East African Scholars Journal of Engineering and Computer Sciences
Abbreviated Key Title: East African Scholars J Eng Comput Sci
ISSN: 2617-4480 (Print) & ISSN: 2663-0346 (Online)
Published By East African Scholars Publisher, Kenya
Volume-8 | Issue-2 | Mar-Apr-2025 | DOI: https://doi.org/10.36349/easjecs.2025.v08i02.004

OPEN ACCESS

Original Research Article

Computational Models Generation for Designing of Plant Based Anticancer Agents

Alka Singh[1]*, Ravindra Singh Yadav[2]

[1]Research Scholar, Department of Computer Science and Engineering, P.K University, Shivpuri (M.P)
[2]Department of Computer Science and Engineering, P.K University, Shivpuri (M.P)

Article History
Received: 06.03.2025
Accepted: 11.04.2025
Published: 20.04.2025

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: The objective of this abstract is to offer an overview of the significance of using computational models in the process of developing anticancer drugs that are derived from fruits and vegetables. This is a branch of research that integrates traditional medical knowledge with modern approaches that are used in the process of medication creation. By using computational methods such as molecular docking, quantitative structure-activity relationship (QSAR) studies, and molecular dynamics simulations, it may be possible to get a better understanding of the complex interactions that take place between compounds originating from plants and cancer targets. The process of discovering potential anticancer medications is sped up by these models, which also provide an efficient path for lead optimization. Specifically, they do this by conducting a rigorous investigation of the chemical landscape of a broad range of plant compounds. Both the relevance of computational tools in the process of expediting drug discovery and the potential of plant-based medicines as a rich source of new and targeted anticancer medications are brought to light by this integrated approach. Not only does it emphasize the value of computational tools, but it also illustrates the promise of plant-based medicines.

Keywords: Computer-aided drug design, Drug design, QSAR, Anti-cancer, Drug discovery.

INTRODUCTION

Since cancer continues to be a significant obstacle in terms of global health, it is imperative that novel techniques be taken in order to create anticancer drugs that are successful. The conventional methods of drug development need a significant amount of time and resources that are spent. When seen in this light, computer models have emerged as extremely useful tools for identifying and optimizing possible medication candidates.

The purpose of the research topic or objective known as "Computational Models Generation for Designing of Plant-Based Anticancer Agents" is to examine and execute computational approaches with the intention of systematically designing and identifying possible anticancer drugs that are derived from plant chemicals. To be more specific, the purpose of the study is to make use of sophisticated computational models, such as molecular docking and machine learning techniques, in order to conduct an analysis of huge datasets of compounds originating from plants. The primary objective is to identify and prioritize molecules that possess substantial anticancer capabilities, with the end goal of simplifying the process of drug discovery. Ultimately, the purpose of this research is to contribute to the creation of novel and effective anticancer medicines that are derived from plant-based natural products. This research aims to address the obstacles that are associated with traditional drug discovery methods by harnessing the power of computational methodologies.

In order to reduce the amount of time needed for innovative drug candidate discovery, characterization, and structural optimization, computer-aided drug design, or CADD, is a highly helpful tool in rational drug design [1-5]. Rational medication design may also benefit from the use of CADD. Prodrugs are often made to improve the parent drug molecules' bioavailability or selectivity [6-8]. The study of molecules that interact with the biological target of interest is the indirect means via which ligand-based drug design aims to promote the

***Corresponding Author:** Alka Singh
Research Scholar Department of Computer Science and Engineering, P.K University, Shivpuri (M.P)

production of pharmacologically active drugs [9]. On the other hand, structure-based drug design techniques directly discover or optimize therapeutic candidates based on their understanding of the target molecule's three-dimensional structure [10-12].

Selecting a good target molecule linked to a disease is the first step in any drug creation process. A prospective therapeutic target is often a major protein in a biochemical pathway connected to the disease state [13-15]. Lead chemicals are substances that are either intended to stimulate or inhibit a particular biochemical pathway based on the nature of the illness condition [16-17], [1819]. Optimizing the lead compounds to maximize the interaction with the target molecule is the next phase in the drug development process. CADD may be very helpful in directing the lead optimization procedure.

BASICS OF QSAR

The QSAR method and pharmacophore modeling are the most widely used techniques for ligandbased drug design. A computer tool called QSAR quantifies the link between a series of chemicals' chemical structures and a chemical or biological process. The QSAR idea is that identical structural or physiochemical features produce similar activity [20-21]. First, a set of chemical entities or lead molecules with the necessary biological activity is found. A quantifiable association exists between active molecule physico-chemical properties and biological activity. The QSAR model optimizes active chemicals for biological activity. The anticipated chemicals are then experimentally tested for activity. Thus, QSAR may help identify chemical changes with better activity.

The general methodology of QSAR is built upon a series of consecutive steps (Fig. 1):

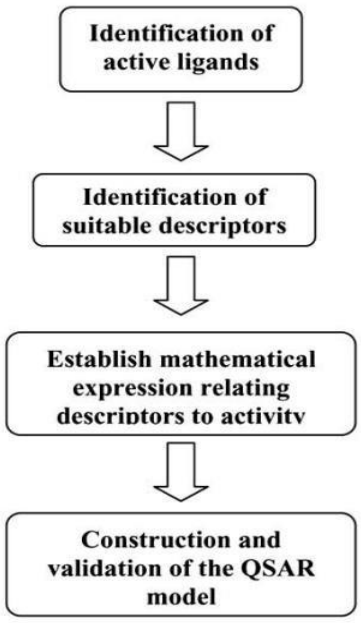

Figure 1. Typical workflow of QSAR methods

- Identify ligands with experimentally measured values of the desired biological activity. Ideally these ligands are of a congeneric series but should be of adequate chemically diversity to have a large variation in activity.
- Identify and determine molecular descriptors associated with various structural and physicochemical properties of the molecules under study.
- Discover correlations between molecular descriptors and the biological activity that can explain the variation in activity in the data set.
- Test the statistical stability and predictive power of the QSAR model.

Ligand Based Drug Design

Ligand-based drug design is a method that is used when there is a lack of information on the threedimensional structure of the receptor. This method is dependent on the knowledge of compounds that bind to the biological target of interest. Within the realm of ligand-based drug design, the most significant and extensively used methods are pharmacophore modeling and three-dimensional quantitative structure activity relationships, often known as 3D QSAR. In addition, they are able to provide predictive models that are appropriate for lead identification and optimization [22]. Additional information on these methodologies and their application to the design and development of 5-LOX inhibitors is offered in a different section of the study.

3D QSAR

As the name implies, the 3D QSAR approach uses descriptors to characterize a molecule's

threedimensional properties in order to create a QSAR model. The three-dimensional features of the ligands in the three-dimensional QSAR approach may be described by a range of geometric, physical, and quantum chemical descriptors. Following that, a pharmacophore that explains the biological action of the ligands is created by combining these molecular descriptors. The threedimensional spatial orientation of different properties, such acceptors or donors of hydrogen bonds, that are necessary for the intended biological activity is known as a pharmacophore [23-24]. To create the final 3D QSAR model, the produced pharmacophore model is evaluated for statistical significance and stability. A number of review publications are already available that go into great detail about several 3D QSAR modeling methodologies [25-35]. The main 3D QSAR methods that are presently being used for drug design will be briefly described in the section that follows in order to prevent duplication. The CSP-SAR approach developed in our laboratory and its applications will be thoroughly explained in the closing part.

