In-Silico Screening of Novel Drug Against Ovarian Cancer by Phytochemicals from Carica Papaya

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Abstract

Most of the women population suffer from many kinds of reproductive health issues. The cause of the diseases may be genetic or acquired causes. Ovarian cancer is a genetic aberration caused in females generation after generation. Various genes cause the genetic disorder, mainly BRCA 1 and BRCA 2. These major genes are present in chromosome 17q. 77% of the epithelial ovarian cancer tumor genes are in chromosome 17q. The disorder can be a germline mutation in females who express this disease before age 30. By DNA sequencing technology, the functioning of BRCA1 and BRCA2 can be discovered along with the involvement of the additional genes that compromise the homologous recombination (HR) pathway. Epithelial ovarian cancer (EOC) is the deadliest gynecological cancer and presents a major clinical challenge due to limited treatment options. Folate receptor alpha (FRα), encoded by the FOLR1 gene in chromosome 11q13.4, is an attractive therapeutic target due to its prevalent and high expression in EOC cells. The folate receptors FOLR1 and FOLR2 are overexpressed in multiple cancers. The overexpression of FOLR1 is often associated with increased cancer progression and poor patient prognosis. There is emerging evidence that FOLR1 is involved in signaling pathways that are independent of one-carbon metabolism.

Keywords: Epithelial Ovarian Cancer, FOLR1, FOLR2, chromosome 11, BRCA 1 and BRCA 2

1. INTRODUCTION

Gynecological malignancy is a major cause of death in current days. 1/5th of cases are hereditary susceptibility. 65- 85% of cases are due to germ-line mutation in BRCA genes. In studies; it is been observed that there are more suppressor genes and oncogenes associated with hereditary ovarian cancer. Ovarian cancer represents the leading cause of cancer death among gynecological malignancies. Almost 16 genes are known to be involved in the hereditary ovarian tumorigenesis. Along with BRCA1 and BRCA2, another gene called OVCAS1 is also an ovarian cancer susceptibility gene mapped in the 3p25-p22 gene locus. According to a survey 45 -55% of cases are caused due to BRCA1 mutation and 20-30% of genes are caused due to BRCA2 mutation. Here, we are analyzing the genes and designing a drug that is effective against the tumor-causing activity of the cell.

1.1. Drug design

Drug designing, also known as rational drug design, is the process of creating new medications based on an understanding of the biological and chemical principles underlying a particular disease. The goal is to design drugs that target specific molecules involved in the disease process while minimizing side effects. The process involves several steps:

1. **Identification of Drug Targets:**
a. Understanding the biological pathways and molecular mechanisms involved in a disease.
b. Identifying specific molecules (proteins, enzymes, receptors) that play a crucial role in the disease.

2. **Target Validation:**
a. Confirming that the selected target is indeed relevant to the disease.
b. Verifying that modifying the target leads to the desired therapeutic effect.

3. **Lead Identification:**
a. Finding or designing molecules (leads) that have the potential to interact with the target.
b. High-throughput screening, virtual screening, and other computational methods are often used to identify potential lead compounds.

4. **Lead Optimization:**
a. Improving the properties of lead compounds, such as efficacy, specificity, and safety.
b. Medicinal chemistry techniques are employed to modify the chemical structure of the leads.

5. **Preclinical Testing:**
a. Assessing the safety and efficacy of lead compounds in laboratory settings using in vitro and animal models.
b. Investigating pharmacokinetics, toxicity, and other parameters.

6. **Clinical Trials:**
a. Conducting human trials to evaluate the safety and efficacy of the drug.
b. Clinical trials typically have several phases, starting with small groups of healthy volunteers and progressing to larger groups of patients.

7. **Regulatory Approval:**
a. Submitting the data from clinical trials to regulatory agencies for approval.
b. If approved, the drug can be marketed and made available to the public.

8. **Post-Marketing Surveillance:**
a. Monitoring the drug's safety and effectiveness once it is available on the market.
b. Addressing any emerging issues or side effects.

Technological advancements, including computational biology, bioinformatics, and structural biology, have significantly accelerated the drug design process. These tools allow researchers to model the interactions between drugs and their targets, predict the pharmacokinetics and toxicity of compounds, and streamline the identification of potential drug candidates.

1.2. Molecular docking

Molecular docking analysis has been one of the most basic and important strategies for drug discovery. It allows the prediction of molecular interactions that hold together a protein and a ligand in the bound state. The relevant basic theories, including sampling algorithms and scoring functions, are also mentioned. Comparative analysis of different molecular docking approaches, especially those including backbone flexibility in receptors, has also been included in the discussion. Considering the significance

of the application of such tools and strategies, a solved practical exercise along with a detailed outline of the protocol to follow has been provided in the final section of the chapter. All the calculations have been performed using free wares such as AutoDock, so any and every reader can practice and validate their docking study.

Current limitations to the widespread use of molecular docking

Molecular docking is a computational technique used in drug design to predict the binding modes and affinities of small molecules to target proteins. While it has proven to be a valuable tool, some several limitations and challenges affect its widespread use and reliability. Some of these limitations include:

Scoring Functions Accuracy:

- The accuracy of scoring functions, which are used to estimate the binding affinity between a ligand and a target, is often limited. Predicting the binding energy with high precision remains a challenge.

Flexibility and Dynamics:

- Molecular docking often assumes rigid structures for both ligands and receptors. In reality, proteins and ligands can undergo conformational changes, and accounting for such flexibility in docking studies is a complex task.

Solvent Effects:

- Many molecular docking methods overlook the role of solvent molecules in the binding process. In reality, water molecules and other solvents can significantly influence ligand-protein interactions.

Treatment of Protein Flexibility:

- Accurately representing the flexibility of the protein is challenging. Ignoring protein flexibility or using simplified models can lead to inaccurate predictions.

Scalability:

- Some molecular docking methods are computationally expensive, especially when dealing with large datasets or extensive conformational sampling. This can limit their applicability for high-throughput virtual screening.

Ligand Parameterization:

- The accurate parameterization of ligands is crucial for reliable docking results. However, obtaining accurate force field parameters for diverse chemical structures can be challenging.

Incomplete Binding Site Information:

- In cases where the binding site of the target protein is not well-defined or known, docking predictions may be less accurate.

Protein-Ligand Covalent Interactions:

- Traditional docking methods may struggle to accurately predict binding modes involving covalent interactions, which are crucial for certain drug design scenarios.

Post-translational Modifications:

- Molecular docking often does not consider post-translational modifications or the influence of specific protein states, which can be critical in understanding real-world biological systems.

Validation and Benchmarking:

- The lack of standardized procedures for validating and benchmarking docking methods makes it challenging to compare different approaches and assess their performance consistently.

- Researchers are continually working on improving the accuracy and reliability of molecular docking methods by addressing these limitations. Integrating experimental data, enhancing scoring functions,

and incorporating more advanced techniques such as molecular dynamics simulations can contribute to overcoming some of these challenges.

1.3. Types of molecular docking

Molecular docking is a versatile computational technique used in drug discovery and molecular biology to predict the binding mode and affinity of a small molecule (ligand) with a target macromolecule (often a protein). There are several types of molecular docking methods, each with its own approach and level of complexity. Here are some common types:

1. Rigid Docking:

Assumes that both the ligand and the target binding site are rigid during the docking process. This is a computationally faster approach but may not capture the full range of protein flexibility.

2. Semi-Flexible Docking:

Allows flexibility in the ligand while keeping the protein rigid. This considers the adaptability of the ligand to the target site while simplifying the treatment of protein flexibility.

3. Flexible Docking:

Considers flexibility in both the ligand and the target protein. This approach attempts to account for conformational changes in both the ligand and the binding site during the docking simulation.

4. Induced Fit Docking:

Takes into account conformational changes in both the ligand and the protein upon binding. It involves multiple steps, where the binding site and/or ligand are allowed to adapt their conformations iteratively during the simulation.

5. High-Throughput Docking:

Designed for screening large compound libraries quickly. It often involves simplified scoring functions and faster computational methods to handle a large number of ligands efficiently.

6. Ligand-Based Docking:

Involves docking ligands into the target protein structure but without explicit consideration of the protein conformation. It relies on pre-existing knowledge of ligand structures and their interactions.

7. Protein-Ligand Interaction Fingerprints:

Focuses on identifying specific interaction patterns between ligands and proteins. It generates fingerprints or descriptors based on these interaction patterns for ligand comparison and classification.

8. Blind Docking:

Involves docking ligands into a target protein without prior knowledge of the binding site location. This method explores the entire protein surface to identify potential binding sites.

9. Grid-Based Docking:

Involves discretizing the search space into a grid, which helps in efficiently exploring possible ligand binding orientations. Autodock is an example of a widely used grid-based docking software.

10. Fragment-Based Docking:

Utilizes smaller molecular fragments rather than complete ligands for docking. Fragments are docked individually and then linked to form larger molecules with improved binding affinity.

11. Covalent Docking:

Deals with ligands that form covalent bonds with the target protein. This is important for certain drug design scenarios where covalent interactions are desired.

The choice of docking method depends on the specific goals of the study, the available computational resources, and the level of accuracy required. Researchers often use a combination of these methods to gain a more comprehensive understanding of ligand-protein interactions.

1.4. Phytochemicals

Phytochemicals are naturally occurring compounds found in plants that contribute to their color, flavor, and disease resistance. These chemicals have gained attention for their potential health benefits. While not essential for human survival like vitamins and minerals, phytochemicals are believed to have positive effects on human health. There are thousands of known phytochemicals, and they can be classified into various groups, including:

- Flavonoids: These are widely distributed in fruits, vegetables, and beverages such as tea and wine. Flavonoids have antioxidant properties and may help protect cells from damage.
- Carotenoids: Found in fruits and vegetables with orange, yellow, and red pigments, carotenoids like beta-carotene are converted into vitamin A in the body, which is important for vision and immune function.
- Glucosinolates: Present in cruciferous vegetables like broccoli, cabbage, and cauliflower, glucosinolates are compounds that may have anti-cancer properties.
- Phenolic acids: Found in fruits, vegetables, and whole grains, phenolic acids have antioxidant properties and may contribute to heart health.
- Terpenes: These compounds are found in the essential oils of plants and have diverse functions, including antimicrobial and anti-inflammatory properties.
- Saponins: Present in legumes and some vegetables, saponins have been studied for their potential role in cholesterol reduction and immune modulation.
- Lignans: Found in seeds, particularly flaxseeds, as well as in whole grains and vegetables, lignans have antioxidant properties and may have cardiovascular benefits.

Research suggests that a diet rich in a variety of phytochemicals may contribute to overall health and reduce the risk of chronic diseases, including certain types of cancer and heart disease. However, it's essential to remember that the specific health benefits of phytochemicals can vary, and more research is needed to fully understand their mechanisms and effects on human health. Eating a diverse and colorful range of fruits, vegetables, whole grains, nuts, and seeds is a good way to incorporate a broad spectrum of phytochemicals into your diet.

1.5. Uses of phytochemicals

Phytochemicals have various uses and applications, primarily in the realms of nutrition, medicine, and industry. Here are some of the key uses:

- Nutritional Benefits: Phytochemicals contribute to the health-promoting properties of fruits, vegetables, whole grains, nuts, seeds, and herbs. They provide color, flavor, and aroma to foods while also offering potential health benefits. Including phytochemical-rich foods in the diet can help reduce the risk of chronic diseases like cancer, heart disease, and diabetes.
- Disease Prevention and Treatment: Many phytochemicals exhibit bioactive properties that can help prevent and treat various diseases. For example, antioxidants such as flavonoids and carotenoids help neutralize harmful free radicals in the body, reducing oxidative stress and inflammation linked to

chronic diseases. Some phytochemicals also have anti-inflammatory, antimicrobial, and anti-cancer properties.

- Pharmaceuticals: Phytochemicals serve as important sources of compounds used in pharmaceutical drugs. Medicines derived from plants or inspired by plant compounds are used to treat a wide range of conditions, including pain, inflammation, infections, cardiovascular diseases, and cancer. For example, the anti-cancer drug paclitaxel (Taxol) is derived from the bark of the Pacific yew tree.
- Functional Foods and Dietary Supplements: Phytochemical-rich foods are often incorporated into functional foods and dietary supplements aimed at improving health and well-being. These products may contain concentrated extracts of phytochemicals or be fortified with specific plant-derived compounds to provide targeted health benefits.
- Cosmetics and Personal Care Products: Phytochemicals are used in cosmetics and personal care products for their antioxidant, anti-inflammatory, and skin-nourishing properties. Plant extracts and essential oils are common ingredients in skincare products, hair care products, and fragrances.
- Food Preservation: Some phytochemicals have natural antimicrobial properties that can help preserve food and prevent spoilage. Plant-derived compounds such as polyphenols and flavonoids are used as natural preservatives in food processing.
- Industrial Applications: Phytochemicals are utilized in various industrial applications, including the production of dyes, pigments, fragrances, and natural pesticides. Plant extracts may also be used in environmentally friendly alternatives to synthetic chemicals in manufacturing processes.

Overall, phytochemicals play a crucial role in promoting human health, supporting diverse industries, and contributing to sustainable practices in agriculture and manufacturing. Continued research into the properties and applications of phytochemicals holds promise for developing innovative products and therapies for various purposes.

1.6. AMET Studies

ADMET stands for Absorption, Distribution, Metabolism, Excretion, and Toxicity. These studies are an integral part of drug development and are conducted to understand how a potential drug candidate behaves within the body. Here's a brief overview of each component:

- Absorption: Examines how a drug is taken up by the body, typically through routes such as oral ingestion.
- Distribution: Investigates how the drug is distributed throughout the body, including how it reaches target tissues and organs.
- Metabolism: Focuses on the chemical transformations a drug undergoes in the body, often in the liver. This helps determine the stability and potential for toxicity of the drug.
- Excretion: Studies the elimination of the drug and its metabolites from the body, usually through urine or feces.
- Toxicity: Assesses the potential harmful effects of the drug on various organs and systems within the body.

ADMET studies play a crucial role in predicting the safety and efficacy of a drug candidate before it advances to clinical trials. Understanding these aspects helps researchers optimize drug structures and dosages, ensuring that the drug has the desired therapeutic effects with minimal side effects.

1.7. Importance of ADMET studies

ADMET studies (Absorption, Distribution, Metabolism, Excretion, and Toxicity) play a crucial role in drug development and are considered essential components of the drug discovery process. Here are the key reasons highlighting the importance of ADMET studies:

- **Predicting Drug Efficacy:**

Absorption: Understanding how a drug is absorbed into the bloodstream helps predict its bioavailability, which directly impacts its efficacy. Poor absorption can lead to insufficient therapeutic levels in the body.

- **Optimizing Drug Formulation:**

Distribution: Knowledge of how a drug is distributed in various tissues and organs is critical for optimizing its formulation. This information helps in determining the right dosage and formulation for effective treatment.

- **Metabolism and Bioactivation:**

Metabolism: Investigating how a drug is metabolized in the body provides insights into its stability and potential for drug-drug interactions. Metabolism can also impact the duration of drug action and the formation of active or toxic metabolites.

- **Minimizing Side Effects:**

Excretion: Understanding the excretion pathways helps in predicting the drug's elimination half-life and potential accumulation in the body. This information is vital for minimizing adverse effects and ensuring drug safety.

