSION

This project delves into the potential therapeutic applications of *Dodonaea viscosa*, a plant with a rich source of bioactive compounds. Our investigation began by sourcing phytochemicals from *Dodonaea viscosa* via the IMPPAT database. Using the SwissADME tool, we meticulously filtered these compounds to identify those with favorable drug-like properties, focusing on their absorption, distribution, metabolism, excretion, and toxicity (ADME) profiles. This screening step narrowed down the selection to a promising subset of 11 compounds.

We then selected four molecular targets with established relevance to various therapeutic areas: 4Y0A (bacterial infections), 4JPS (cancer), 5KIR (inflammation), and 4PNZ (diabetes). Molecular docking studies were performed to simulate the interactions between the 11 *Dodonaea viscosa* compounds and these target proteins. These simulations provided valuable insights into binding affinities and modes of interaction, suggesting that some of these compounds may be capable of modulating the activity of these targets.

To gain further structural insights, we conducted pharmacophore analysis to identify essential chemical features contributing to the observed biological activity. We focused on features such as hydrogen bond acceptors/donors, aromatic rings, aliphatic groups, and ionizable groups within the active compounds.

Two phytochemicals from *Dodonaea viscosa* displayed particularly strong docking results, suggesting the potential for therapeutic intervention in the diseases related to their corresponding targets. Further research is crucial to experimentally validate these computational findings. This would involve utilizing in vitro and in vivo models to verify the efficacy of these compounds and to explore their mechanisms of action. Additionally, we can look into the potential for synergistic effects by studying the combination of these compounds.

In conclusion, this project offers promising evidence that *Dodonaea viscosa* harbors phytochemicals with the potential to address various health conditions. Our computational approach successfully identified compounds with favorable ADME properties and affinity towards key drug targets. These findings warrant further exploration and could contribute to the development of novel therapeutic agents derived from this medicinal plant.

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