CoMFA

One of the most popular 3D QSAR approaches is CoMFA [36]. CoMFA was the first QSAR approach to link molecule biological activity to 3D shape-dependent steric and electrostatic characteristics. The molecules' 3D structures are aligned on a 3D grid, and steric and electrostatic potential energies are determined at each grid point. CoMFA usually assumes the bioactive conformer is the minimal energy conformer. For systems with known crystal structures, crystal coordinates may determine bioactive conformers. Field values for potential energy terms are determined at each grid point for each molecule and associated with biological activity. CoMFA models are developed using PCA or PLS. We next evaluate the CoMFA model for statistical significance and robustness. Aligning bioactive conformers is crucial to CoMFA model performance and prediction [37-40]. The bioactive conformation is not always the lowest energy conformation in the absence of the receptor [41-43], hence CoMFA's selection of bioactive conformers and alignment approach may give incorrect models. CoMFA's application is limited by ignoring ligand dynamics. The energy function of CoMFA does not explicitly account for hydrophobicity or hydrogen bond interactions [44-46]. CoMFA calculates steric and electrostatic interaction using Lennard-Jones and Coulombic potential functions, which might result in unreasonably large energy terms owing to their hyperbolic natures. To prevent such behavior, CoMFA assigns an arbitrary cutoff value for these potential functions [47-48].

CoMSIA

Similar to CoMFA, Comparative Molecular Similarity Indices (CoMSIA) [49] is a 3D QSAR method. Nevertheless, in addition to steric and coulombic contributions, the molecular field expression of CoMSIA also contains hydrophobic, hydrogen-bond donor and acceptor components, unlike CoMFA. By comparing each ligand molecule with a common probe that has a radius of 1Å and charge, hydrophobicity, and hydrogen bond characteristics equal to 1, CoMSIA also computes the similarity indices rather than contact energies [50]. CoMSIA describes the steric, electrostatic, and hydrophobic components of the energy function using a bell-shaped Gaussian function. This enables CoMSIA to avoid using an arbitrary cutoff value for the energy computations, in contrast to CoMFA. The ligand-protein binding relationship is described by similarity indices that correlate to CoMSIA molecular fields [51].

Catalyst

3D QSAR's conformational flexibility has been taken into account. One well-known 3D QSAR application, CATALYST [52], uses conformational variation to build models. Using the poling approach, CATALYST samples the conformational space of ligands [53]. At a predetermined threshold of 20 kcal/mol above the global minimum conformation, this process yields 250 conformers. Functional group spatial orientations are used to create the pharmacophore hypothesis, and estimated and observed activity levels are used to assess QSAR models. The primary functional categories or pharmacophoric attributes are:

1. Hydrogen-bond acceptor
2. Hydrogen-bond donor
3. Positively charges group (basic)
4. Negatively charged group (acidic)
5. Aromatic ring
6. Aliphatic hydrophobic moieties
7. Aromatic hydrophobic moieties

Pharmacophore production involves constructive and subtractive steps. A pharmacophore hypothesis is built using molecules with activity above a threshold value during the constructive phase. Any pharmacophore that fits more than half of the inactive compounds is excluded in the subtractive phase. Based on prediction inaccuracy, feature weight, and complexity, each pharmacophore is priced.

CATALYST overcomes major 3D QSAR technique disadvantages. However, CATALYST has several limitations. Flexible ligand molecules may not be able to use all 250 conformers generated by CATALYST's conformation generator. Thus, CATALYST may not contain the bioactive conformer of active drugs, resulting in erroneous pharmacophore models. CATALYST does not develop combinations of physico-chemical and pharmacophoric models.

CSP-SAR

Principle. CSP-SAR is a unique 3D QSAR model development approach based on our Conformationally Sampled Pharmacophore (CSP) method [54-56]. This technique overcomes ligand alignment issues for conformationally flexible ligands. In the absence of the target molecule, a ligand molecule's

active or bound conformation may not be the lowest-energy conformer [57]. The conformational space of each ligand must be rigorously sampled to optimize the presence of bioactive conformers in the model. CSP considers all available conformations of each ligand molecule for pharmacophore creation, unlike other approaches. CSP maximizes the bioactive conformer's model inclusion probability.

The CSP technique relies on descriptors that contain chosen pharmacophore properties and all available conformations of each ligand. The descriptors must be considered as probability distributions that encompass all potential distances between two pharmacophore characteristics, angles between three, etc. We will use CSP data on bile acid conjugates and associated transporter (Apical Sodium-dependent Bile acid Transporter or ASBT) to explain this notion [58]. Fig. (**2**) shows three conjugates of the bile acid **9**, **2** and with three pharmacophore points (the original research evaluated 30 points on 13 compounds). Three conjugates from Fig. (**2**) will be used in this example. MD simulations were performed on each conjugate to acquire all potential conformations and establish descriptor probability distributions based on pharmacophore properties in Fig. (**3**). Compounds **9** (red), **2** (blue), and **21** (turquoise) have one-dimensional descriptors for the NG-OA distance and OA-NG-CG angles [59]. The probability distributions show that each conjugate samples a variety of conformations. These distributions reflect the descriptors, and their overlap (see next paragraph) may be employed as independent variables for model construction. Additional descriptors may be created in two or more dimensions. See Fig. (**4**) for 2D probability distributions for the two structural descriptors in Fig. (**3**). The distributions show that **9** and **2** share considerable structural similarity to the provided descriptors, but 21 did not sample conformational space related to either **9** or **2**. According to this qualitative study, **9** and **2** should have comparable activity as **21**. Notably, this approach did not need ligand alignment, just a comparison of the specified pharmacophore feature probability distributions. Another benefit of CSP is that structural alignment is not required.

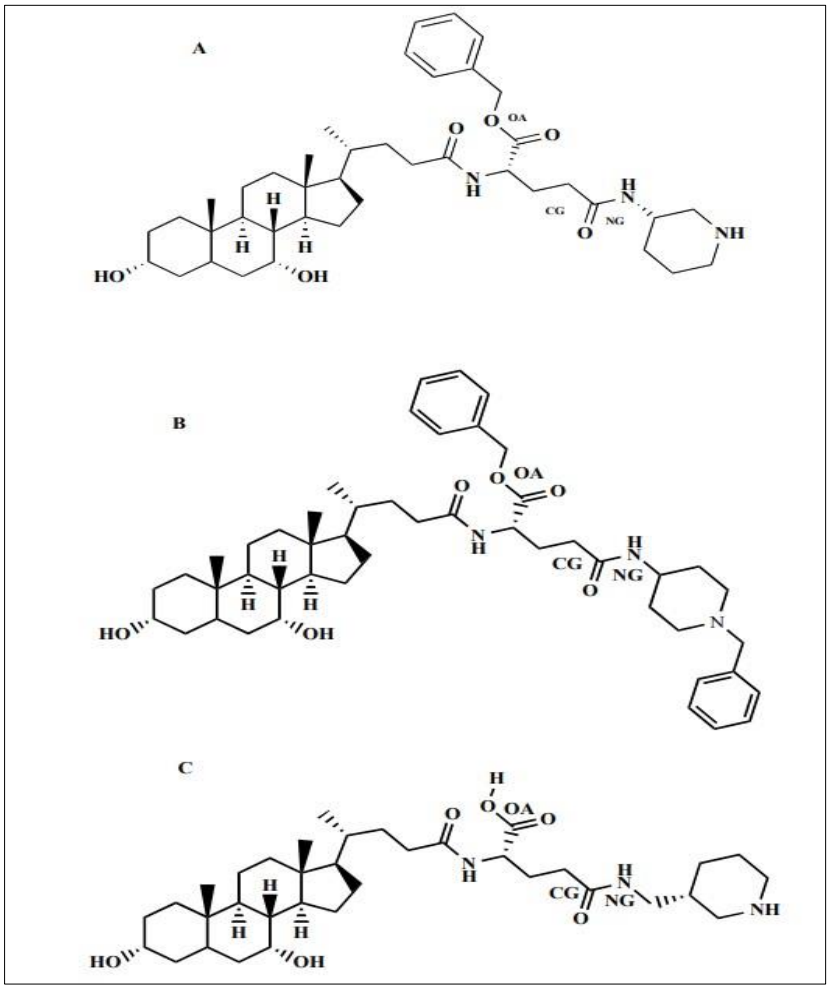

Figure 2: Structures of three bile acid conjugates (A) 9, (B) 2 and (C) 21 used by Gonzalez and coworkers [20]. OA, CG and NG