- **Early Identification of Toxicity:**

Toxicity Studies: ADMET studies contribute significantly to the early identification of potential toxicities associated with a drug candidate. This helps in making informed decisions about whether to advance or discontinue the development of a particular compound.

- **Regulatory Requirements:**

Regulatory agencies such as the FDA (Food and Drug Administration) and EMA (European Medicines Agency) require comprehensive ADMET data during the drug approval process. Adequate ADMET data is essential for demonstrating the safety and efficacy of a drug.

- **Cost and Time Savings:**

Identifying issues related to absorption, distribution, metabolism, excretion, or toxicity early in the drug development process can save substantial time and resources. It allows researchers to focus on compounds with higher chances of success and avoid investing in candidates with unfavorable ADMET profiles.

- **Enhancing Drug Development Success:**

A thorough understanding of a drug candidate's ADMET properties contributes to a more informed decision-making process during drug development. This, in turn, increases the likelihood of successful clinical trials and regulatory approval.

In summary, ADMET studies are integral to the drug development pipeline, providing valuable insights that contribute to the optimization of drug candidates, ensuring their safety and efficacy, and ultimately improving the success rate of bringing new drugs to market.

1.8. Ovarian cancer

Ovarian cancer is a type of cancer that begins in the ovaries, which are the female reproductive organs

that produce eggs. It is often called the "silent killer" because symptoms may not appear until the disease has progressed to an advanced stage.

Symptoms of ovarian cancer can include bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, frequent urination, and changes in bowel habits. However, these symptoms can also be caused by other, less serious conditions, which can make ovarian cancer difficult to detect in its early stages.

Treatment for ovarian cancer typically involves surgery to remove the tumor, followed by chemotherapy or radiation therapy to kill any remaining cancer cells. The specific treatment plan will depend on factors such as the stage of the cancer, the patient's overall health, and whether the cancer has spread to other parts of the body.

Early detection is key to improving the prognosis for ovarian cancer, so it's important for women to be aware of the symptoms and to see their doctor if they experience any persistent or unusual symptoms. Additionally, women with a family history of ovarian cancer or certain genetic mutations may be at higher risk and may benefit from genetic counseling and screening tests.

1.9.Lipinski's rule of five

The Lipinski Rule of Five, also known as the Rule of Five or simply Ro5, is a set of criteria used to evaluate the drug-likeness of a chemical compound. These rules were formulated by Christopher A. Lipinski, a pharmaceutical chemist, and are commonly employed in the early stages of drug development to predict whether a compound is likely to have favorable oral bioavailability.

The Lipinski Rule of Five consists of the following criteria:

1. Molecular Weight (MW): The molecular weight should be less than 500 Daltons.
2. Lipophilicity (LogP): The octanol/water partition coefficient (LogP) should be less than five .
3. Hydrogen Bond Donors (HBD): The number of hydrogen bond donor atoms (usually nitrogen and oxygen atoms with hydrogen) should be less than 5.
4. Hydrogen Bond Acceptors (HBA): The number of hydrogen bond acceptor atoms (usually nitrogen and oxygen atoms) should be less than 10.

The basic idea behind these rules is that compounds meeting these criteria are more likely to have favorable absorption and permeation properties, which are crucial for oral bioavailability. However, it's important to note that the Lipinski Rule of Five is a guideline rather than a strict rule, and many successful drugs may not adhere to all of these criteria.

Researchers and pharmaceutical developers use the Lipinski Rule of Five as a screening tool to identify compounds with a higher likelihood of success in drug development, but other factors, such as specific therapeutic targets, pharmacokinetics, and toxicological considerations, are also taken into account during the drug development process.

1.10.   FOLR 1 gene

The FOLR1 gene encodes a protein called folate receptor alpha (FRα), which is involved in the transport of folate (vitamin B9) into cells. Folate is crucial for various cellular processes, including DNA synthesis and repair. The FOLR1 gene is particularly expressed in certain tissues, including the placenta, kidney, lung, and breast.

Mutations or alterations in the FOLR1 gene can affect folate metabolism and cellular processes dependent on folate, potentially leading to health issues. For example, abnormal FOLR1 expression has

been associated with various cancers, including ovarian and lung cancer, where FRα is often overexpressed.

Therapeutically, the high expression of FRα in some cancers has made it a target for specific drug delivery systems, such as folate-linked drugs, which can selectively target cancer cells overexpressing FRα while sparing normal cells.

Folate receptors are proteins found on the surface of certain cells that have a high affinity for folate, also known as vitamin B9 or folic acid. These receptors play a crucial role in the cellular uptake of folate, which is essential for various biological processes such as DNA synthesis, cell division, and amino acid metabolism.

There are several types of folate receptors, but one of the most studied is the folate receptor alpha (FRα). FRα is overexpressed in many types of cancer cells, including ovarian, lung, breast, and colorectal cancers, making it an attractive target for cancer therapy. This overexpression is thought to be a result of increased demand for folate in rapidly dividing cancer cells.

Researchers have developed targeted therapies, such as antibody-drug conjugates (ADCs) and folate receptor-targeted drugs, that specifically bind to folate receptors on cancer cells. These therapies deliver cytotoxic drugs directly to cancer cells while minimizing damage to healthy tissues, potentially improving treatment efficacy and reducing side effects compared to traditional chemotherapy.

Furthermore, folate receptor-targeted imaging agents have been developed for diagnostic purposes, allowing for the visualization and detection of folate receptor-expressing tumors using imaging techniques such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

Overall, folate receptors play a significant role in both normal cellular function and disease processes, particularly in cancer, making them promising targets for both therapeutic intervention and diagnostic imaging.

2. AIM:

To analyze drug properties of phytochemicals extracted from Carica papaya against folate receptor protein for epithelial ovarian cancer.

3. OBJECTIVES:

1. Analyse the FOLR 1 gene
2. To analyze the structure and orientation of folate receptor protein
3. Phytochemical studies of Carica papaya
4. Molecular docking analysis
5. ADME analysis of the selected compounds.

4. REVIEW OF LITERATURE:

1. *Shreelekha Dutta et; al. (2017) studied Molecular docking prediction, and in vitro studies elucidate the anti-cancer activity of phytoestrogens,*

The study is aimed at evaluating the chemosensitization and apoptotic effect of aglycone-rich extracts of dietary phytoestrogens (derived from soybean and flaxseed) on estrogen receptor-positive, MCF-7 and

estrogen receptor-negative, MDA-MB-231 cells. The extracts show potent activity on both the cell lines, hence, in silico studies have been carried out to find the possible reason for their activity.

2. *C. Baskaran et, al. (2012) Computational molecular docking studies on anticancer drugs,*

Cancer is characterized by the uncontrollable proliferation of abnormal cells. Lung cancer is a prevalent form of malignant neoplasm worldwide. Nonsmall-cell lung cancers often contain oncogenic fusion genes composed of EML4 and anaplastic lymphoma kinase (ALK), which account for 2 to 7% of such tumors. ALK proteins are crucial in inhibiting the apoptosis process in cancer. Crizotinib, Sunitinib malate, Tandutinib, and other drugs are commonly used to treat nonsmall-cell lung cancer. These drugs target the role of ALK in promoting cell growth and proliferation in malignant cells. Their primary function is to counteract the effects of ALK on these cells.

3. *Sourav Mukherjee et; al. studied Structure-Based Virtual Screening, Molecular Docking, and Molecular Dynamics Simulation of VEGF inhibitors for the clinical treatment of Ovarian Cancer,*

Vascular endothelial development factor (VEGF) and its receptor assume a significant part both in physiologic and pathologic angiogenesis, which is recognized in ovarian disease movement and metastasis improvement. The current examination means to distinguish a potential vascular endothelial development factor inhibitor which is assuming a pivotal part in animating the immunosuppressive microenvironment in growth cells of the ovary and to look at the viability of the recognized inhibitor for the therapy of ovarian disease utilizing different in silico approaches. Twelve laid-out VEGF inhibitors were gathered from different literary works. The compound AEE788 shows incredible liking towards the objective protein because of the docking study. AEE788 was additionally utilized for structure-based virtual screening to get an all the more fundamentally comparable compound with high proclivity. Among the 80 virtual screened compounds, CID 88265020 explains much preferable partiality over the laid out compound AEE788. In view of sub-atomic elements reenactment, pharmacophore, and near harmfulness examination of both the best-laid out compound and the best virtual screened compound showed a trifling variety in related properties. The virtual screened compound CID 88265020 has a high fondness with the most minimal re-rank score and holds a colossal potential to hinder the VGFR and can be executed for imminent future examinations in ovarian disease.

4. *Priyadurairaj et,al. (2020) studied the Effect of ethanolic extract of Carica papaya Leaves and their cytotoxicity and apoptotic potential in human ovarian cancer cell lines-PA-1,*

The current study aims to evaluate the effectiveness of Carica papaya ethanolic extract for wound healing, cell cycle blockage, apoptotic, antiproliferative, and cytotoxicity in ovarian cancer PA-1 cell lines. Supplies and Procedures: For the aforementioned experiment, PA-1 cells were treated according to the procedure both with and without the sample (to serve as a control). Results: The antiproliferative result shows that the growth inhibitory effect (IC50) values are attained at a concentration of 100 μg, and PA-1 cell viability declines in a concentration-dependent way. After the sample was treated with PA-1 cells, an increase in apoptotic cells was seen using double staining techniques. The test sample greatly inhibited the cell cycle's G2/M phase.

5. *Sheikh Fauziya et, al; (2013) studied PAPAYA (CARICA PAPAYA): SOURCE MATERIAL FOR ANTICANCER,*

Around the world, papaya (Carica papaya Linn.) is renowned for its remarkable nutritional and therapeutic qualities. The entire plant is used medicinally, including the leaves, fruits, seeds, bark, latex, and juice. The papaya is regarded as a nutritional fruit because of its many benefits. Papain, lycopene, isothiocyanate, and other vital minerals, vitamins, carbohydrates, carotenoids, and flavonoids are all

present in the entire papaya plant. The body and immune system are nourished by these very nourishing fruits. According to an in vitro study, papaya physiochemicals have anticancer properties and can cure a variety of cancer cell lines. Papain, an enzyme found in abundance in papayas, has anti-cancer properties. Protein and fibrin cancer cell walls are broken down into amino acids by papain. In addition to papain, it also contains highly reactive lycopene.

6. *Thao T. T. Nguyen et, al; (2012) studied the Anticancer activity of Carica papaya,*

Carica papaya is extensively grown in tropical and subtropical regions and is utilized both as a food source and in traditional medicine for treating various illnesses. The increasing number of anecdotal reports regarding its potential in cancer treatment and prevention, supported by numerous successful cases, highlights the need for scientific validation of its pharmacological properties. A thorough bibliographic search was carried out using the keywords "papaya," "anticancer," and "antitumor," in addition to cross-referencing. No clinical or animal studies on cancer were found, with only seven in vitro cell-culture-based studies being documented; these studies suggest that extracts from C. papaya could potentially impact the growth of different cancer cell lines. Nonetheless, several studies have concentrated on specific compounds found in papaya, revealing bioactivity with anticancer properties. This review presents a summary of investigations based on extracts or specific compounds from papaya, underscoring the need for further research to explore the bioactive components in C. papaya for their anticancer effects.

5. DISEASE AND PHYTOCHEMICALS:

5.1. Ovarian cancer

Ovarian cancer is a group of diseases that originates in the ovaries or the related areas of the fallopian tubes and the peritoneum. Women have two ovaries that are located in the pelvis, one on each side of the uterus. The ovaries make female hormones and produce eggs for reproduction. Women have two fallopian tubes which are a pair of long, slender tubes on each side of the uterus. Eggs pass from the ovaries through the fallopian tubes to the uterus. The peritoneum is the tissue lining that covers organs in the abdomen.

When ovarian cancer is found in its early stages, treatment works best. Ovarian cancer often causes signs and symptoms, so it is important to pay attention to your body and know what is normal for you. Symptoms may be caused by something other than cancer, but the only way to know is to see your doctor, nurse, or other health care professional.

Some mutations (changes in genes) can raise your risk for ovarian cancer. Mutations in the breast cancer susceptibility genes 1 and 2 (BRCA1 and BRCA2), and those associated with Lynch syndrome, are the most common mutations that raise ovarian cancer risk.

Ovarian cancers come in a variety of different tumor types and subtypes. The most common tumor type is adenocarcinoma, and the most common subtype is serous adenocarcinoma. Most serous adenocarcinomas are high-grade (aggressively growing) tumors.

Fig 1: ultrasound scan report of ovarian cancer tumor

5.1.1. Symptoms

When ovarian cancer first develops, it might not cause any noticeable symptoms. When ovarian cancer symptoms happen, they're usually attributed to other, more common conditions. Signs and symptoms of ovarian cancer may include:

- Abdominal bloating or swelling
- Quickly feeling full when eating
- Weight loss
- Discomfort in the pelvic area
- Fatigue
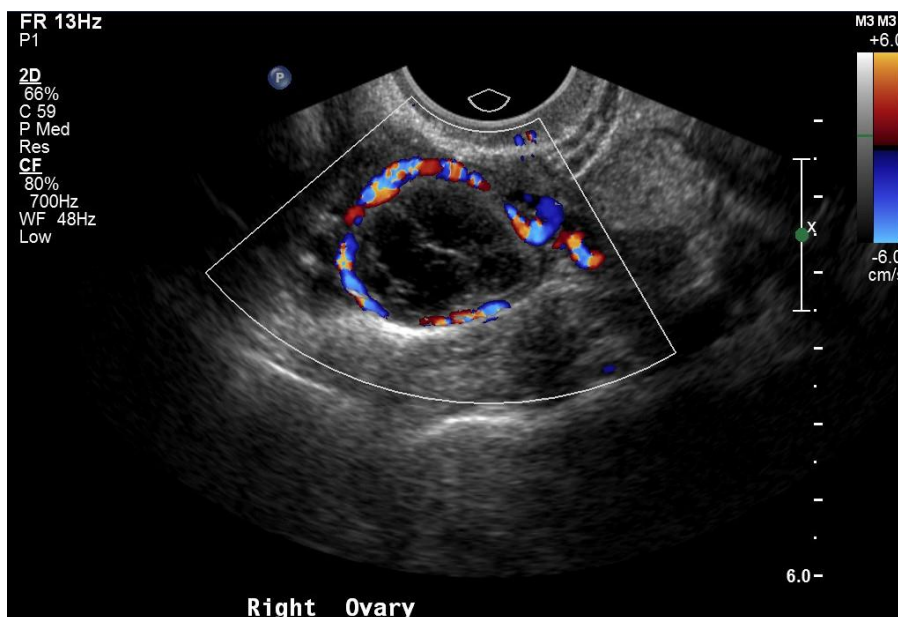- Back pain
- Changes in bowel habits, such as constipation
- A frequent need to urinate

Fig 2: ultrasound scan report of ovarian cancer tumour

5.1.2. Causes

It's not clear what causes ovarian cancer, though doctors have identified things that can increase the risk of the disease.

Doctors know that ovarian cancer begins when cells in or near the ovaries develop changes (mutations) in their DNA. A cell's DNA contains the instructions that tell the cell what to do. The changes tell the cells to grow and multiply quickly, creating a mass (tumor) of cancer cells. The cancer cells continue living when healthy cells die. They can invade nearby tissues and break off from an initial tumor to spread (metastasize) to other parts of the body.