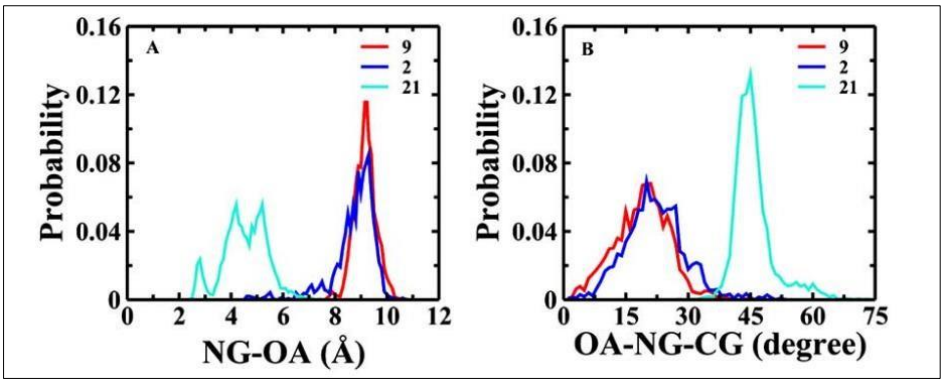

Figure 3: 1D probability distributions of distance between pharmacophoric points NG (basic nitrogen) and OA (α-acid) and angle between pharmacophoric points OA, NG and CG (amide carbon) for hASBT inhibitors; compound 2 (blue), 9 (red) and 21 (turquoise)

While use of the CSP approach in a qualitative manner is of utility, as described below, quantitative analysis is required to predict inhibition constants, potencies and so on. This requires that the degree of overlap of the probability distributions of the individual ligands be determined, yielding overlap coefficients that may be used directly in regression analysis. 1D overlap coefficient of a single structure descriptor between two ligands can be calculated using the following relation for discrete probability density functions, represent three pharmacophore feature points used in the study.

$$OC = \sum_{i=1}^{N} \min(P^{Ai}, P^{Bi}) \quad (1)$$

where $P^{Ai}$and P^{Bi} are the probability in bin i for compounds A and B and N is the total number of bins. Similarly, 2D overlap coefficients between two different structural descriptors can be calculated based on Eq. 2 [60]:

$$\sum ij\ Pijk.Pijl$$

$$OC = \sqrt{\sum_{ij}(P_{ijk})^2 \cdot \sum_{ij}(P_{ijl})^2} \quad (2)$$

where P is the normalized probability at pixel ij from the 2D distributions for compounds k (the reference chemical) and l. Usually the most powerful compound is selected to be the reference compound. Thus, overlap coefficients quantify ligand similarity to the reference chemical in their sampling conformation space (see below). Consider the 2D distributions in Fig. (**4**), 2D overlap coefficients for **2** and **21** were computed with regard to **9**; **2** provided an overlap coefficient of 0.688 whereas this value for **21** is 0. The research found that **9** (0.953μM) and **2** (2.26μM) were effective hASBT inhibitors, whereas **21** (31.8μM) exhibited intermediate efficacy. In that study, which used 13 ligands and multiple regression analysis, the CSP-SAR method was able to obtain quantitative and qualitative correlations with experimental data, providing a physical understanding of the compounds' biological activity.

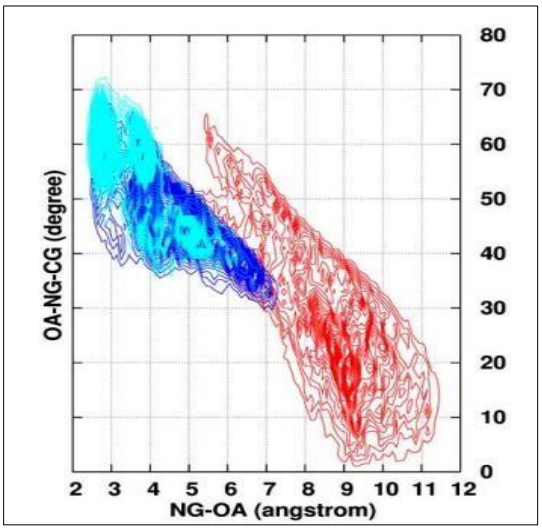

Figure 4. 2D probability distributions of distance between pharmacophoric points NG (basic nitrogen) and OA (α-acid) and angle between pharmacophoric points OA, NG and CG (amide carbon) for hASBT inhibitors; compound 2 (blue), 9 (red) and 21 (turquoise)

The overlap coefficients, structural descriptors, may be easily linked with physical property descriptors, a final CSP benefit. Physical parameters like polar surface area, dipole moment, and free energy of solvation may be determined for each ligand and used in regression analysis. Calculating the physical characteristic for each ligand conformation and utilizing the average results for regression analysis may be necessary. Physical attributes are easily included in the CSP technique, another strength.

REVIEW OF LITERATURE

Das *et al.,* 2023 [61] Drug discovery using phytocompounds is common due to their chemical and functional diversity. Multiple phytocompounds have been employed to produce novel cancer treatments. New anti-cancer leads, which phytocompounds can provide, are a priority for pharmaceutical companies and researchers worldwide. Due to their efficiency, reduced time, and cost-effectiveness, computational approaches like virtual screening (VS), molecular dynamics (MD), pharmacophore modeling, Quantitative structure–activity relationship (QSAR), Absorption Distribution Metabolism Excretion and Toxicity (ADMET), network biology, and machine learning (ML) have grown in popularity. This paper summarizes in silico findings on plant-based compounds for cancer lead discovery. This review discusses studies published in the last 5–6 years that use computational methods and emerging methods like network pharmacology and ML to find Phyto molecules as cancer leads. This study includes lists public databases and webservers for phytocompound-related drug development. This review should help pharmacologists, medicinal chemists, molecular biologists, and others transform natural products (NPs) into clinically viable lead molecules.

Ntie-Kang *et al.,* 2014 [62] Anticancer chemicals that occur naturally account for approximately half of the chemotherapeutic medications that have been introduced to the market for the treatment of cancer up to this point. Computer-based or in silico virtual screening approaches are frequently utilized in the protocols that are used for lead and hit finding. A comprehensive investigation was conducted to examine the "drug-likeness" of around 400 compounds derived from African medicinal plants. These compounds have demonstrated anticancer, cytotoxic, and antiproliferative properties in vitro and/or in animal. In order to determine whether or not the compounds have the ability to bind to anticancer drug targets, in silico modeling was used to investigate the interactions that occurred between the compounds and 14 different targets. Docking and binding affinity calculations were performed, and the results were compared to known anticancer drugs, which included around one thousand naturally occurring plant-based chemicals from all over the world. According to the findings, various medicinal plants found in Africa have the potential to serve as a valuable starting point for the development of anticancer medications. The limited data collection that was produced, which was given the moniker Afro Cancer, has been made accessible to research groups that are working on virtual screening.

De Araújo *et al.,* 2020 [63] Computer-Aided Drug Design (CADD) methods are compared to highthroughput screening for candidate medications due to their versatility, low cost, and ability to lower in vitro screening and synthesis step costs. Secondary metabolism of plants and other organisms produces huge amounts of unique chemical compounds having biological and pharmacological effects for practically every disease, including cancer. Vimblastine, vincristine, taxol, podophyllotoxin, captothecin, and cytarabine help cancer treatment. This review updates Ligand-Based Drug Design and Structure-Based Drug Design for flavonoids, alkaloids, and coumarins to uncover oncology-relevant compounds or fragments. Multiple databases were methodically searched. The search focused on papers from the past decade. Cancer-related chemical structures (coumarin, flavonoids, and alkaloids) and the infinite synthetic possibilities for analogous compounds create a huge chemical environment to explore, making it difficult for screening studies to select compounds with better target activity. Virtual screening tests utilizing CADD are the cheapest and most effective means to select compounds with better activity and "drug ability".

Chavda *et al.,* 2021 [64] The properties that program necrosis in natural chemical substances have been extensively studied. To determine pharmacological activity, concentrated plant extracts without active moieties are used to screen compounds. Modern medicine has focused on isolating and purifying one or two complicated active and isomeric compounds for 20 years. Multi-target medicines have evolved rapidly from an innovative approach in the early 2000s to one of the most popular drug development trends in 2021. However, fragment-based drug discovery is being studied for target-based drug discovery of strong natural anticancer medicines. This technique stresses well-defined fragments above natural mixes. This paper summarizes the latest advances in natural anticancer drugs, including computer-assisted and fragment-based structural elucidation and a multi-target exploration technique for natural compounds.

Ulucan-Karnak *et al.,* 2023 [65] Around the world, millions of individuals are afflicted with cancer. In order to identify medicine that is both effective and affordable, a significant amount of research is carried out. Over the course of the last few decades, natural compounds derived from plants have garnered a lot of attention as potential innovative medicinal agents. Because of the wide variety of chemical compounds that nature contains, it is a tremendous source of potential medicinal molecules. When it comes to the progression of medication discovery, anticancer plant metabolites are currently being considered as potential replacements for

chemically manufactured pharmaceuticals. Bioinformatics-based technologies have the capability of identifying compounds that have the potential to fight cancer. The use of computational methods could thereby pave the way for the rapid and cost-effective discovery of prospective drug candidates and molecular targets within the pharmaceutical industry. We will present an introduction of the use of herbal resources for the treatment of cancer, as well as methodologies for drug design, with a special focus on structure-based drug design, and examples of how drug design can be applied to plant-based molecules.

Rahman *et al.,* 2022 [66] Immune system and cancer research has led to new treatments. Future drugs will kill and stop cancer cell growth with precise signals. Machine learning speeds up therapeutic research for difficult ailments. Machine learning could investigate cancer genomes and develop subtype-specific drugs. New drug development is costly, risky, and time-consuming. Costs over $1 billion to make drugs over 15 years. Thus, CADD may improve design speed, cost, and efficiency. From hit identification to optimization, many scanning systems use ligand screening and structural virtual screening to improve drug development productivity and analysis. This review examined numerous computational anticancer medication methods. Machine learning in fundamental and translational cancer research is too far off for tailored treatment and fast data processing. Every cancer patient requires safe, effective treatment. Recently developed computational drug discovery technologies improve cancer drug design and treatment. Computeraided anticancer medication development is covered here. Transcriptomics, toxicogenomics, functional genomics, and biological networks predict anticancer medication and therapy combinations. Knowledge of databases and computational approaches may aid cancer treatment development.

Mangal *et al.,* 2013 [67] Pharmaceutical corporations and biomedical researchers favor plantderived compounds for therapeutic development since they are assumed to be optimized during evolution. To complement the other databases, we have collected and compiled a central resource Naturally Occurring Plant-based Anti-cancer Compound-Activity-Target database (NPACT, http://crdd.osdd.net/raghava/npact/) with experimentally validated plant-derived natural compounds with anti-cancerous activity (in vitro and in vivo). Each of its 1574 compound entries includes structure, manually curated published data on in vitro and in vivo experiments, reference for user referral, inhibitory values ($IC_{50}/ED_{50}/EC_{50}/GI_{50}$), properties (physical, elemental, and topological), cancer types, cell lines, protein targets, commercial suppliers, and drug likeness. We offer an online similarity tool and other ways to view or query NPACT. Each record links to Super Natural, Herbal Ingredients' Targets, Comparative Toxicogenomic Database, PubChem, and NCI60 GI_{50} data to make data retrieval easier.

Prada-Gracia *et al.,* 2016 [68] New medication development is complicated, dangerous, expensive, and time-consuming. Conventional drug discovery can take 15 years and cost over a billion dollars. Fortunately, new methods have changed this. Computational methods are essential to many drug development projects because to the many new technology and methods that have improved drug discovery. Many discovery initiatives use ligand- or structure-based virtual screening for hit identification and lead optimization. These computational approaches have had a big impact on creating possible anticancer medications and therapeutic candidates, providing valuable cancer insights. In this study, we examine rational design and describe some of the most representative compounds identified by it. Case studies of successful anticancer drug design reveal that research improvements and in silico drug design can develop novel anticancer medications.

De *et al.,* 2019 [69] The utilization of in silico tools in the process of developing medications that are effective against cancer. The compilation of many computer-aided drug design strategies that have been utilized in the process of developing anti-cancer medications. The use of structurebased, ligand-based, hybrid protein-ligand pharmacophore techniques, homology modeling, and molecular docking can be of great assistance at various stages of the drug discovery pipeline, resulting in significant time and cost savings. In addition, in silico tools have applications in the field of medication development for cancer patient treatment. PUMA inhibitors were identified with the assistance of structure-based pharmacophore modeling. Additionally, a structure-based approach was utilized for the development of Bcl-2 inhibitors, with high throughput screening. This approach was utilized to derive the most relevant protein-protein interactions, anti-mitotic agents, and I-Kappa-B Kinase β (IKK- β) inhibitors. Additionally, they were utilized to screen for a new class of aromatase inhibitors, which have the potential to be important targets in cancer therapy. It has been discovered that the utilization of computational tools in the process of designing anti-cancer medications is successful.

Vibala *et al.,* 2020 [70] Cancer is one of the leading causes of death and is rising. Multiple cancer treatments are available, yet none are effective. One of the biggest problems in chemotherapy is drug toxicity. However, plant and plant derivative cancer treatments are effective and safe. Most cancer-targeted medication development nowadays uses plant and plant natural components. Some natural compounds and their equivalents are effective anticancer agents. This review highlights recent plant species with invitro or invivo anticancer activities. Invention of plant-based medications takes time and money. Many labor-intensive

high-throughput technologies are being developed. Bioinformatics and bioscience are essential to high-throughput data creation. This is frequent in drug discovery and design. Bioinformatics and computational methods are rarely applied in plant-based research and technology. The aforesaid medicinalplant research methods are covered in this review. Using these strategies in medicinal plant research may lead to cheaper and simpler medication design.

RESEARCH METHODOLOGY

The research study titled "Computational Models Generation for Designing of Plant-Based Anticancer Agents" makes use of a comprehensive collection of computational approaches in order to generate models that can anticipate the possible anticancer effects of chemicals derived from plants. The following is an overview of the primary computational methods that were utilized in the research:

3.1 Molecular Docking:

- **Purpose:** Molecular docking is employed to simulate the interaction between plant-derived compounds and specific cancer-related molecular targets.
- **Methodology:** Computational algorithms predict the preferred orientation and binding affinity of the plant compounds within the active site of target proteins.
- **Outcome:** The results provide insights into the potential of each compound to interact with the target, guiding the selection of candidates for further investigation.