5.1.3. Types of ovarian cancer

The type of cell where the cancer begins determines the type of ovarian cancer you have and helps your doctor determine which treatments are best for you. Ovarian cancer types include:

- *Epithelial ovarian cancer*. This type is the most common. It includes several subtypes, including serous carcinoma and mucinous carcinoma.
- *Stromal tumors*. These rare tumors are usually diagnosed at an earlier stage than other ovarian cancers.
- *Germ cell tumors*. These rare ovarian cancers tend to occur at a younger age.

5.1.4. Risk factors

Factors that can increase your risk of ovarian cancer include:

- *Older age*. The risk of ovarian cancer increases as you age. It's most often diagnosed in older adults.
- *Inherited gene changes*. A small percentage of ovarian cancers are caused by gene changes you inherit from your parents. The genes that increase the risk of ovarian cancer include BRCA1 and BRCA2. These genes also increase the risk of breast cancer. Several other gene changes are known to increase the risk of ovarian cancer, including gene changes associated with Lynch syndrome and the genes BRIP1, RAD51C, and RAD51D.
- *Family history of ovarian cancer*. If you have blood relatives who have been diagnosed with ovarian cancer, you may have an increased risk of the disease.
- *Being overweight or obese*. Being overweight or obese increases the risk of ovarian cancer.
- *Postmenopausal hormone replacement therapy*. Taking hormone replacement therapy to control menopause signs and symptoms may increase the risk of ovarian cancer.
- *Endometriosis*. Endometriosis is an often painful disorder in which tissue similar to the tissue that lines the inside of your uterus grows outside your uterus.
- *Age when menstruation started and ended*. Beginning menstruation at an early age or starting menopause at a later age, or both, may increase the risk of ovarian cancer.
- *Never having been pregnant*. If you've never been pregnant, you may have an increased risk of ovarian cancer.

5.1.5. Prevention

There's no sure way to prevent ovarian cancer. But there may be ways to reduce your risk:

- *Consider taking birth control pills*. Ask your doctor whether birth control pills (oral contraceptives) may be right for you. Taking birth control pills reduces the risk of ovarian cancer. But these medications do have risks, so discuss whether the benefits outweigh those risks based on your situation.
- *Discuss your risk factors with your doctor*. If you have a family history of breast and ovarian cancers, bring this up with your doctor. Your doctor can determine what this may mean for your own

risk of cancer. You may be referred to a genetic counselor who can help you decide whether genetic testing may be right for you. If you're found to have a gene change that increases your risk of ovarian cancer, you may consider surgery to remove your ovaries to prevent cancer.

5.2. Carica papaya

Papaya, (Carica papaya) is a succulent fruit of a large plant of the family Caricaceae. Though its origin is rather obscure, the papaya may represent the fusion of two or more species of Carica native to Mexico and Central America. Today it is cultivated throughout the tropical world and into the warmest parts of the subtropics. The papaya fruit is slightly sweet, with an agreeable musky tang, which is more pronounced in some varieties and in some climates than in others. It is a popular breakfast fruit in many countries and is also used in salads, pies, sherbets, juices, and confections. The unripe fruit can be cooked like squash.

Fig 3: *Carica papaya*

Kingdom:	Plantae
Clade:	Tracheophytes
Clade:	Angiosperms
Clade:	Eudicots
Clade:	Rosids
Order:	Brassicales
Family:	Caricaceae
Genus:	*Carica*
Species:	*C. papaya*

Table 1: Scientific Classification Of *Carica papaya*

5.2.1. Physical description

The papaya plant is considered a tree, though its palmlike trunk, up to 8 metres (26 feet) tall, is not as woody as the designation generally implies. The plant is crowned by deeply lobed leaves, sometimes 60 cm (2 feet) across, borne on hollow petioles (leaf stalks) 60 cm long. Normally, the species is dioecious, male and female flowers being produced on separate plants, but hermaphroditic forms are known, and numerous irregularities in the distribution of the sexes are common. Male flowers are borne in clusters on stalks 90 cm long; the flowers are funnel-shaped, about 2.5 mm (0.1 inch) long, and whitish, with 10 stamens in the throat. The female flowers are considerably larger, on very short stalks, and often solitary

in the leaf axils; they have five fleshy petals that are united toward the base and a large cylindrical or globose superior ovary that is crowned by five fan-shaped sessile stigmas.

The fruit is commonly spherical to cylindrical in form, is 75 to 500 mm (3 to 20 inches) or even more in length, and sometimes weighs as much as 9 to 11.5 kg (20 to 25.5 pounds). The very juicy flesh is deep yellow or orange to salmon-coloured. Along the walls of the large central cavity are attached numerous round, wrinkled black seeds.

The unripe fruit contains a milky juice in which is present a protein-digesting enzyme known as papain, which greatly resembles the animal enzyme pepsin in its digestive action. This juice is used in the preparation of various remedies for indigestion and in the manufacture of meat tenderizers.

5.2.2. Cultivation

Papayas are usually grown from seed. Their development is rapid, with fruit being produced before the end of the first year. Under favorable conditions, a plant may live five years or more. The papaya ringspot virus nearly wiped out papaya crops around the world, first hitting Hawaiian plantations in the 1940s and soon spreading. A genetically modified (GMO) variety named the Rainbow papaya was developed in the early 2000s with resistance to the virus. It was one of the first GMO fruits in commercial production, and the majority of exported papayas are now GMO crops.

5.2.3. Benefits

Protection against heart disease

Papayas contain high levels of antioxidants such as vitamin A, vitamin C, and vitamin E. Diets high in antioxidants may reduce the risk of heart disease. The antioxidants prevent the oxidation of cholesterol. When cholesterol oxidizes, it's more likely to create blockages that lead to heart disease. Additionally, papaya's high fiber content may reduce the risk of heart disease. High-fiber diets lower cholesterol levels. Other papaya benefits include folic acid, which is needed to convert the amino acid homocysteine into less harmful amino acids. (Amino acids are molecules that help make up proteins.) High levels of homocysteine, an amino acid mostly found in meat products, are a risk factor for heart disease. Eating papaya may lower homocysteine levels, reducing this risk factor.

Digestion and reduced inflammation

Papayas contain two enzymes, papain, and chymopapain. Both enzymes digest proteins, meaning they can help with digestion and reduce inflammation. Papain is an ingredient in some over-the-counter supplements to help with minor upset stomach. Both papain and chymopapain also help reduce inflammation. They may help ease acute pain, like that from burns or bruises, and might help with chronic inflammatory conditions such as arthritis and asthma.

Immune system

Eating foods high in vitamin C can help boost your immune system, allowing the body to fight off bacterial and viral illnesses. Papaya has a good amount of this antioxidant. Papaya is also a good source of vitamin A, which is important for a healthy and functional immune system.

Potentially protects against prostate cancer

Lycopene is a natural pigment found in red and orange foods. Tomatoes, watermelon, and papaya are good sources of lycopene. Some experts believe that eating more lycopene reduces the risk of prostate cancer, but some research has been inconclusive. However, in other studies, eating a diet high in lycopene along with green tea was found to reduce the risk of prostate cancer significantly.

Papaya seed benefits

Papaya seeds have traditionally been used as a natural remedy to combat intestinal parasites. Some studies suggest that compounds in papaya seeds may have antiparasitic effects, helping eliminate harmful organisms from the digestive tract. Some research also suggests that papaya seeds may have a protective effect on the liver. Certain compounds in the seeds, such as flavonoids and phenolic acids, might support liver health and function. Papaya seeds contain bioactive compounds that may have anti-inflammatory properties. These compounds may help reduce inflammation in the body and provide relief from inflammatory conditions.

Papaya enzyme benefits

Papaya enzymes, particularly papain, are known for their digestive properties. They help break down dietary proteins in the stomach. This can lead to reduced bloating, gas, and indigestion. Applying creams or ointments that contain papaya enzyme is believed to promote wound healing. The enzymes may help remove dead or damaged tissue, aiding in the healing process. Some skincare products contain papaya enzymes due to their exfoliating properties. Papain helps remove dead skin cells, leaving the skin smoother and more radiant.

5.2.4. Nutrition

A medium-sized papaya contains more than 200% of the vitamin C you need per day. This vitamin helps reduce the risk of heart disease and boosts the immune system. Papayas are also a good source of:

- Folate
- Vitamin A
- Fiber
- Copper
- Magnesium
- Potassium
- Pantothenic acid
- Nutrients per serving

Medium-sized papaya (approximately 275 grams) contains about:

- 119 calories
- 1.3 grams of protein
- 30 grams of carbohydrates
- Less than 1 gram of fat
- 4.7 grams of dietary fiber
- 21.58 grams of sugar

6. MATERIALS AND METHOD

7.1 DATABASES

1. GENBANK

GenBank is a database of genetic sequence data. It's maintained by the National Center for Biotechnology Information (NCBI), which is part of the United States National Library of Medicine (NLM), a branch of the National Institutes of Health (NIH). GenBank serves as an archive for DNA and RNA sequences submitted by researchers from around the world.

- Data Repository: GenBank collects, annotates, and distributes DNA sequences and their associated information, such as sequence features and references.

- Sequence Types: It contains sequences from a variety of organisms, including viruses, bacteria, plants, animals, and humans.
- Collaborative Effort: GenBank is a collaborative effort, with data submitted by scientists and researchers worldwide. Submissions are reviewed to ensure accuracy and quality.
- Sequence Accession Numbers: Each sequence in GenBank is assigned a unique accession number, which serves as its identifier. These accession numbers are used in scientific publications to refer to specific sequences.
- Search and Retrieval: Users can search GenBank using various criteria, such as keywords, accession numbers, organism names, and sequence similarity. Sequence data can be retrieved in different formats for analysis and research.
- Annotation: GenBank provides annotations for sequences, including information about genes, coding regions, regulatory elements, and other features. These annotations help researchers interpret the sequence data.
- Integration with Other Databases: GenBank is integrated with other databases and tools provided by NCBI, such as PubMed (for literature search), BLAST (for sequence similarity search), and Entrez (for integrated search across multiple NCBI databases).

Overall, GenBank plays a crucial role in the field of molecular biology and bioinformatics by providing a centralized repository of genetic sequence data for research, education, and various applications in biotechnology and medicine.
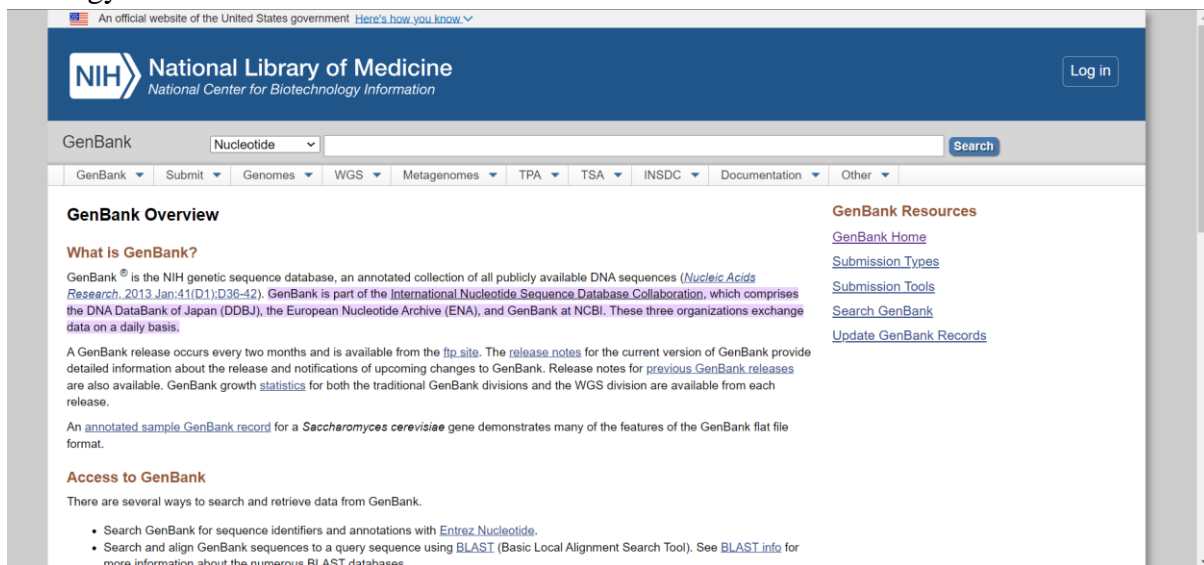
Fig 4: Genbak

2. RCSB PDB

The Protein Data Bank (PDB) is an archive of experimentally determined three-dimensional (3D) structures of biological macromolecules, primarily proteins and nucleic acids. It provides a resource for researchers to access and analyze structural data, aiding in understanding the structure-function relationships of biological molecules.

- Data Repository: The PDB serves as a central repository for 3D structural data of biological macromolecules determined using techniques such as X-ray crystallography, nuclear magnetic resonance (NMR) spectroscopy, and cryo-electron microscopy (cryo-EM).

- International Collaboration: The PDB is maintained through an international collaboration involving research institutions and organizations worldwide. It is managed by the Worldwide Protein Data Bank (wwPDB) consortium, which includes members from several countries.
- Structural Information: Each entry in the PDB contains detailed structural information about a bio-molecule, including the coordinates of atoms, bond lengths, angles, and other geometric parameters.
- Accession Codes: Each structure deposited in the PDB is assigned a unique alphanumeric identifier known as a PDB ID. This identifier is used to reference the structure in scientific publications and databases.
- Data Deposition and Validation: Researchers submit their experimentally determined structures to the PDB along with supporting experimental data. The submitted data undergoes validation and annotation processes to ensure quality and accuracy.
- Search and Retrieval: Users can search the PDB database using various criteria such as PDB ID, keywords, organism name, protein name, and sequence similarity. The PDB website provides tools for searching, browsing, and downloading structural data.
- Integration with Other Resources: The PDB is integrated with other bioinformatics resources and databases, such as UniProt, RCSB Sequence Clusters, and RCSB Chemical Components Dictionary, to provide comprehensive information about biological macromolecules.
- Structural Analysis: Researchers use the PDB to study protein structure, function, and dynamics, as well as to design drugs, understand disease mechanisms, and engineer proteins for various applications.

Overall, the Protein Data Bank plays a critical role in structural biology and bioinformatics by providing a valuable resource for accessing, analyzing, and sharing structural information about biological macromolecules.
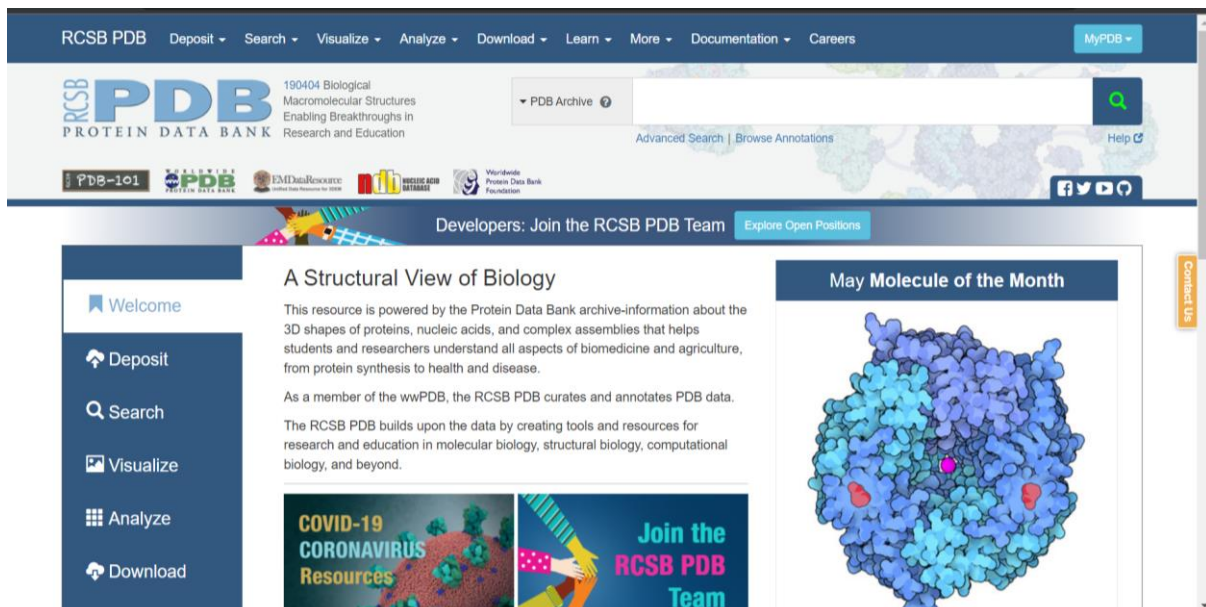
Fig 5: RCSB PDB

3. CAST P

CASTp (Computed Atlas of Surface Topography of proteins) database or tool. CASTp is a web-based resource and algorithm used for the calculation and analysis of protein surface pockets and binding sites.

- Surface Topography Analysis: CASTp allows users to analyze the surface topography of proteins, specifically focusing on identifying and characterizing surface pockets, voids, and clefts.

- Binding Site Identification: One of the primary applications of CASTp is the identification and analysis of potential binding sites or pockets on protein surfaces. These binding sites are crucial for understanding protein-ligand interactions, such as drug binding to target proteins.

- Accessibility and Visualization: CASTp provides users with accessible web-based tools for submitting protein structures and performing surface analysis. Results are often presented visually, allowing users to inspect and analyze the identified pockets and their properties.

- Calculation Methodology: The CASTp algorithm calculates the surface accessibility of a protein by rolling a probe sphere across its surface. It identifies cavities by considering both geometric and physicochemical properties of the protein surface.

- Applications: CASTp is used in various areas of structural biology and drug discovery, including protein-ligand docking studies, rational drug design, and understanding protein function based on surface features.

- Integration: While CASTp primarily provides a standalone web-based tool, its results can also be integrated with other bioinformatics resources and software for further analysis and interpretation of protein structures and functions.

Overall, CASTp serves as a valuable resource for structural biologists, biochemists, and drug discovery researchers, offering insights into protein surface characteristics and potential binding sites that are crucial for understanding protein function and designing therapeutics.
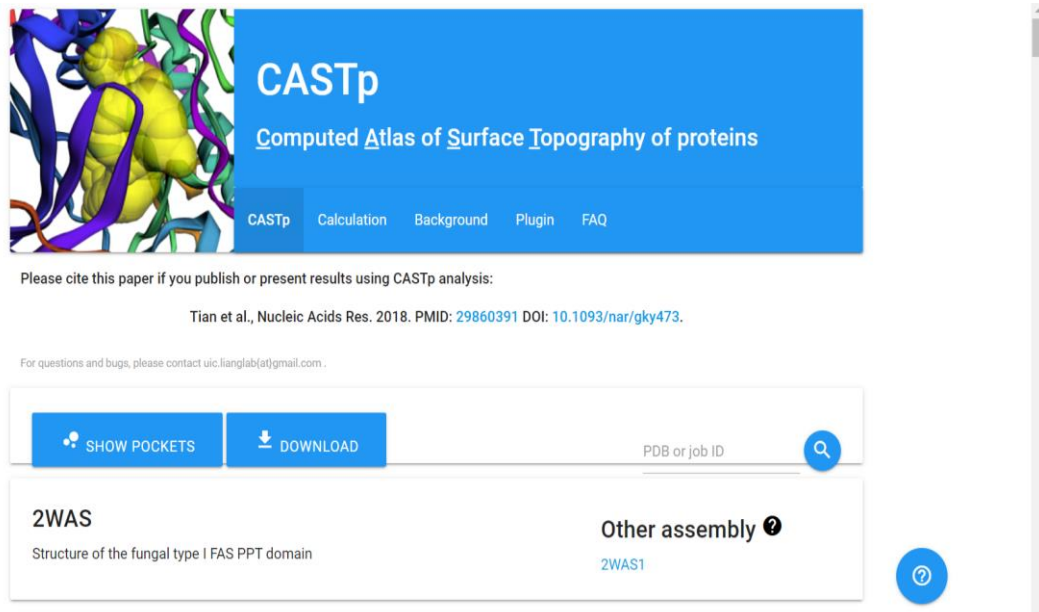
Fig 6:Cast p

4. PUBCHEM

PubChem is a comprehensive database of chemical compounds, maintained by the National Center for Biotechnology Information (NCBI), which is part of the United States National Library of Medicine (NLM), a branch of the National Institutes of Health (NIH). Here are some key points about PubChem:

- Chemical Compound Repository: PubChem serves as a repository for information on chemical compounds, including small organic molecules, peptides, carbohydrates, and more. It aggregates data from various sources, including chemical vendors, literature, and public submissions.

- Structural Information: Each compound in PubChem is annotated with detailed structural information, including 2D and 3D chemical structures, as well as molecular formulas, weights, and chemical properties.

- Biological Activities: PubChem provides data on the biological activities of chemical compounds, including assays, bioassays, and screening results. This information is crucial for drug discovery and chemical biology research.

- Compound Identifiers: Each compound in PubChem is assigned a unique identifier known as a PubChem CID (Compound Identifier). This identifier allows users to unambiguously reference and retrieve information about specific compounds.

- Integration with Other Databases: PubChem is integrated with other bioinformatics resources and databases, such as PubMed, NCBI Gene, and the Protein Data Bank (PDB). This integration enables users to explore relationships between chemical compounds, genes, proteins, and biological pathways.

- Search and Retrieval: Users can search PubChem using various criteria, such as chemical names, molecular formulas, chemical structures, and biological activities. PubChem offers web-based search tools, APIs (Application Programming Interfaces), and downloadable datasets for accessing its vast repository of chemical data.

- Data Submission: Researchers and organizations can submit data to PubChem, contributing to the expansion and enrichment of the database. Data submission is subject to curation and validation processes to ensure data quality and accuracy.

- Applications: PubChem is widely used in drug discovery, chemical informatics, toxicology, and pharmacology research. Researchers leverage its extensive collection of chemical and biological data to identify lead compounds, explore structure-activity relationships, and investigate the mechanisms of drug action.

Overall, PubChem plays a vital role in the field of chemical biology and bioinformatics, providing researchers with a valuable resource for exploring the properties, activities, and relationships of chemical compounds in various biological and biomedical contexts.
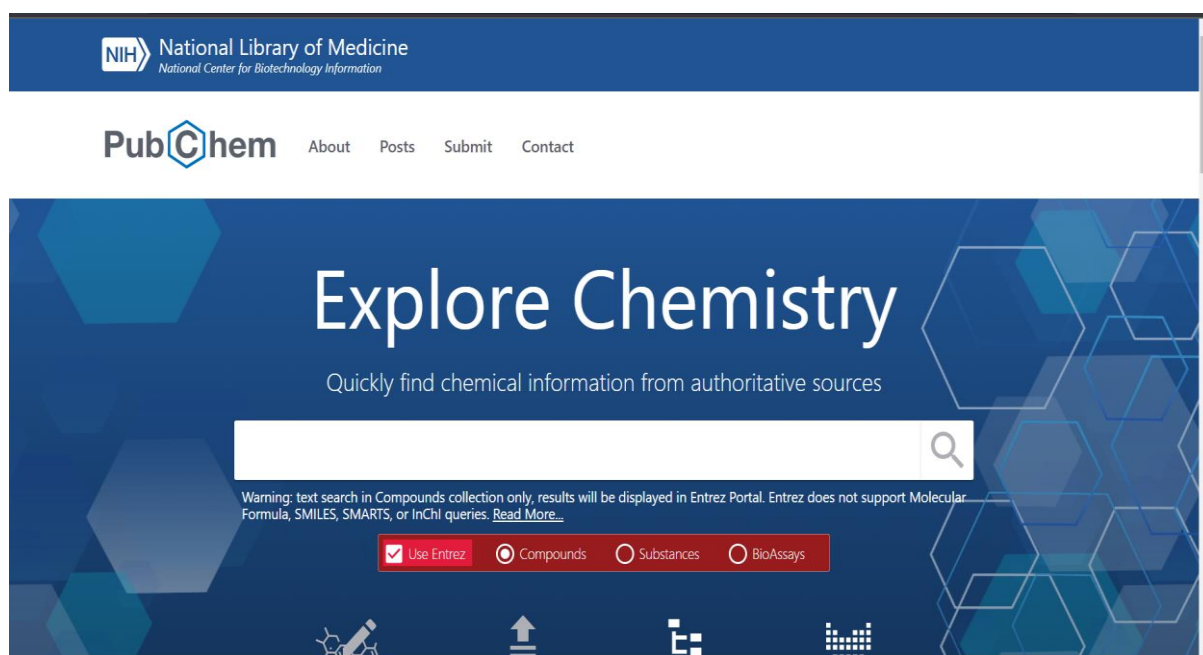
Fig 7: PubChem

5. PYRX

PyRx, or Python Prescription, is an open-source software tool designed for virtual screening and molecular docking studies. It provides a user-friendly interface for molecular modeling tasks and integrates various computational chemistry tools and libraries.

- Graphical User Interface (GUI): PyRx offers a graphical user interface that enables users to perform molecular docking and virtual screening tasks without the need for extensive programming or command-line expertise.

- Molecular Docking: One of the primary functionalities of PyRx is molecular docking, a computational technique used to predict the binding mode and affinity of small molecules (ligands) to a target protein or macromolecule.

- Virtual Screening: PyRx facilitates virtual screening, a process where large libraries of compounds are screened computationally to identify potential drug candidates that may bind to a target of interest.

- Integration with Autodock Vina: PyRx is built upon Autodock Vina, a popular molecular docking software. It provides a user-friendly interface for setting up docking experiments, running simulations, and analyzing results using Autodock Vina's underlying algorithms.

- Chemical Libraries: PyRx supports the use of chemical libraries or databases containing small molecule compounds for virtual screening studies. Users can import compound libraries in various formats for screening against protein targets.

- Visualization and Analysis: PyRx offers visualization tools to analyze docking results, including interactive 3D visualization of protein-ligand complexes and graphical representations of binding interactions.

- Scripting and Automation: While PyRx emphasizes ease of use through its GUI, it also supports scripting and automation through Python scripting. Advanced users can extend PyRx's functionality and perform custom computational workflows using Python scripting.

- Open-Source and Community-Driven: PyRx is an open-source project, and its development is supported by a community of contributors. This allows for transparency, collaboration, and ongoing improvement of the software.

Overall, PyRx provides a valuable tool for researchers and practitioners in computational chemistry, drug discovery, and molecular modeling. Its intuitive interface, coupled with powerful docking algorithms and visualization capabilities, makes it accessible for users ranging from beginners to advanced researchers in the field.
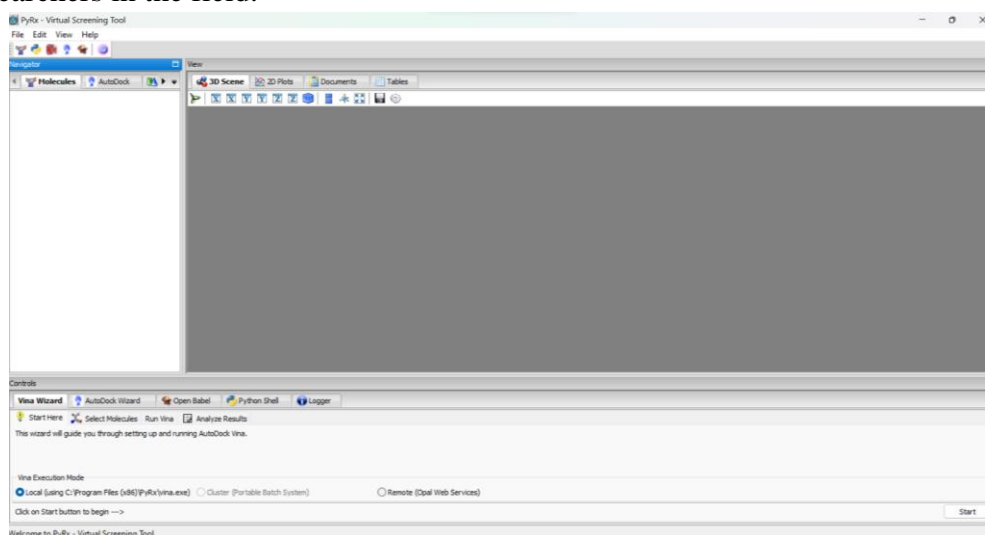
Fig 8: PyRx

6. SWISS ADME

SwissADME is a free web tool developed by the Swiss Institute of Bioinformatics (SIB) that allows users to predict various pharmacokinetic and drug-likeness properties of small molecules. Here are some key features and functionalities of SwissADME:

- Drug-likeness Prediction: SwissADME predicts the drug-likeness of small molecules based on various criteria such as Lipinski's rule of five, Ghose's rule, Veber's rule, Egan's rule, and Muegge's rule. These rules are widely used in medicinal chemistry to assess the likelihood of a compound becoming a drug candidate.
- Pharmacokinetic Properties: SwissADME predicts pharmacokinetic properties such as absorption, distribution, metabolism, and excretion (ADME) parameters. These include oral bioavailability, blood-brain barrier permeability, P-glycoprotein substrate status, and cytochrome P450 inhibition.
- Chemical Space Exploration: The tool provides users with the ability to explore the chemical space of their compounds, including physicochemical properties such as molecular weight, logP (lipophilicity), polar surface area (PSA), and number of hydrogen bond donors and acceptors.
- Bioavailability Radar: SwissADME offers a bioavailability radar plot that visually represents the drug-likeness and pharmacokinetic properties of a compound. This radar plot helps users quickly assess the overall drug-like profile of their molecules.
- Interactive Interface: The web interface of SwissADME is user-friendly and interactive, allowing users to input chemical structures in various formats (e.g., SMILES, SDF) and obtain predictions for multiple properties simultaneously.

- Batch Processing: SwissADME supports batch processing, enabling users to analyze multiple compounds in one go. This feature is useful for high-throughput screening studies or analyzing libraries of small molecules.
- Export and Visualization: Results generated by SwissADME can be exported in various formats for further analysis or visualization. Users can download reports containing predicted properties and radar plots for individual compounds or batches.
- Integration with Other Tools: SwissADME is integrated with other bioinformatics resources and databases, allowing users to seamlessly access additional information about compounds or explore related data.