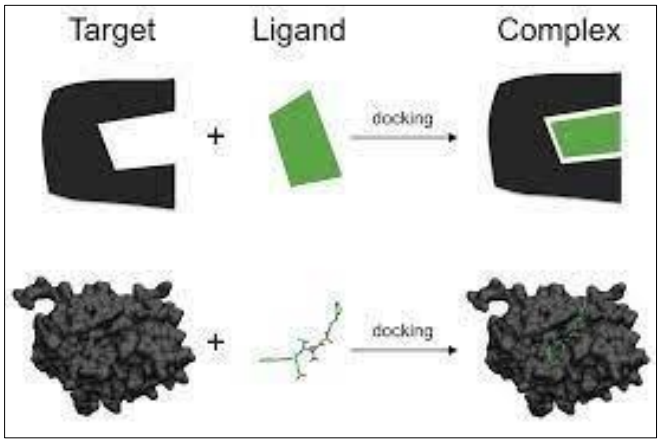

Figure 5: Molecular Docking

3.2 Machine Learning Algorithms:

- **Purpose:** Machine learning models are utilized to analyze and predict the anticancer properties of plant compounds based on a set of defined features.
- **Methodology:** Datasets containing information on the chemical and structural properties of the compounds, as well as their known anticancer activities, are used to train machine learning algorithms.
- **Outcome:** The trained models can then predict the anticancer potential of new, untested compounds, aiding in the identification of promising candidates.

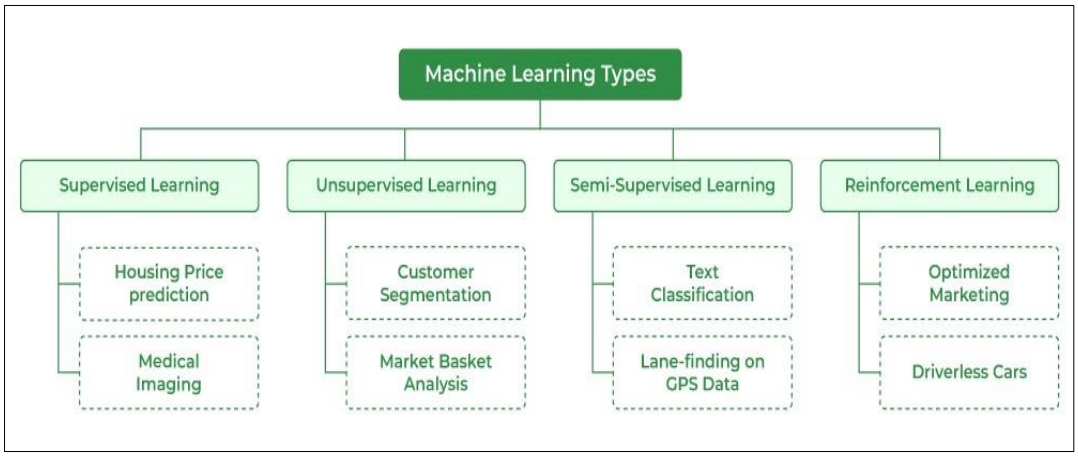

Figure 6: Types of Machine Learning

3.3 Bioinformatics Tools:

- **Purpose:** Bioinformatics tools are applied to analyze biological data, including information on the genetic and molecular aspects of cancer pathways.
- **Methodology:** The integration of bioinformatics involves the interpretation of omics data, pathway analysis, and identification of potential targets associated with cancer.
- **Outcome:** Bioinformatics analysis contributes to the selection of relevant molecular targets for molecular docking studies and guides the overall strategy for identifying plant compounds with anticancer properties.

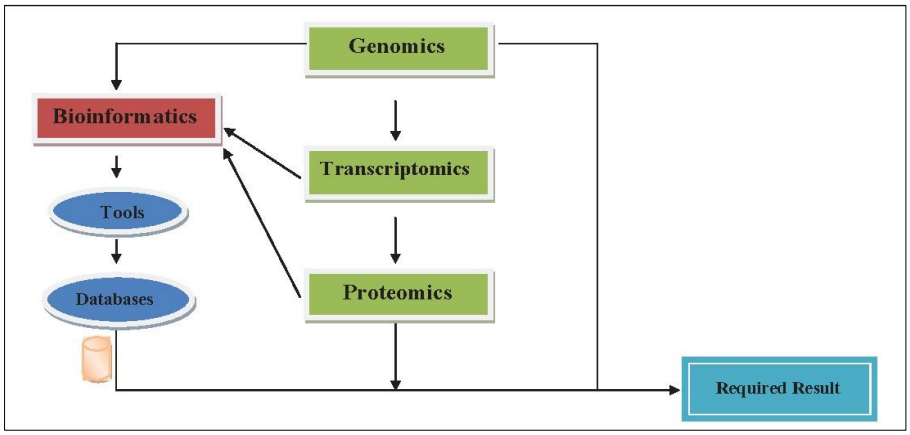

Figure 7: Integration Bioinformatics Tools

3.4 Data Integration and Mining:

- **Purpose:** Integration of diverse datasets from various sources, including chemical databases and biological repositories.
- **Methodology:** Computational techniques for data integration and mining are employed to extract relevant information on the chemical properties, bioavailability, and known activities of plant compounds.
- **Outcome:** The integrated data provide a comprehensive foundation for the subsequent computational analyses, facilitating a more holistic understanding of the potential anticancer properties of the plant compounds.

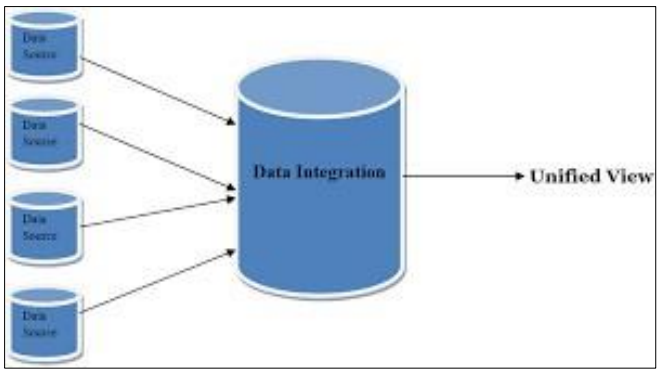

Figure 8: Data Integration in Data Mining

Specify the criteria for selecting plant compounds

In "Computational Models Generation for Designing of Plant-Based Anticancer Agents," plant molecules matching particular criteria are carefully selected. Ethnopharmacological significance favors plants with a traditional medicine background, notably for cancer treatment. Based on biological activities, substances with anticancer characteristics in the literature are included. We seek diverse chemical classes to ensure a broad molecular range for computational analysis and increase the possibility of discovering novel anticancer drugs. Selecting substances that are readily available for experimental validation is based on availability and source. Compounds with good safety profiles are prioritized. Structurally complex chemicals that may interact uniquely with cancer targets are preferred. Compounds must meet target specificity, bioavailability, and druglikeness criteria to be developed. Finally, computational feasibility favors chemicals suitable for investigation analytical procedures. The study uses these criteria to gather a varied and promising set of plant chemicals for computer modeling to find effective plant-based anticancer medicines.

Describe how the anticancer properties were assessed

The evaluation of anticancer qualities in the article "Computational Models Generation for Designing of Plant-Based Anticancer Agents" requires the integration of computational methodologies in a methodical manner. For the purpose of predicting the interactions between certain plant chemicals and cancer-related molecular targets, molecular docking studies are utilized. These studies provide insights into the probable binding affinities of cancer-related molecules. It is possible to make predictions about the anticancer potential of plant compounds by using machine learning models that have been trained on datasets that include the chemical and structural features of botanical substances. Putting the computational findings into context within the setting of cancer-related pathways is made easier with the incorporation of bioinformatics technologies. The trustworthiness of the computational predictions is further improved by the process of validation against experimental data and statistical studies. A thorough awareness of the possible influence that plant compounds may have on molecular targets and pathways associated with cancer is provided by this holistic approach, which not only prioritizes plant compounds based on their projected anticancer efficacy but also provides a comprehensive understanding of the potential impact that these compounds may have.