Overall, SwissADME is a valuable tool for medicinal chemists, pharmacologists, and drug discovery researchers interested in assessing the drug-likeness and pharmacokinetic properties of small molecules during the early stages of drug development.
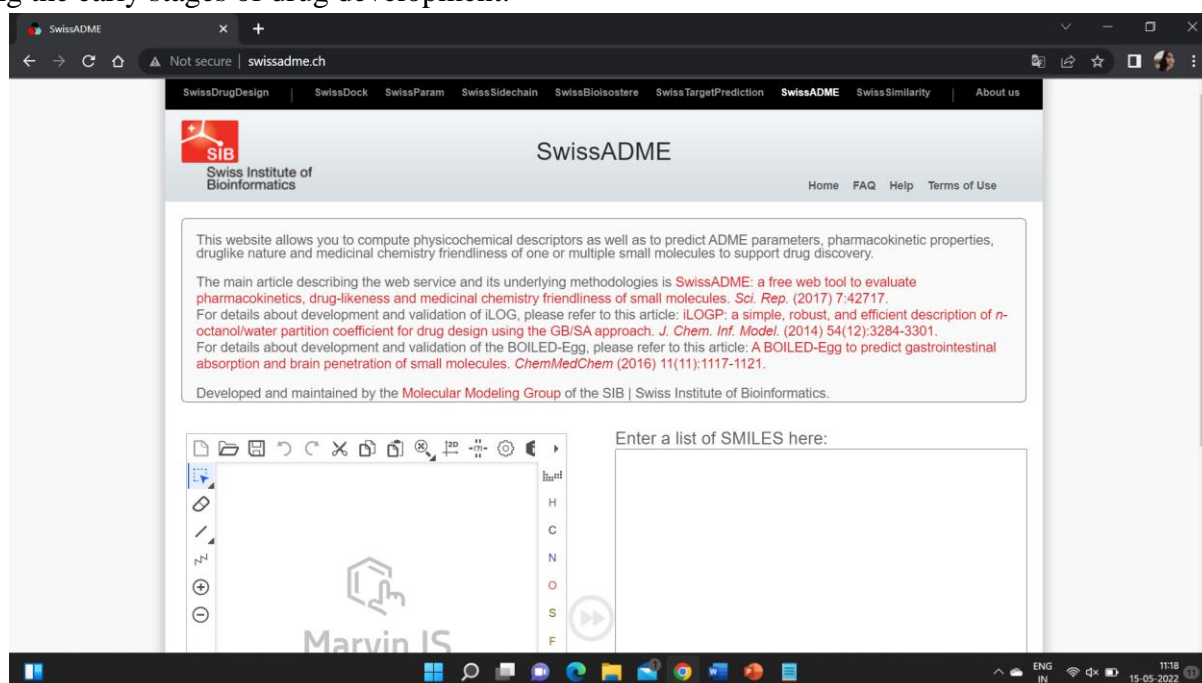
Fig 9: Swiss ADME

7.2 METHODOLOGY

1. Target gene identification and protein structure analysis

Define the biological target and understand its role in disease then identify the molecular target, such as a protein or enzyme. Gain insights into the structural characteristics and biological function of the target.

2. Target 3D structure extraction from PDB

The target protein sequence is analyzed from pdb and the structure is extracted in .pdb form.

3. Phytochemicals are determined from the Database

Gather and curate databases of molecular structures of known ligands. Prepare the 3D structure of the target protein using experimental or computational methods.

4. Virtual Screening of Ligands

Employ computational algorithms to screen chemical libraries for potential ligands. Dock ligands into the target binding site and assess their binding affinity and interactions. Utilize methods such as molecular docking and molecular dynamics simulations.

5. Molecular docking

The ligand phytochemicals and the target are supposed to be docked. For docking pyrx software can be used.

6. ADME-Tox Prediction

Predict the absorption, distribution, metabolism, excretion, and toxicity (ADME-Tox) properties of lead compounds. Assess potential risks and safety profiles to prioritize lead compounds for further development.

7. Experimental Validation

Synthesize lead compounds and test their biological activities in vitro. Validate binding affinity, pharmacological effects, and therapeutic potential. Use biochemical assays, cell-based assays, animal studies, and clinical trials for validation.

Gene Analysis (GENBANK)

↓

Protein Structure Analysis (PDB)

↓

Active Site Prediction (CAST P)

↓

Selection Of Natural Ligands From Medicinal Plants (PUBCHEM)

↓

Protein-ligand Docking (PYRX)

↓

Receptor-ligand Interaction Studies

↓

ADMET studies

↓

Drugs found to be non-carcinogenic
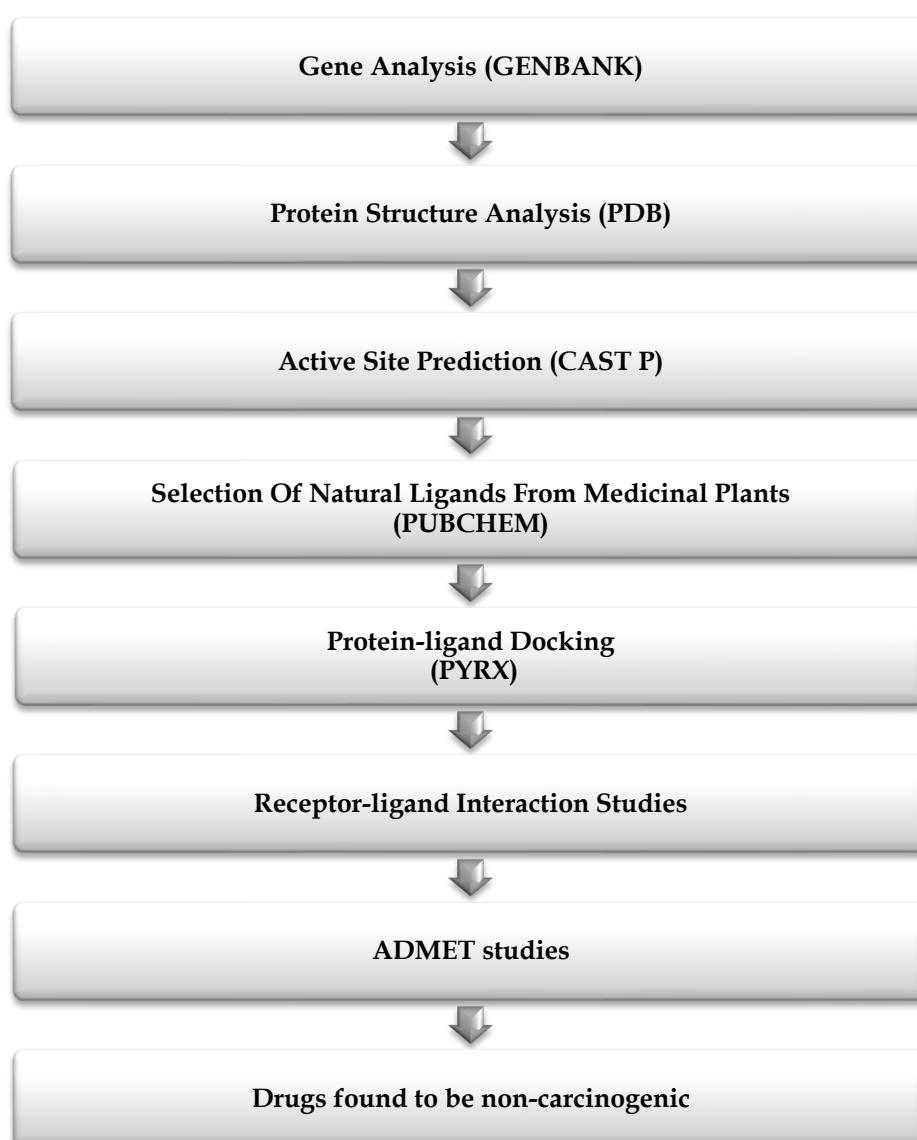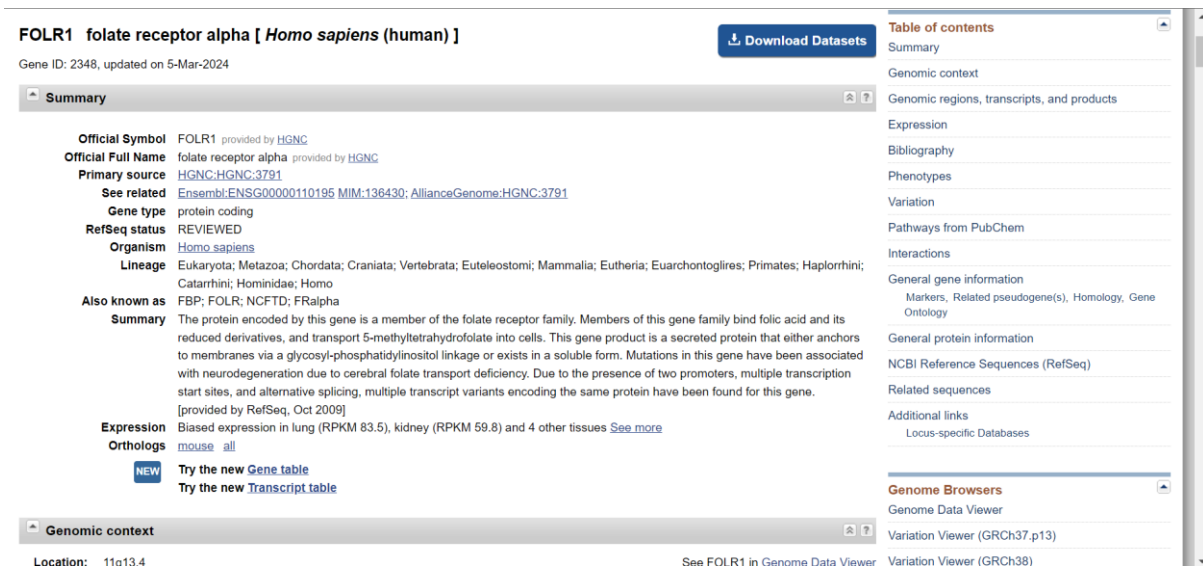
8. RESULTS AND DISCUSSION

Target – folate receptor protein (FOLR 1 gene)

Folate receptor alpha (FRα), encoded by the FOLR1 gene, is an attractive therapeutic target due to its prevalent and high expression in EOC cells. This is visualized by Pymol software.

Target Name	PDB ID
Folate Receptor Protein	4KM6
Target Gene	**Genbank Id**
FOLR 1	2348

Table 2: target gene and protein

Fig 10: target gene (FOLR 1)

Fig 11: Target Protein

Active site

The active site of folate receptor protein and active site amino acid residues are analyzed and visualized by cast p.
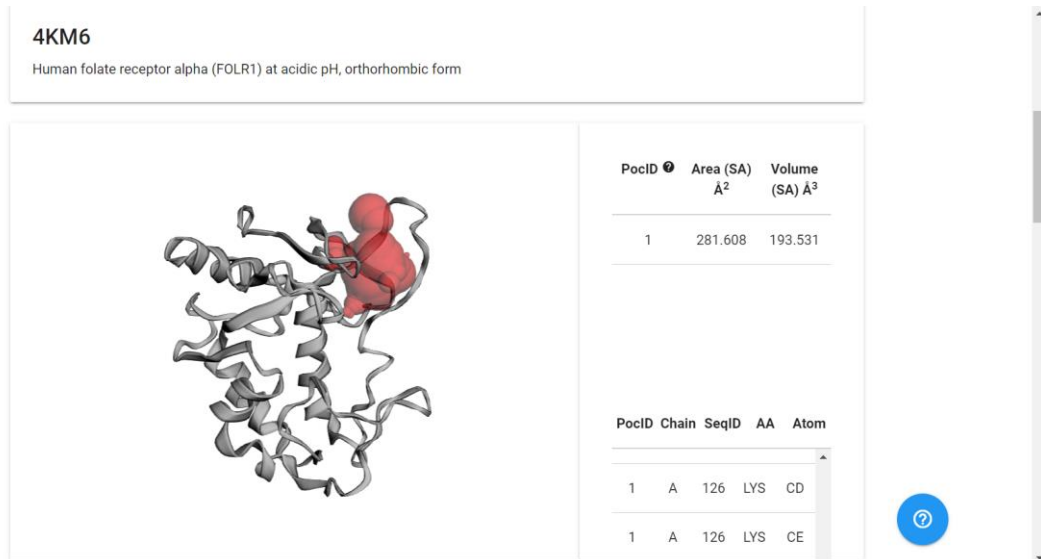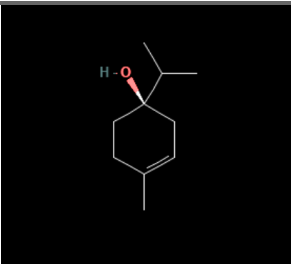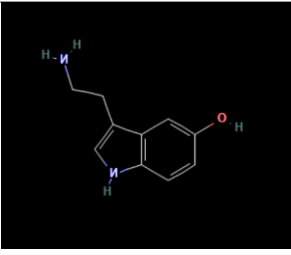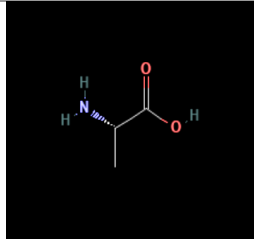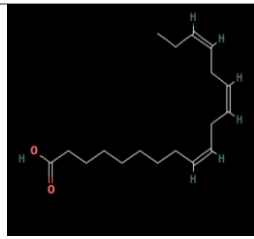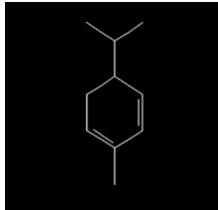