Plant-Based Anticancer Agents

Bioactive chemicals obtained from plants can inhibit or reduce cancer cell development. Oncology is interested in these medicines due to their various chemical structures and methods of action. Plants are rich in secondary metabolites such alkaloids, flavonoids, terpenoids, and polyphenols, which have many pharmacological effects, including anticancer characteristics. These plantderived chemicals are studied for their ability to disrupt cancer-related cell cycle regulation, apoptosis, angiogenesis, and metastasis. Traditional pharmacological methods and current computational methods are used to identify and optimize plant-based anticancer medicines that may be more effective and less harmful. The study of plant-based anticancer medicines is part of an increasing interest in combining traditional medicine with modern drug discovery.

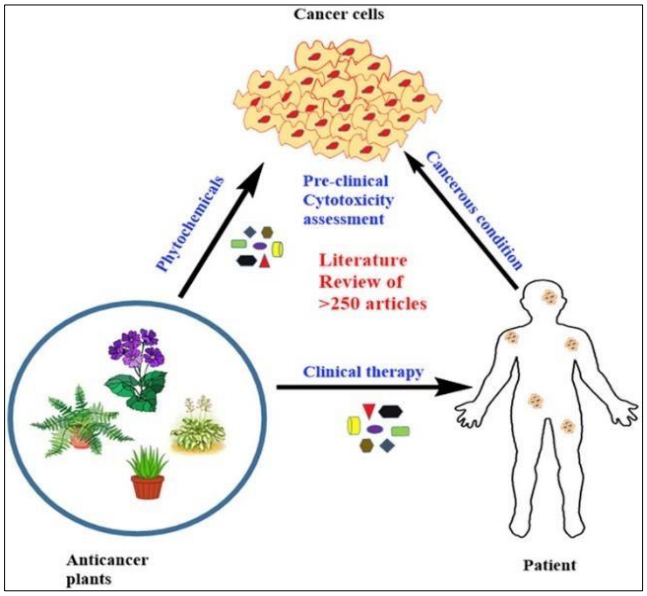

Figure 9. Plant-derived anticancer agents

Computational Models Generation

Generating mathematical or computational models to simulate and forecast complicated systems, phenomena, or processes is computational model generation. In "Computational Models

Generation for Designing of Plant-Based Anticancer Agents," mathematical frameworks or algorithms are used to anticipate plant chemicals' cancer cell growth inhibitory effects. These models use molecular docking, machine learning, and bioinformatics to analyses massive plant chemical datasets, understand their interactions with cancer-related molecular targets, and rank candidates for experimental validation. The goal is to use computational methods to speed drug discovery, find promising plant-based anticancer chemicals, and develop novel and effective therapy regimens. These computational models efficiently screen and prioritize anticancer drugs, speeding up the drug discovery pipeline.

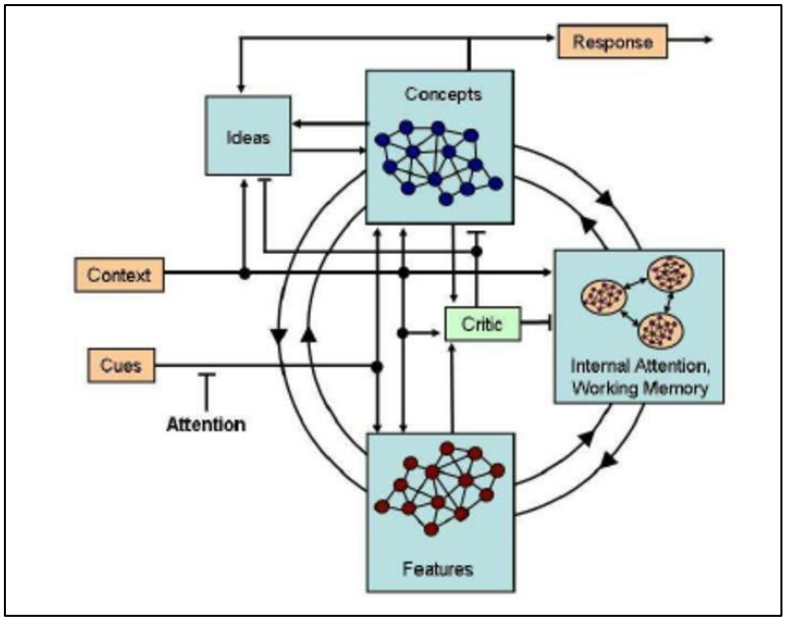

Figure 10: Architecture of the computational model

RESULTS AND DISCUSSION

Ligand-based drug design is inherently a complicated problem as this approach is restricted to considering only one side of the actual biochemical process. Receptor molecules and/or ligands have often been shown to go through substantial conformational changes in order to promote their interaction [71-75]. More current methodologies include several conformations during model creation, whereas earlier pharmacophore approaches generally did not account for ligand conformational flexibility by employing just minimal energy conformations of the ligands. Even while these approaches provide a great deal of improvement, they are still constrained by the fact that they involve a narrow range of conformations and need ligand alignment. By include all ligand conformations that are available and using the overlap of probability distributions of pharmacophore characteristics in model creation, the CSP approach essentially gets around these restrictions. Furthermore, physicochemical characteristics may be easily integrated using the CSPSAR approach. Several research conducted in our labs and by other scientists have shown the usefulness of this strategy.

It is clear that ligand-based drug design is an effective method for learning about the properties of ligands that are critical to their biological activity in the absence of the receptor structure. Examining a therapeutic target's ligands' structural and physico-chemical characteristics may reveal the kinds of interactions crucial to the desired pharmacological response. Furthermore, the methodology may forecast distinct chemical structures with properties that facilitate the interaction with the target molecule. As previously indicated, there are several ways to approach the process of ligand-based modeling. Nevertheless, it is highly recommended that one has a solid understanding of the underlying idea behind the chosen technique in order to properly apply these methods to complex biological systems.

CONCLUSION AND FUTURE SCOPE

In conclusion, there is a lot of potential to advance drug discovery and development via the use of computer models in the creation of plant-based anticancer medicines. The drug development process has been optimized by the systematic identification of promising therapeutic compounds made possible by the synergy between medicinal plant research and computational techniques. Future work on improving and verifying computational models and integrating cutting-edge technologies like machine learning and artificial intelligence will be focused on improving prediction accuracy. Computational biologists, pharmacologists, and botanists working together will increase the number of medicinal plants in the database and improve the models to include more bioactive components. Furthermore, by combining virtual screening with lead optimization using these models, it will be possible to identify attractive candidates for experimental validation more quickly, leading to more effective and focused anticancer tactics. The manufacture and testing of anticipated compounds will become more efficient as technology advances, saving time and money on medication development. All things considered, the combination of plant-based drug discovery with computer modeling not only constitutes a recent success, but also paves the way for a creative future in the search for potent natural anticancer medicines.

REFERENCES

1. Chang, C.; Ekins, S.; Bahadduri, P.; Swaan, P.W. Pharmacophorebased discovery of ligands for drug transporters. Adv. Drug Deliv. Rev., 2006, 58, 1431-1450.
2. Ekins, S.; Mirny, L.; Schuetz, E.G. A ligand-based approach to understanding selectivity of nuclear hormone receptors PXR, CAR, FXR, LXRa, and LXRb. Pharm. Res., 2002, 19, 17881800.
3. Ekins, S.; Waller, C.L.; Swaan, P.W.; Cruciani, G.; Wrighton, S.A.; Wikel, J.H. Progress in predicting human ADME parameters in silico. J. Pharmacol. Toxicol. Methods, 2000, 44, 251272.
4. van de Waterbeemd, H.; Gifford, E. ADMET in silico modelling: towards prediction paradise? Nat. Rev. Drug Discov., 2003, 2, 192- 204.
5. Ekins, S. Computer applications in pharmaceutical research and development. John Wiley & Sons; Hoboken, NJ, 2006.
6. Balakrishnan, A.; Polli, J.E. Apical sodium dependent bile acid transporter (ASBT, SLC10A2): a potential prodrug target. Mol. Pharm., 2006, 3, 223-230.
7. Takakura, Y.; Hashida, M. Macromolecular drug carrier systems in cancer chemotherapy: macromolecular prodrugs. Crit. Rev. Oncol. Hematol., 1995, 18, 207-231.
8. Tolle-Sander, S.; Lentz, K.A.; Maeda, D.Y.; Coop, A.; Polli, J.E. Increased acyclovir oral bioavailability via a bile acid conjugate. Mol. Pharm., 2004, 1, 40-48.
9. Kurogi, Y.; Guner, O.F. Phamacophore modeling and threedimensional database searching for drug design using catalyst. Curr. Med. Chem., 2001, 8, 1035-1055.
10. Marrone, T.J.; Briggs, J.M.; McCammon, J.A. Structure-based drug design: computational advances. Annu. Rev. Pharmacol. Toxicol., 1997, 37, 71-90.
11. Gane, P.J.; Dean, P.M. Recent advances in structure-based rational drug design. Curr. Opin.
12. Struct. Biol., 2000, 10, 401-404.
13. Jhoti, H.; Leach, A.R. Structure-based Drug Discovery. Springer: 2007.
14. Balakrishnan, A.; Polli, J.E. Apical sodium dependent bile acid transporter (ASBT, SLC10A2): a potential prodrug target. Mol. Pharm., 2006, 3, 223-230.
15. Zhong, S.; Macias, A.T.; MacKerell, A.D., Jr. Computational identification of inhibitors of protein-protein interactions. Curr. Top. Med. Chem., 2007, 7, 63-82.
16. Chen, F.; Hancock, C.N.; Macias, A.T.; Joh, J.; Still, K.; Zhong, S.; MacKerell, A.D. Jr.; Shapiro, P. Characterization of ATPindependent ERK inhibitors identified through in silico analysis of the active ERK2 structure. Bioorg. Med. Chem. Lett., 2006, 16, 6281-6287.
17. Hafner, C.; Schmitz, G.; Meyer, S.; Bataille, F.; Hau, P.; Langmann, T.; Dietmaier, W.; Landthaler, M.; Vogt, T. Differential gene expression of Eph receptors and ephrins in benign human tissues and cancers. Clin. Chem., 2004, 50, 490-499.
18. Dobrzanski, P.; Hunter, K.; Jones-Bolin, S.; Chang, H.; Robinson, C.; Pritchard, S.; Zhao, H.; Ruggeri, B. Antiangiogenic and antitumor efficacy of EphA2 receptor antagonist. Cancer Res., 2004, 64, 910-919.
19. Cheng, N.; Brantley, D.; Fang, W.B.; Liu, H.; Fanslow, W.; Cerretti, D.P.; Bussell, K.N.; Reith, A.; Jackson, D.; Chen, J. Inhibition of VEGF-dependent multistage carcinogenesis by soluble EphA receptors. Neoplasia, 2003, 5, 445-456.
20. Torres, G.E.; Gainetdinov, R.R.; Caron, M.G. Plasma membrane monoamine transporters: structure, regulation and function. Nat. Rev. Neurosci., 2003, 4, 13-25.
21. Akamatsu, M. Current state and perspectives of 3D-QSAR. Curr. Top. Med. Chem., 2002, 2, 1381-1394.
22. Verma, R. P.; Hansch, C., Camptothecins: A SAR/QSAR Study. Chem. Rev. 2009, 109, 213235.
23. Acharya, C.; Coop, A.; Polli, J.E.; Mackerell, A.D. Jr. Recent advances in ligand-based drug design: relevance and utility of the conformationally sampled pharmacophore approach. Curr. Comput. Aided Drug Des., 2011, 7(1), 10-22.
24. Chang, C.; Swaan, P.W. Computational approaches to modeling drug transporters. Eur. J. Pharm. Sci., 2006, 27, 411-424.
25. Wermuth, C.G.; Langer, T. Pharmacophore identification. In 3DQSAR in Drug Design. Theory, Methods, and Applications. ESCOM Science Publishers: 1993.
26. Ekins, S.; Mirny, L.; Schuetz, E.G. A ligand-based approach to understanding selectivity of nuclear hormone receptors PXR, CAR, FXR, LXRa, and LXRb. Pharm. Res., 2002, 19, 17881800.
27. Ekins, S.; Waller, C.L.; Swaan, P.W.; Cruciani, G.; Wrighton, S.A.; Wikel, J.H. Progress in predicting human ADME parameters in silico. J. Pharmacol. Toxicol. Methods, 2000, 44, 251272.
28. Kurogi, Y.; Guner, O.F. Phamacophore modeling and threedimensional database searching for drug design using catalyst. Curr. Med. Chem., 2001, 8, 1035-1055.
29. Mason, J.S.; Good, A.C.; Martin, E.J. 3-D pharmacophores in drug discovery. Curr. Pharm. Des., 2001, 7, 567-597.
30. Akamatsu, M. Current state and perspectives of 3D-QSAR. Curr. Top. Med. Chem., 2002, 2, 1381-1394.
31. Winkler, D.A. Overview of Quantitative Structure-Activity Relationships (QSAR). In Molecular Analysis and Genome Discovery, Rapley, R.; Harbron, S., Eds. 2004.
32. Winkler, D.A. The role of quantitative structure-activity relationships (QSAR) in biomolecular discovery. Brief. Bioinform., 2002, 3, 73-86.
33. Chang, C.; Swaan, P.W. Computational approaches to modeling drug transporters. Eur. J. Pharm. Sci., 2006, 27, 411-424.