Fig 12: Active Site
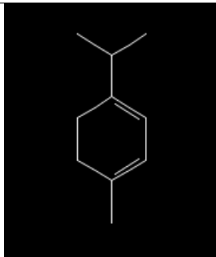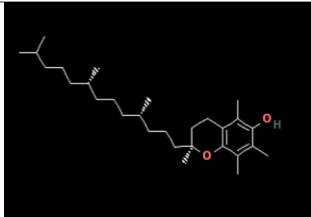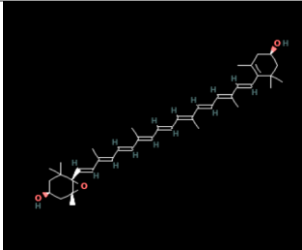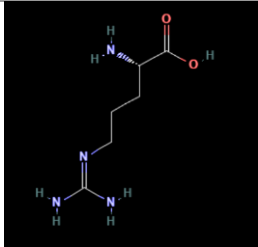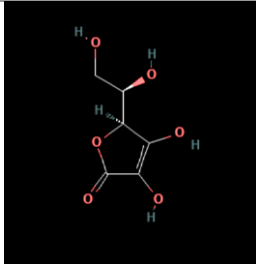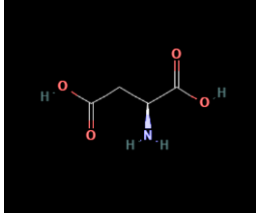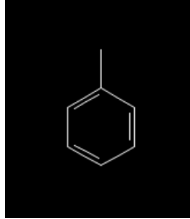
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1	A	40	ALA	CB
1	A	41	LYS	CG
1	A	41	LYS	CE
1	A	41	LYS	NZ
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1	A	45	GLU	OE1
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1	A	46	LYS	O
1	A	47	PRO	CA
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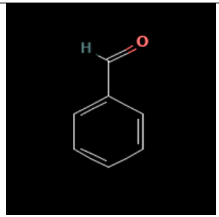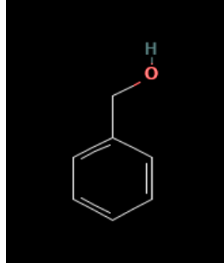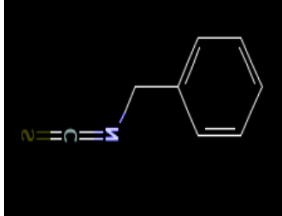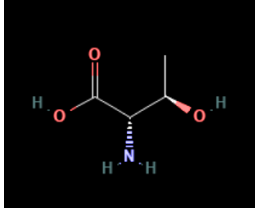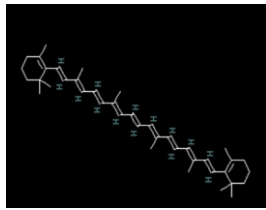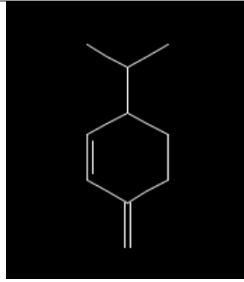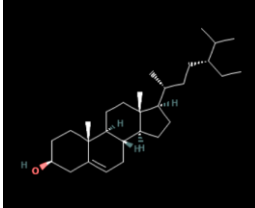
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1	A	71	SER	OG
1	A	73	GLU	O
1	A	73	GLU	CB
1	A	74	ALA	O
1	A	75	HIS	CA
1	A	75	HIS	CB
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1	A	78	VAL	CG2
1	A	79	SER	N
1	A	79	SER	CA
1	A	79	SER	CB
1	A	108	GLU	CB
1	A	108	GLU	CG
1	A	108	GLU	CD
1	A	125	ARG	CG
1	A	125	ARG	CD
1	A	125	ARG	NE
1	A	126	LYS	CG
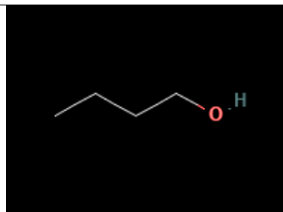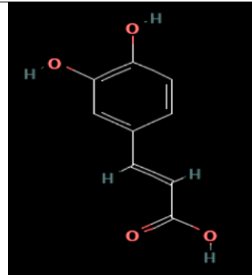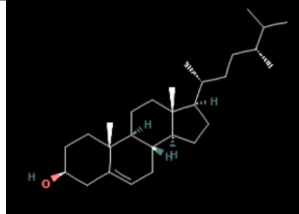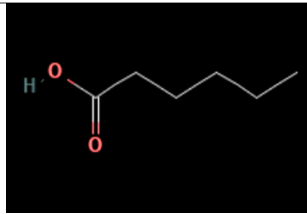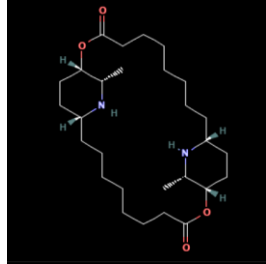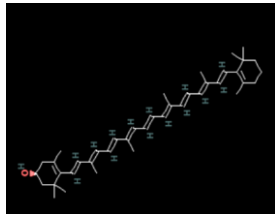
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1	A	126	LYS	CE
1	A	126	LYS	NZ
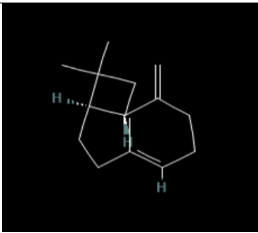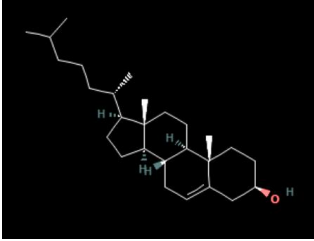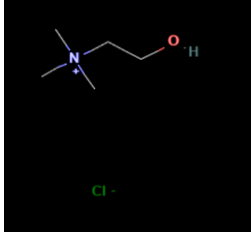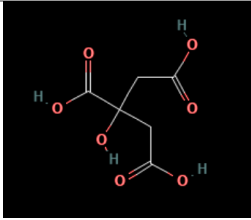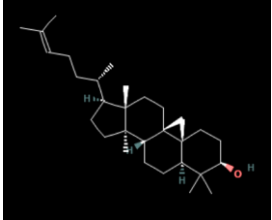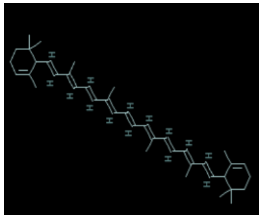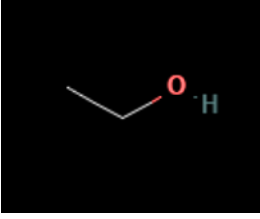
Table 3: active site

Ligand – phytochemicals
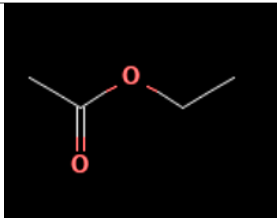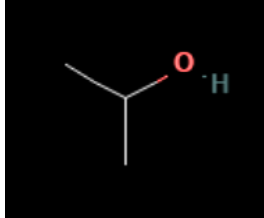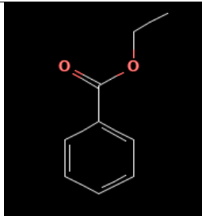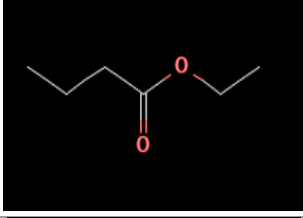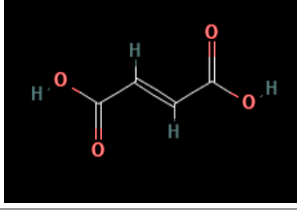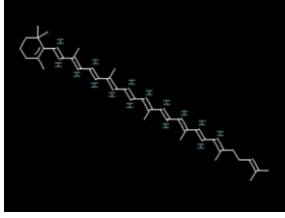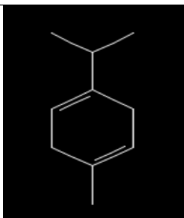
Sl no:	Chemicals	Properties	2D Structure
1.	4-TERPINEOL	Molecular Formula: $C_{10}H_{18}O$ Molecular Weight: 154.25 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
2.	5-HYDROXYTRYP-TAMINE	Molecular Formula: $C_{10}H_{12}N_2O$ Molecular Weight: 176.21 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 2	
3.	ALANINE	Molecular Formula: $C_3H_7NO_2$ Molecular Weight: 89.09 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 3	
4.	ALPHA-LINOLENIC-ACID	Molecular Formula: $C_{18}H_{30}O_2$ Molecular Weight: 278.4 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
5.	ALPHA-PHELLANDRENE	Molecular Formula: $C_{10}H_{16}$ Molecular Weight 136.23 Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
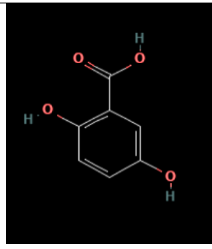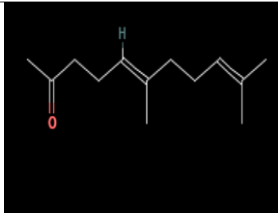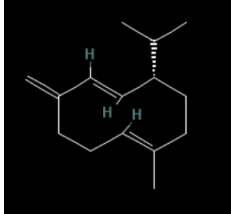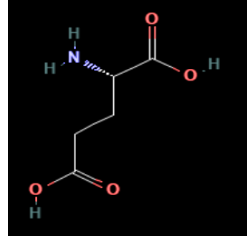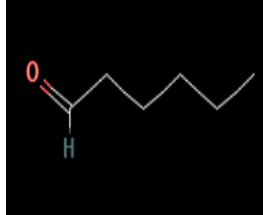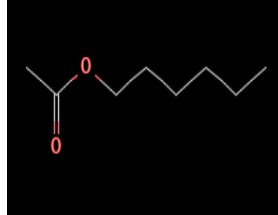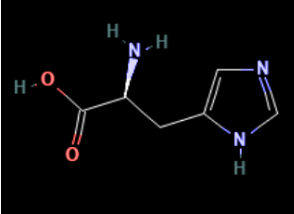
6.	ALPHA-TERPINENE	Molecular Formula: $C_{10}H_{16}$ Molecular Weight 136.23 Hydrogen Bond Donor Count 0 Hydrogen Bond Acceptor Count 0	
7.	ALPHA-TOCOPHEROL	Molecular Formula: $C_{29}H_{50}O_2$ Molecular Weight: 430.7 g/mol Hydrogen Bond Donor Count:1 Hydrogen Bond Acceptor Count: 2	
8.	ANTHERAXAN-THIN	Molecular Formula: $C_{40}H_{56}O_3$ Molecular Weight: 584.9 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 3	
9.	ARGININE	Molecular Formula: $C_6H_{14}N_4O_2$ Molecular Weight: 174.20 g/mol Hydrogen Bond Donor Count: 4 Hydrogen Bond Acceptor Count: 4	
10	ASCORBIC-ACID	Molecular Formula: $C_6H_8O_6$ Molecular Weight: 176.12 g/mol Hydrogen Bond Donor Count: 4 Hydrogen Bond Acceptor Count: 6	
11	ASPARTIC-ACID	Molecular Formula: $C_4H_7NO_4$ Molecular Weight: 133.10 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 5	
12	TOLUENE	Molecular Formula: C_7H_8 Molecular Weight: 92.14 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
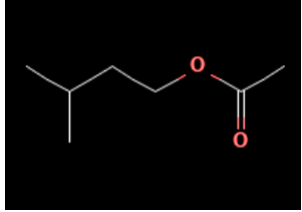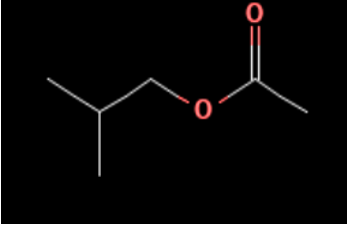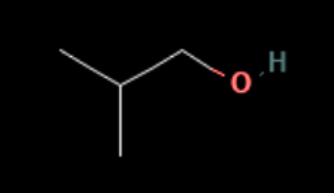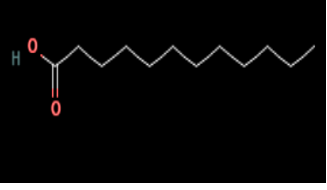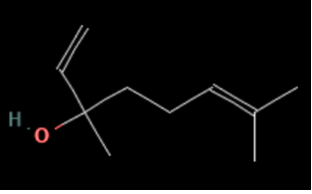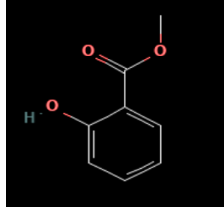
13	BENZALDEHYDE	Molecular Formula: C_7H_6O Molecular Weight: 106.12g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 1	
14	BENZYL-ALCOHOL	Molecular Formula: C_7H_8O Molecular Weight: 108.14 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
15	BENZYL-ISOTHIOCYANATE	Molecular Formula: C_8H_7NS Molecular Weight: 149.21 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
16	THREONINE	Molecular Formula: $C_4H_9NO_3$ Molecular Weight: 119.12 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	
17	BETA-CAROTENE	Molecular Formula: $C_{40}H_{56}$ Molecular Weight: 536.9 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
18	BETA-PHELLANDRENE	Molecular Formula: $C_{10}H_{16}$ Molecular Weight: 136.23 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
19	BETA-SITOSTEROL	Molecular Formula: $C_{29}H_{50}O$ Molecular Weight: 414.7 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
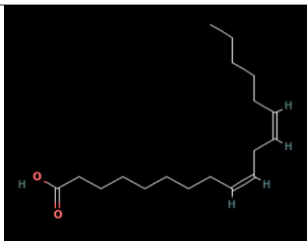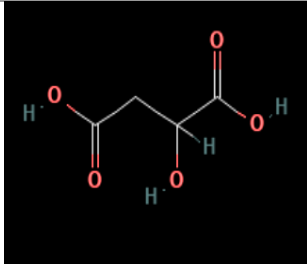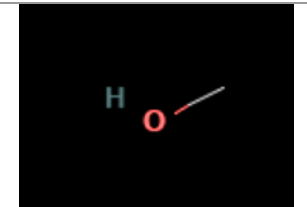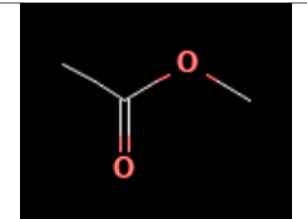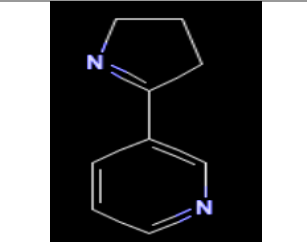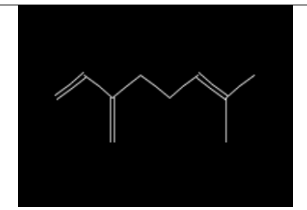
20	BUTYL-ALCOHOL	Molecular Formula: $C_4H_{10}O$ Molecular Weight: 74.12 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
21	CAFFEIC-ACID	Molecular Formula: $C_9H_8O_4$ Molecular Weight: 180.16 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	
22	CAMPESTEROL	Molecular Formula: $C_{28}H_{48}O$ Molecular Weight: 400.7 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
23	CAPROIC-ACID	Molecular Formula: $C_6H_{12}O_2$ Molecular Weight: 116.16 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
24	CARPAINE	Molecular Formula: $C_{28}H_{50}N_2O_4$ Molecular Weight: 478.7 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 6	
25	CHYMOPAPAIN	Molecular Formula: $C_6H_6O_8S_2$ Molecular Weight: 270.2 g/mol Hydrogen Bond Donor Count: 4 Hydrogen Bond Acceptor Count: 8	
26	CRYPTOXANTHIN	Molecular Formula: $C_{40}H_{56}O$ Molecular Weight: 552.9 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
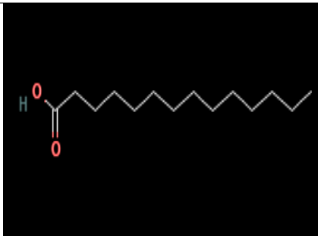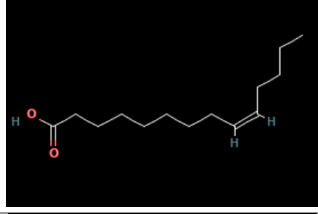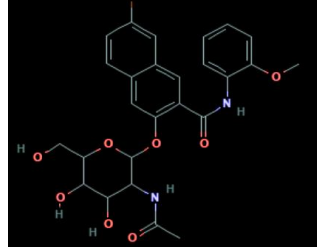
27	CARYOPHYLLENE	Molecular Formula: $C_{15}H_{24}$ Molecular Weight: 204.35 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
28	CHOLESTEROL	Molecular Formula: $C_{27}H_{49}O$ Molecular Weight: 386.7 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
29	CHOLINE	Molecular Formula: $C_5H_{14}NO.Cl$ Molecular Weight: 139.62 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
30	CITRIC-ACID	Molecular Formula: $C_6H_8O_7$ Molecular Weight: 192.12 g/mol Hydrogen Bond Donor Count: 4 Hydrogen Bond Acceptor Count: 7	
31	CYCLOARTENOL	Molecular Formula: $C_{30}H_{50}O$ Molecular Weight: 426.7 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
32	EPSILON-CAROTENE	Molecular Formula: $C_{40}H_{56}$ Molecular Weight: 536.9 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
33	ETHANOL	Molecular Formula: C_2H_6O Molecular Weight: 46.07 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
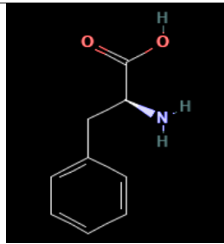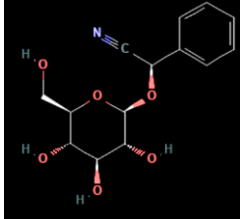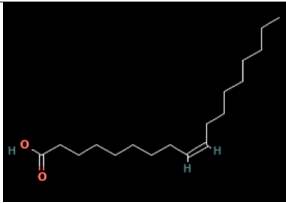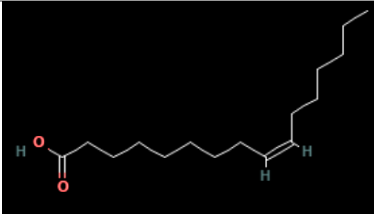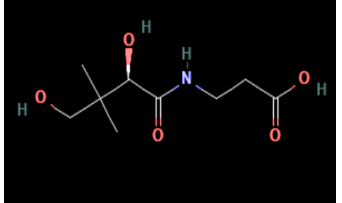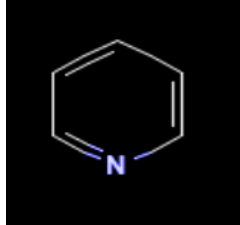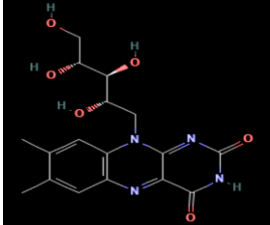
34	ETHYL-ACETATE	Molecular Formula: $C_4H_8O_2$ Molecular Weight: 88.11 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
35	ISOPROPYL-ALCOHOL	Molecular Formula: C_3H_8O Molecular Weight: 60.10 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
36	ETHYL-BENZOATE	Molecular Formula: $C_9H_{10}O_2$ Molecular Weight: 105.17 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
37	ETHYL-BUTYRATE	Molecular Formula: $C_6H_{12}O_2$ Molecular Weight: 116.16 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 4	
38	FUMARIC-ACID	Molecular Formula: $C_4H_4O_4$ Molecular Weight: 116.07 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 4	
39	GAMMA-CAROTENE	Molecular Formula: $C_{40}H_{56}$ Molecular Weight: 536.9 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
40	GAMMA-TERPINENE	Molecular Formula: $C_{10}H_{16}$ Molecular Weight: 136.23 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
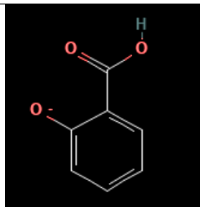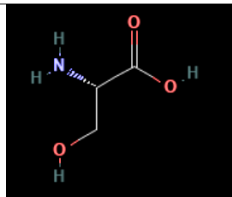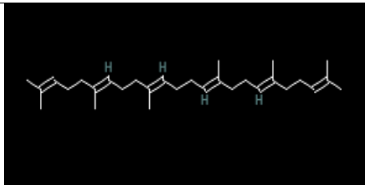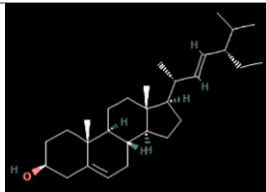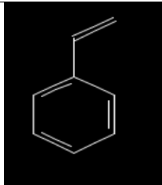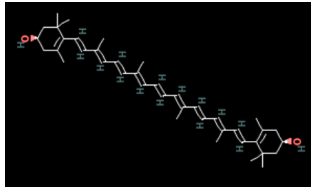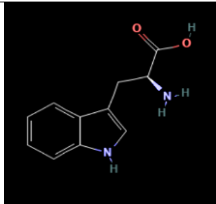
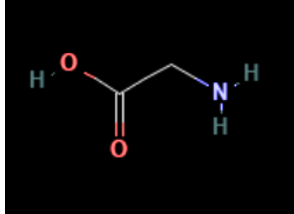| 41	GENTISIC-ACID	Molecular Formula: $C_7H_6O_4$ Molecular Weight: 154.12 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	
42	GERANYL-ACETONE	Molecular Formula: $C_{13}H_{22}O$ Molecular Weight: 194.31g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 1	
43	GERMACRENE-D	Molecular Formula: $C_{15}H_{24}$ Molecular Weight: 204.35 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
44	GLYCINE	Molecular Formula: $C_2H_5NO_2$ Molecular Weight: 75.07 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 3	
45	GLUTAMIC-ACID	Molecular Formula: $C_5H_9NO_4$ Molecular Weight: 147.13 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 5	
46	HEXANAL	Molecular Formula: $C_6H_{12}O$ Molecular Weight: 100.16 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 1	
47	HEXYL-ACETATE	Molecular Formula: $C_8H_{16}O_2$ Molecular Weight: 144.21 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
48	HISTIDINE	Molecular Formula: $C_6H_9N_3O_2$ Molecular Weight: 155.15 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	

49	ISOAMYL-ACETATE	Molecular Formula: $C_7H_{14}O_2$ Molecular Weight: 130.18g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
50	ISOBUTYL-ACETATE	Molecular Formula: $C_6H_{12}O_2$ Molecular Weight: 116.16 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
51	ISOBUTYL-ALCOHOL	Molecular Formula: $C_4H_{10}O$ Molecular Weight: 74.12 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
52	ISOLEUCINE	Molecular Formula: $C_6H_{13}NO_2$ Molecular Weight: 131. 17 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 3	
53	LAURIC-ACID	Molecular Formula: $C_{12}H_{24}O_2$ Molecular Weight: 200.32 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
54	LINALOOL	Molecular Formula: $C_{10}H_{18}O$ Molecular Weight: 154.25 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
55	METHYL-SALICYLATE	Molecular Formula: $C_8H_8O_3$ Molecular Weight: 152.12 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 3	

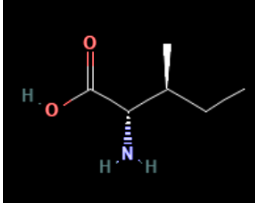| 56	LINOLEIC-ACID	Molecular Formula: $C_{18}H_{32}O_2$ Molecular Weight: 280.4 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
57	MALIC-ACID	Molecular Formula: $C_4H_6O_5$ Molecular Weight: 134.09 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 5	
58	METHANOL	Molecular Formula: CH_4O Molecular Weight: 32.042 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
59	METHIONINE	Molecular Formula: $C_5H_{11}NO_2S$ Molecular Weight: 149.21 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 4	
60	METHYL-ACETATE	Molecular Formula: $C_3H_6O_2$ Molecular Weight: 74.08 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
61	MYOSMINE	Molecular Formula: $C_9H_{10}N_2$ Molecular Weight: 146.19 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
62	MYRCENE	Molecular Formula: $C_{10}H_{16}$ Molecular Weight: 136.23 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	

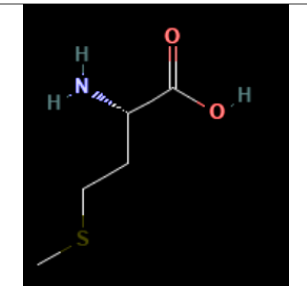| 63	MYRISTIC-ACID	Molecular Formula: $C_{14}H_{28}O_2$ Molecular Weight: 228.37 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
64	MYRISTOLEIC-ACID	Molecular Formula: $C_{14}H_{26}O_2$ Molecular Weight: 226.35 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
65	N-ACETYL-HEXOSAMIDASE	Molecular Formula: $C_{26}H_{27}BrN_2O_8$ Molecular Weight: 575.4 g/mol Hydrogen Bond Donor Count:5 Hydrogen Bond Acceptor Count: 8	
66	NEOXANTHIN	Molecular Formula: $C_{40}H_{56}O_4$ Molecular Weight: 600.9 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	
67	NIACIN	Molecular Formula: $C_6H_5NO_2$ Molecular Weight:123.11 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 3	
68	NICOTINE	Molecular Formula: $C_{10}H_{14}N_2$ Molecular Weight: 162.23 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 2	
69	OCTANOIC-ACID	Molecular Formula: $C_8H_{16}O_2$ Molecular Weight: 144.21 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	

70	PHENYLALANINE	Molecular Formula: $C_9H_{11}NO_2$ Molecular Weight: 165.91 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 3	
71	PRUNASIN	Molecular Formula: $C_{14}H_{17}NO_6$ Molecular Weight: 295.29 g/mol Hydrogen Bond Donor Count:4 Hydrogen Bond Acceptor Count: 7	
72	OLEIC-ACID	Molecular Formula: $C_{18}H_{34}O_2$ Molecular Weight: 282.5 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
73	PALMITIC-ACID	Molecular Formula: $C_{16}H_{32}O_2$ Molecular Weight: 256.42 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
74	PALMITOLEIC-ACID	Molecular Formula: $C_{16}H_{30}O_2$ Molecular Weight: 254.41 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 2	
75	PANTOTHENIC-ACID	Molecular Formula: $C_9H_{17}NO_5$ Molecular Weight: 219.23 g/mol Hydrogen Bond Donor Count:4 Hydrogen Bond Acceptor Count:5	
76	PYRIDINE	Molecular Formula: C5H5N Molecular Weight: 79.1 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 1	
77	RIBOFLAVIN	Molecular Formula: C17H20N4O6 Molecular Weight: 376.4 g/mol Hydrogen Bond Donor Count:5 Hydrogen Bond Acceptor Count: 7	

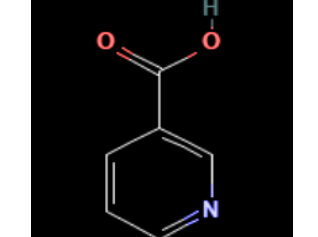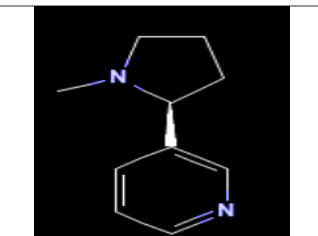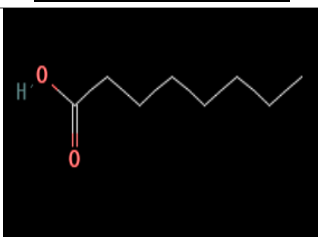|			
78	SALICYLATES	Molecular Formula: $C_7H_5O_3^-$ Molecular Weight:137.11 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 3	
79	SERINE	Molecular Formula: $C_3H_7NO_3$ Molecular Weight: 105.09g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	
80	SQUALENE	Molecular Formula: $C_{30}H_{50}$ Molecular Weight: 410.7 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
81	STIGMASTEROL	Molecular Formula: $C_{29}H_{48}O$ Molecular Weight: 412.7 g/mol Hydrogen Bond Donor Count: 1 Hydrogen Bond Acceptor Count: 1	
82	STYRENE	Molecular Formula: C_8H_8 Molecular Weight: 104.15 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
83	ZEAXANTHIN	Molecular Formula: $C_{40}H_{56}O_2$ Molecular Weight: 568.9 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 2	
84	TRYPTOPHAN	Molecular Formula: $C_{11}H_{12}N_2O_2$ Molecular Weight: 204.22 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 3	
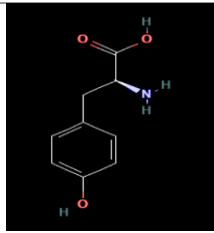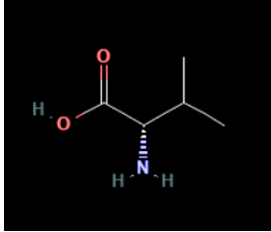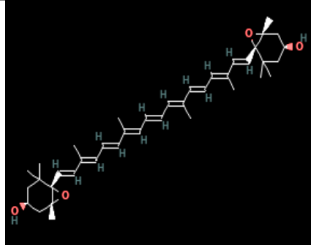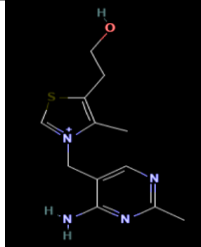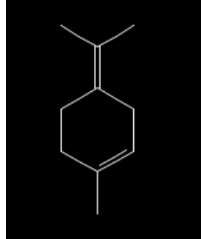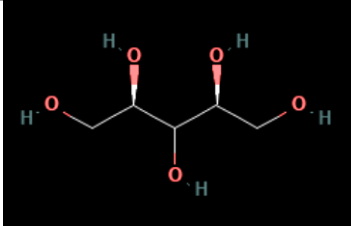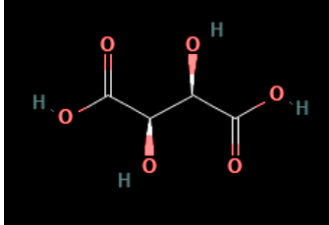
85	TYROSINE	Molecular Formula: C9H11NO3 Molecular Weight: 181.19 g/mol Hydrogen Bond Donor Count: 3 Hydrogen Bond Acceptor Count: 4	
86	VALINE	Molecular Formula: C5H11NO2 Molecular Weight: 117015 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 3	
87	VIOLAXANTHIN	Molecular Formula: C40H56O4 Molecular Weight: 600.9 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 4	
88	THIAMIN	Molecular Formula: $C_{12}H_{17}N_4OS^+$ Molecular Weight: 265.36 g/mol Hydrogen Bond Donor Count: 2 Hydrogen Bond Acceptor Count: 5	
89	TERPINOLENE	Molecular Formula: C10H16 Molecular Weight: 136.23 g/mol Hydrogen Bond Donor Count: 0 Hydrogen Bond Acceptor Count: 0	
90	XYLITOL	Molecular Formula: C5H12O5 Molecular Weight: 152.15 g/mol Hydrogen Bond Donor Count: 5 Hydrogen Bond Acceptor Count: 5	
91	TARTARIC-ACID	Molecular Formula: C4H6O6 Molecular Weight: 150.09 g/mol Hydrogen Bond Donor Count:4 Hydrogen Bond Acceptor Count: 6	

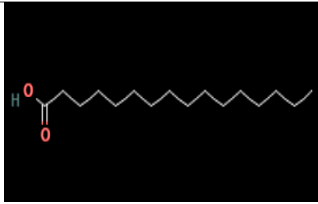**Table 4: ligand-phytochemicals**

Molecular Docking

The phytochemicals are docked with target Folate Receptor Protein. The best phytochemicals are screened according to the docking score value. The least score value ligand s is taken as the best phytochemical. The ligands and the docking score values are listed below:

PUBCHEM ID	CHEMICAL COMPOUNDS	DOCKING SCORE
5325830	4-terpineol	-4.9
5202	5-hydroxytryptamine	-6.1
5950	Alanine	-4.2
5280934	Alpha-linolenic-acid	-4.5
7460	Alpha-phellandrene	-6.6
7462	Alpha-terpinene	-4.7
14985	Alpha-tocopherol	-5.7
5281223	Antheraxanthin	-7.7
6322	Arginine	-6.3
54670067	Ascorbic-acid	-5.8
5960	Aspartic-acid	-5.3
1140	Toluene	-6.4
240	Benzaldehyde	-4.6
244	Benzyl-alcohol	-4.2
2346	Benzyl-isothiocyanate	-6.7
6288	Threonine	-4.8
5280489	Beta-carotene	-7.7
11142	Beta-phellandrene	-6.5
222284	Beta-sitosterol	-6.9
263	Butyl-alcohol	-4.3
689043	Caffeic-acid	-6.5
173183	Campesterol	-6.9
8892	Caproic-acid	-5.8
442630	Carpaine	-7.9
9002	Chymopapain	-6.2
5281235	Cryptoxanthin	-7.6
5281515	Caryophyllene	-5.7
5997	Cholesterol	-6.8
6209	Choline	-3.7
311	Citric-acid	-6.1
92110	Cycloartenol	-7.8
446439	Epsilon-carotene	-7.5
702	Ethanol	-3
8857	Ethyl-acetate	-4.3
3776	Isopropyl-alcohol	-3.7
7165	Ethyl-benzoate	-7.1
7762	Ethyl-butyrate	-4.2