34. Hopfinger, A.J.; Wang, S.; Tokarski, J.S.; Jin, B.; Albuquerque, M.; Madhav, P.J.; Duraiswami, C. Construction of 3D-QSAR models using the 4D-QSAR analysis formalism. J. Am. Chem. Soc., 1997, 119, 10509-10524.
35. de Groot, M.J.; Ekins, S. Pharmacophore modeling of cytochromes P450. Adv. Drug Deliv. Rev., 2002, 54, 367-383.
36. Van Drie, J.H. Pharmacophore discovery: lessons learned. Curr. Pharm. Des., 2003, 9, 16491664.
37. Cramer, R.D.; Patterson, D.E.; Bunce, J.D. Comparative molecularfield analysis (Comfa). 1. Effect of shape on binding of steroids to carrier proteins. J. Am. Chem. Soc., 1988, 110, 59595967.
38. Akamatsu, M. Current state and perspectives of 3D-QSAR. Curr. Top. Med. Chem., 2002, 2, 1381-1394.
39. Gohda, K.; Mori, I.; Ohta, D.; Kikuchi, T. A CoMFA analysis with conformational propensity:
40. an attempt to analyze the SAR of a set of molecules with different conformational flexibility using a 3DQSAR method. J. Comput. Aided Mol. Des., 2000, 14, 265-275.
41. Yasuo, K.; Yamaotsu, N.; Gouda, H.; Tsujishita, H.; Hirono, S., Structure-based CoMFA as a predictive model - CYP2C9 inhibitors as a test case. J. Chem. Inf. Model., 2009, 49, 853-864.
42. Ghose, A.K.; Viswanadhan, V.N.; Wendoloski, J.J. A knowledgebased approach in designing combinatorial or medicinal chemistry libraries for drug discovery. J. Comb. Chem., 1999, 1, 55-68.
43. Bostrom, J.; Norrby, P.O.; Liljefors, T. Conformational energy penalties of protein-bound ligands. J. Comput. Aided Mol. Des., 1998, 12, 383-396.
44. MacKerell, A.D. Jr. Empirical force fields for biological macromolecules: overview and issues.
45. J. Comput. Chem., 2004, 25, 1584-1604.
46. Hasegawa, K.; Arakawab, M.; Funatsu, K. Rational choice of bioactive conformations through use of conformation analysis and 3-way partial least squares modeling. Chemom. Intell. Lab. Syst., 2000, 50, 253-261.
47. Akamatsu, M. Current state and perspectives of 3D-QSAR. Curr. Top. Med. Chem., 2002, 2, 1381-1394.
48. Ghose, A.K.; Viswanadhan, V.N.; Wendoloski, J.J. A knowledgebased approach in designing combinatorial or medicinal chemistry libraries for drug discovery. J. Comb. Chem., 1999, 1, 55-68.
49. Klebe, G.; Abraham, U.; Mietzner, T. Molecular similarity indices in a comparative analysis (CoMSIA) of drug molecules to correlate and predict their biological activity. J. Med. Chem., 1994, 37, 4130-4146.
50. Folkers, G.; Merz, A.; Rognan, D. CoMFA: Scope and Limitations in 3D QSAR in Drug Design. 1993.
51. Flower, D.R. Predicting chemical toxicity and fate. 2002.
52. Klebe, G.; Abraham, U.; Mietzner, T. Molecular similarity indices in a comparative analysis (CoMSIA) of drug molecules to correlate and predict their biological activity. J. Med. Chem., 1994, 37, 4130-4146.
53. Flower, D.R. Drug design: cutting edge approaches. 2002.
54. Klebe, G.; Abraham, U. Comparative molecular similarity index analysis (CoMSIA) to study hydrogen-bonding properties and to score combinatorial libraries. J. Comput. Aided Mol. Des., 1999, 13, 1-10.
55. Catalyst: Accelrys Inc. (SanDiego, CA), 2002.
56. Smellie, A.; Teig, S.L.; Towbin, P. Poling: promoting conformational variation. J. Comput. Chem., 1995, 16, 171-187.
57. Bernard, D.; Coop, A.; MacKerell, A.D. Jr. Conformationally sampled pharmacophore for peptidic delta opioid ligands. J. Med. Chem., 2005, 48, 7773-7780.
58. Bernard, D.; Coop, A.; MacKerell, A.D. Jr. 2D conformationally sampled pharmacophore: a ligand-based pharmacophore to differentiate delta opioid agonists from antagonists. J. Am. Chem. Soc., 2003, 125, 3101-3107.
59. Bernard, D.; Coop, A.; MacKerell, A.D. Jr. Quantitative conformationally sampled pharmacophore for delta opioid ligands: reevaluation of hydrophobic moieties essential for biological activity. J. Med. Chem., 2007, 50, 1799-1809.
60. Nicklaus, M.C.; Wang, S.; Driscoll, J.S.; Milne, G.W.A. Conformational changes of small molecules binding to proteins. Bioorg. Med. Chem., 1995, 3, 411-428.
61. González, P. M.; Acharya, C.; MacKerell, A.D. Jr.; Polli, J.E. Inhibition requirements of the human apical sodium-dependent bile acid transporter (hASBT) using aminopiperidine conjugates of glutamyl-bile acids. Pharm. Res., 2009, 26, 1665-1678.
62. González, P. M.; Acharya, C.; MacKerell, A.D. Jr.; Polli, J.E. Inhibition requirements of the human apical sodium-dependent bile acid transporter (hASBT) using aminopiperidine conjugates of glutamyl-bile acids. Pharm. Res., 2009, 26, 1665-1678.
63. Bernard, D.; Coop, A.; MacKerell, A.D. Jr. Quantitative conformationally sampled pharmacophore for delta opioid ligands: reevaluation of hydrophobic moieties essential for biological activity. J. Med. Chem., 2007, 50, 1799-1809.
64. Das, A. P., & Agarwal, S. M. (2023). Recent advances in the area of plant-based anti-cancer drug discovery using computational approaches. *Molecular Diversity*, 1-25.
65. Ntie-Kang, F., Nwodo, J. N., Ibezim, A., Simoben, C. V., Karaman, B., Ngwa, V. F., ... & Mbaze, L. M. A. (2014). Molecular modeling of potential anticancer agents from African medicinal plants. *Journal of chemical information and modeling*, *54*(9), 2433-2450.

66. de Araújo, R. S., da Silva-Junior, E. F., de Aquino, T. M., Scotti, M. T., Ishiki, H. M., Scotti, L., & Mendonça-Junior, F. J. B. (2020). Computer-aided drug design applied to secondary metabolites as anticancer agents. *Current Topics in Medicinal Chemistry*, *20*(19), 1677-1703.
67. Chavda, V. P., Ertas, Y. N., Walhekar, V., Modh, D., Doshi, A., Shah, N., ... & Chhabria, M. (2021). Advanced computational methodologies used in the discovery of new natural anticancer compounds. *Frontiers in Pharmacology*, *12*, 702611.
68. Ulucan-Karnak, F., Yilmaz-Sercinoglu, Z., Sercinoglu, O., & Ali, A. (2023). Computational Approaches Used in Anticancer Plants. In *Plant-Derived Anticancer Drugs in the OMICS Era* (pp. 215-250). Apple Academic Press.
69. Rahman, M. M., Islam, M. R., Rahman, F., Rahaman, M. S., Khan, M. S., Abrar, S., ... & Chellappan, D. K. (2022). Emerging promise of computational techniques in anti-cancer research: at a glance. *Bioengineering*, *9*(8), 335.
70. Mangal, M., Sagar, P., Singh, H., Raghava, G. P., & Agarwal, S. M. (2013). NPACT: naturally occurring plant-based anti-cancer compound-activity-target database. *Nucleic acids research*, *41*(D1), D1124-D1129.
71. Prada-Gracia, D., Huerta-Yépez, S., & Moreno-Vargas, L. M. (2016). Application of computational methods for anticancer drug discovery, design, and optimization. *Boletín Médico Del Hospital Infantil de México (English Edition)*, *73*(6), 411-423.
72. De, B., Bhandari, K., Mendonça, F. J., Scotti, M. T., & Scotti, L. (2019). Computational studies in drug design against cancer. *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents)*, *19*(5), 587-591.
73. Vibala, B. V., Praseetha, P. K., & Vijayakumar, S. (2020). Evaluating new strategies for anticancer molecules from ethnic medicinal plants through in silico and biological approachA review. *Gene Reports*, *18*, 100553.
74. Remy, I.; Wilson, I.A.; Michnick, S.W. Erythropoietin receptor activation by a ligand-induced conformation change. Science, 1999, 283, 990-993.
75. Kuiper, G.G.; Carlsson, B.; Grandien, K.; Enmark, E.; Haggblad, J.; Nilsson, S.; Gustafsson, J.A. Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors alpha and beta. Endocrinology, 1997, 138, 863-870.
76. Kunishima, N.; Shimada, Y.; Tsuji, Y.; Sato, T.; Yamamoto, M.; Kumasaka, T.; Nakanishi, S.; Jingami, H.; Morikawa, K. Structural basis of glutamate recognition by a dimeric metabotropic glutamate receptor. Nature, 2000, 407, 971-977.
77. Palczewski, K.; Kumasaka, T.; Hori, T.; Behnke, C.A.; Motoshima, H.; Fox, B.A.; Le Trong, I.; Teller, D.C.; Okada, T.; Stenkamp, R.E.; Yamamoto, M.; Miyano, M. Crystal structure of rhodopsin: a G protein-coupled receptor. Science, 2000, 289, 739-745.
78. Humphries, M.J. Integrin activation: the link between ligand binding and signal transduction. Curr. Opin. Cell Biol., 1996, 8, 632-640.

Cite This Article: Alka Singh & Ravindra Singh Yadav (2025). Computational Models Generation for Designing of Plant Based Anticancer Agents. *East African Scholars J Eng Comput Sci*, *8*(2), 39-52.