444972	Fumaric-acid	-5
5280791	Gamma-carotene	-7
7461	Gamma-terpinene	-4.6
3469	Gentisic-acid	-5.8
1549778	Geranyl-acetone	-4.5
5317570	Germacrene-d	-5.9
750	Glycine	-3.9
33032	Glutamic-acid	-5.5
6184	Hexanal	-3.7
8908	Hexyl-acetate	-4
6274	Histidine	-6.2
31276	Isoamyl-acetate	-5.7
8038	Isobutyl-acetate	-4.5
6560	Isobutyl-alcohol	-3.9
6306	Isoleucine	-4.3
3893	Lauric-acid	-3.9
6549	Linalool	-4.2
4133	Methyl-salicylate	-6.8
5280450	Linoleic-acid	-4.4
525	Malic-acid	-5.3
887	Methanol	-2
6137	Methionine	-3.7
6584	Methyl-acetate	-3.9
442649	Myosmine	-5
31253	Myrcene	-4.3
11005	Myristic-acid	-4.2
5281119	Myristoleic-acid	-4.1
4109091	N-acetyl-hexosamidase	-7.3
5282217	Neoxanthin	-7.3
938	Niacin	-5.4
89594	Nicotine	-4.8
379	Octanoic-acid	-4
6140	Phenylalanine	-5.1
119033	Prunasin	-6.1
445639	Oleic-acid	no reaction
985	Palmitic-acid	-4
445638	Palmitoleic-acid	-4.4
6613	Pantothenic-acid	-5.6
1049	Pyridine	-5.3
493570	Riboflavin	-6.8
54675850	Salicylates	-6.7
5951	Serine	-4.3

638072	Squalene	-5.2
5280794	Stigmasterol	-7.3
7501	Styrene	-6.9
5280899	Zeaxanthin	-7.5
6305	Tryptophan	-5.8
6057	Tyrosine	-6.6
6287	Valine	-4.7
448438	Violaxanthin	-7.2
1130	Thiamin	-5.5
11463	Terpinolene	-6.2
6912	Xylitol	-4.6
444305	Tartaric-acid	-4.9

Table 5: molecular docking scores

Best docking results

Sel No:	Chemical	Docking Score
1	Carpaine	-7.9
2	Cycloartenol	-7.8
3	Beta-Carotene	-7.7
4	Antheraxanthin	-7.7
5	Cryptoxanthin	-7.6
6	Zeaxanthin	-7.5
7	Epsilon-Carotene	-7.5
8	N-Acetyl-Hexosamidase	-7.3
9	Neoxanthin	-7.3
10	Stigmasterol	-7.3
11	Ethyl-Benzoate	-7.1
12	Gamma-Carotene	-7

Table 6: best docking scores

DOCKING SCORE

1. Carpaine

2. Cycloartenol

3. Beta-carotene

4. Antheraxanthin

5. Cryptoxanthin

6. Zeaxanthin

7. Epsilon-Carotene

8. N-Acetyl-Hexosamidase

9. Neoxanthin

10. Stigmasterol

11. Ethyl-Benzoate

12. Gamma-Carotene

ADME Studies

1. Carpaine

Molecule 1

SMILES: O=C1CCCCCCCC2CCC(C(N2)C)OC(=O)CCCCCCCC2CCC(O1)C(C)N2

Physicochemical Properties	
Formula	C28H50N2O4
Molecular weight	478.71 g/mol
Num. heavy atoms	34
Num. arom. heavy atoms	0
Fraction Csp3	0.93
Num. rotatable bonds	0
Num. H-bond acceptors	6
Num. H-bond donors	2
Molar Refractivity	146.37
TPSA	76.66 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	4.71
Log $P_{o/w}$ (XLOGP3)	6.29

Water Solubility	
Log S (ESOL)	-6.77
Solubility	8.12e-05 mg/ml ; 1.70e-07 mol/l
Class	Poorly soluble
Log S (Ali)	-7.69
Solubility	9.81e-06 mg/ml ; 2.05e-08 mol/l
Class	Poorly soluble
Log S (SILICOS-IT)	-5.71
Solubility	9.29e-04 mg/ml ; 1.94e-06 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-4.75 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 2 violations: MR>130, #atoms>70
Veber	Yes
Egan	Yes
Muegge	No; 1 violation: XLOGP3>5

2. Cycloarthenol

Molecule 1

SMILES: CC(=CCCC(C1CCC2(C1(C)CCC13C2CCC2C3(C1)CCC(C2(C)C)O)C)C)C

Physicochemical Properties	
Formula	C30H50O
Molecular weight	426.72 g/mol
Num. heavy atoms	31
Num. arom. heavy atoms	0
Fraction Csp3	0.93
Num. rotatable bonds	4
Num. H-bond acceptors	1
Num. H-bond donors	1
Molar Refractivity	135.14
TPSA	20.23 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	5.17
Log $P_{o/w}$ (XLOGP3)	9.78

Water Solubility	
Log S (ESOL)	-8.38
Solubility	1.77e-06 mg/ml ; 4.14e-09 mol/l
Class	Poorly soluble
Log S (Ali)	-10.12
Solubility	3.20e-08 mg/ml ; 7.50e-11 mol/l
Class	Insoluble
Log S (SILICOS-IT)	-6.87
Solubility	5.77e-05 mg/ml ; 1.35e-07 mol/l
Class	Poorly soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-1.96 cm/s

Druglikeness	
Lipinski	Yes; 1 violation: MLOGP>4.15
Ghose	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

3. Beta-carotene

Molecule 1

SMILES	CC(=CC=CC=C(C=CC=C(C=CC1=C(C)CCCC1(C)C)C)C)=CC=C(C=CC1=C(C)CCCC1(C)C)C

Physicochemical Properties	
Formula	C40H56
Molecular weight	536.87 g/mol
Num. heavy atoms	40
Num. arom. heavy atoms	0
Fraction Csp3	0.45
Num. rotatable bonds	10
Num. H-bond acceptors	0
Num. H-bond donors	0
Molar Refractivity	184.43
TPSA	0.00 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	7.79
Log $P_{o/w}$ (XLOGP3)	13.54

Water Solubility	
Log S (ESOL)	-11.04
Solubility	4.91e-09 mg/ml ; 9.15e-12 mol/l
Class	Insoluble
Log S (Ali)	-13.60
Solubility	1.34e-11 mg/ml ; 2.50e-14 mol/l
Class	Insoluble
Log S (SILICOS-IT)	-7.59
Solubility	1.38e-05 mg/ml ; 2.56e-08 mol/l
Class	Poorly soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	0.04 cm/s

Druglikeness	
Lipinski	No; 2 violations: MW>500, MLOGP>4.15
Ghose	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

4. Antheraxanthin

Molecule 1

SMILES	CC(=CC=CC=C(C=CC=C(C=CC12OC2(C)CC(CC1(C)C)O)C)C)=CC=C(C=CC1=C(C)CC(CC1(C)C)O)C

Physicochemical Properties	
Formula	C40H56O3
Molecular weight	584.87 g/mol
Num. heavy atoms	43
Num. arom. heavy atoms	0
Fraction Csp3	0.50
Num. rotatable bonds	10
Num. H-bond acceptors	3
Num. H-bond donors	2
Molar Refractivity	186.28
TPSA	52.99 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	7.10
Log $P_{o/w}$ (XLOGP3)	10.34

Water Solubility	
Log S (ESOL)	-9.32
Solubility	2.80e-07 mg/ml ; 4.78e-10 mol/l
Class	Poorly soluble
Log S (Ali)	-11.39
Solubility	2.36e-09 mg/ml ; 4.04e-12 mol/l
Class	Insoluble
Log S (SILICOS-IT)	-5.66
Solubility	1.28e-03 mg/ml ; 2.18e-06 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-2.53 cm/s

Druglikeness	
Lipinski	No; 2 violations: MW>500, MLOGP>4.15
Ghose	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

5. Cryptoxanthin

Molecule 1

SMILES: OC1CC(=C(C(C1)(C)C)C=CC(=CC=CC(=CC=CC=C(C=CC=C(C=CC1=C(C)CCCC1(C)C)C)C)C)C)C

Physicochemical Properties	
Formula	C40H56O
Molecular weight	552.87 g/mol
Num. heavy atoms	41
Num. arom. heavy atoms	0
Fraction Csp3	0.45
Num. rotatable bonds	10
Num. H-bond acceptors	1
Num. H-bond donors	1
Molar Refractivity	185.59
TPSA	20.23 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	7.44

Water Solubility	
Log S (ESOL)	-10.33
Solubility	2.61e-08 mg/ml ; 4.73e-11 mol/l
Class	Insoluble
Log S (Ali)	-12.69
Solubility	1.13e-10 mg/ml ; 2.05e-13 mol/l
Class	Insoluble
Log S (SILICOS-IT)	-6.77
Solubility	9.48e-05 mg/ml ; 1.71e-07 mol/l
Class	Poorly soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-0.98 cm/s

Druglikeness	
Lipinski	No; 2 violations: MW>500, MLOGP>4.15
Ghose	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

6. Zeaxanthine

Molecule 1

SMILES: OC1CC(=C(C(C1)(C)C)C=CC(=CC=CC(=CC=CC=C(C=CC=C(C=CC1=C(C)CC(CC1(C)O)C)C)C)C)C)C

Physicochemical Properties	
Formula	C40H56O2
Molecular weight	568.87 g/mol
Num. heavy atoms	42
Num. arom. heavy atoms	0
Fraction Csp3	0.45
Num. rotatable bonds	10
Num. H-bond acceptors	2
Num. H-bond donors	2
Molar Refractivity	186.76
TPSA	40.46 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	7.23

Water Solubility	
Log S (ESOL)	-9.58
Solubility	1.50e-07 mg/ml ; 2.63e-10 mol/l
Class	Poorly soluble
Log S (Ali)	-11.72
Solubility	1.08e-09 mg/ml ; 1.90e-12 mol/l
Class	Insoluble
Log S (SILICOS-IT)	-5.94
Solubility	6.52e-04 mg/ml ; 1.15e-06 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-2.02 cm/s

Druglikeness	
Lipinski	No; 2 violations: MW>500, MLOGP>4.15
Ghose	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

7. Epsilon-carotene

Molecule 1

SMILES: CC(=CC=CC=C(C=CC=C(C=CC1C(=CCCC1(C)C)C)C)C)C=CC=C(C=CC1C(=CCCC1(C)C)C)C

Physicochemical Properties

Formula	C40H56
Molecular weight	536.87 g/mol
Num. heavy atoms	40
Num. arom. heavy atoms	0
Fraction Csp3	0.45
Num. rotatable bonds	10
Num. H-bond acceptors	0
Num. H-bond donors	0
Molar Refractivity	184.43
TPSA	0.00 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	7.88
Log $P_{o/w}$ (XLOGP3)	13.69

Water Solubility

Log S (ESOL)	-11.13
Solubility	3.95e-09 mg/ml ; 7.36e-12 mol/l
Class	Insoluble
Log S (Ali)	-13.76
Solubility	9.39e-12 mg/ml ; 1.75e-14 mol/l
Class	Insoluble
Log S (SILICOS-IT)	-6.69
Solubility	1.09e-04 mg/ml ; 2.03e-07 mol/l
Class	Poorly soluble

Pharmacokinetics

GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	0.14 cm/s

Druglikeness

Lipinski	No; 2 violations: MW>500, MLOGP>4.15
Ghose	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

8. Stigmasterol

Molecule 1

SMILES: CCC(C(C)C)C=CC(C1CCC2C1(C)CCC1C2CC=C2C1(C)CCC(C2)O)C

Physicochemical Properties

Formula	C29H48O
Molecular weight	412.69 g/mol
Num. heavy atoms	30
Num. arom. heavy atoms	0
Fraction Csp3	0.86
Num. rotatable bonds	5
Num. H-bond acceptors	1
Num. H-bond donors	1
Molar Refractivity	132.75
TPSA	20.23 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	5.01
Log $P_{o/w}$ (XLOGP3)	8.56

Water Solubility

Log S (ESOL)	-7.46
Solubility	1.43e-05 mg/ml ; 3.46e-08 mol/l
Class	Poorly soluble
Log S (Ali)	-8.86
Solubility	5.71e-07 mg/ml ; 1.38e-09 mol/l
Class	Poorly soluble
Log S (SILICOS-IT)	-5.47
Solubility	1.40e-03 mg/ml ; 3.39e-06 mol/l
Class	Moderately soluble

Pharmacokinetics

GI absorption	Low
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-2.74 cm/s

Druglikeness

Lipinski	Yes; 1 violation: MLOGP>4.15
Ghose	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88

9. Ethyl-benzoate

Molecule 1

SMILES CCOC(=O)c1ccccc1

Physicochemical Properties	
Formula	C9H10O2
Molecular weight	150.17 g/mol
Num. heavy atoms	11
Num. arom. heavy atoms	6
Fraction Csp3	0.22
Num. rotatable bonds	3
Num. H-bond acceptors	2
Num. H-bond donors	0
Molar Refractivity	42.53
TPSA	26.30 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.25
Log $P_{o/w}$ (XLOGP3)	2.64

Water Solubility	
Log S (ESOL)	-2.64
Solubility	3.44e-01 mg/ml ; 2.29e-03 mol/l
Class	Soluble
Log S (Ali)	-2.84
Solubility	2.16e-01 mg/ml ; 1.44e-03 mol/l
Class	Soluble
Log S (SILICOS-IT)	-2.86
Solubility	2.08e-01 mg/ml ; 1.38e-03 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.34 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 1 violation: MW<160
Veber	Yes
Egan	Yes

9. CONCLUSION AND FUTURE WORKS

Treatment for ovarian cancer is given by chemotherapy, steroid medications, etc. this can lead to various health problems and hormonal imbalances. These side effects can pave the way for many other issues that can end up in severe health issues. Ovarian cancer is one of the deadliest diseases that is seen in women in recent times. the female body's hormonal regulation is done mainly by the ovaries but during the canceric conditions, there are chances of hormonal imbalance. Modern techniques can cause various effects according to the patient's body nature and their hormonal imbalances. The conditions along with the unified medical treatment of cancer lead to harmful effects in the body.

Through these pre-clinical studies, I am put forwarding a new and emerging field of oncological treatment with natural sources. In recent times studies regarding the use of papaya extract in various cancers are studied. It is said to have an impact on the patient positively and the body giving a positive response.

In the above studies, it is clear that the phytochemicals have anti-cancerous effects and can be used as a treatment method and prevention for ovarian cancer.

In future studies, I like to extend the invite studies on cell lines and produce drugs extracted from the phytochemicals of Carica papaya. And further, proceed to clinical trials.

The main moto is to design a drug with fewer or no side effects and give a better cure than synthetic medicine compound

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