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Review Article

COMPUTER-AIDED DRUG DESIGN AND ITS APPLICATIONS IN CANCER RESEARCH: A REVIEW

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ABSTRACT

Computer-aided drug design (CADD) has become a crucial tool in cancer research, leveraging advanced computational techniques to accelerate drug discovery and develop targeted anticancer agents. By simulating molecular interactions and predicting the behavior of potential drug candidates, CADD aids in identifying novel compounds with enhanced specificity and reduced toxicity. Virtual screening, a key element of CADD, allows rapid assessment of thousands of compounds to target specific cancer-related proteins or pathways. Molecular dynamics simulations provide insights into protein conformational changes and their interactions with small molecules, facilitating rational drug design. Molecular docking predicts the binding affinity and orientation of ligands within protein binding sites, streamlining the identification of potential drug candidates and reducing experimental trial and error. Quantitative structure-activity relationship models quantitatively relate chemical structures to biological activities, optimizing drug candidates by refining chemical scaffolds to enhance efficacy and minimize toxicity. CADD's impact on drug development is significant, paving the way for specialized and targeted cancer treatments, offering hope for novel medications with improved effectiveness and fewer adverse effects.

Keywords: Computer-aided drug design, Cancer research, Virtual screening, Molecular dynamics simulations, Quantitative structure-activity relationship.

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INTRODUCTION

Cancer, a complex group of diseases characterized by the uncontrolled growth and spread of abnormal cells, continues to be a major global health challenge. Over the past few decades, significant progress has been made in understanding the molecular mechanisms underlying cancer, leading to the development of more effective treatments. Central to this progress is the field of computer-aided drug discovery (CADD) and its transformative applications in oncology [1]. CADD, often referred to as *in silico* drug discovery, harnesses the power of computational techniques and advanced algorithms to expedite and enhance the drug discovery process. By merging principles of chemistry, biology, and informatics, CADD has reshaped the way new therapeutic agents are identified, optimized, and introduced to clinical practice [2]. Historically, drug discovery was a laborious and costly endeavor, heavily reliant on empirical trial and error. Researchers engaged in high-throughput screening (HTS), synthesizing and testing thousands of compounds in the laboratory to pinpoint potential drug candidates. However, this conventional approach was plagued by its limitations, including high costs, limited success rates, and ethical concerns regarding animal testing. The advent of CADD can be attributed to the exponential growth of computational power and the burgeoning availability of biological data [3]. This progression enabled scientists to simulate and analyze molecular interactions with unprecedented precision. The utilization of CADD tools, such as molecular modeling, virtual screening, and molecular dynamics (MD) simulations, allows researchers to predict how molecules will interact with specific biological targets, including proteins and nucleic acids [4]. These predictions are pivotal throughout various stages of drug discovery, from identifying promising lead compounds to optimizing their properties for clinical use. Moreover, CADD plays a critical role in the development of targeted therapies for intricate diseases like cancer. By comprehending the molecular mechanisms underpinning cancer, researchers can utilize computational techniques to design drugs that selectively target the dysregulated pathways driving tumor growth [5]. This personalized and precision medicine approach holds the promise of more effective cancer treatments with fewer side effects. In this comprehensive review paper, we will delve deeper into the principles and applications of CADD in the context of advancing our understanding and treatment of cancer. The paper will explore various computational tools and strategies employed in CADD, highlighting recent breakthroughs and challenges in the field. It aims to provide insights into the multidimensional role of CADD in cancer research and underscore its potential in shaping the future of cancer treatment.

Streamlined advancements in CADD techniques for cancer research

In the realm of cancer research and drug discovery, the advent of computer-aided drug discovery (CADD) techniques has been transformative. These modern approaches stand in stark contrast to the traditional methods employed in the past. Understanding this transition is essential to appreciate the full scope of CADD's role in cancer research. Traditionally, the methods employed in cancer research were marked by empiricism, serendipity, and labor-intensive testing. Drug discovery often relied on extensive screening of chemical compounds without a clear understanding of their potential efficacy. This approach was not only time-consuming but also costly, as it involved laborious experimentation, and success rates were often limited. Furthermore, ground-breaking cancer treatments were discovered serendipitously. For instance, the discovery of mechlorethamine, one of the first chemotherapeutic agents, occurred as an unintended consequence of nitrogen mustard gas exposure during World War II. This chance discovery prompted further exploration of its potential therapeutic use. In addition, pre-clinical testing of potential cancer treatments frequently involved labor-intensive and sometimes ethically contentious animal testing [6]. This limited the feasibility of HTS, making it challenging to test a large number of compounds systematically. The drug development process was often characterized by a "trial and error" approach. Researchers and pharmaceutical companies invested significant resources in developing and testing compounds, with no guarantee of success. This approach was inefficient and costly, often leading to the abandonment of promising compounds due to unforeseen toxicity or inefficacy.

In contrast, modern CADD techniques have revolutionized cancer research. These techniques leverage the power of computational analysis and predictive modeling. Researchers now employ "*in silico*" (computer-based) screening, which allows for the virtual assessment of the properties of thousands of compounds [7]. This virtual screening accelerates the initial phases of drug discovery, significantly reducing the time and resources required. CADD enables rational drug design by predicting how a compound will interact with its target at a molecular level. This precision allows for the tailored design of compounds with higher efficacy and reduced side effects. Techniques such as molecular docking use advanced algorithms to simulate how potential drug candidates interact with biological targets, providing invaluable insights into the binding affinity and orientation of molecules [8]. MDs simulations have also emerged as a powerful tool in modern cancer research. MD simulations enable the study of dynamic processes at the atomic and molecular levels. Researchers can observe how biomolecules and potential drug candidates interact over time, providing critical insights into drug binding, protein flexibility, and the behavior of biological systems. This dynamic approach complements the static predictions of molecular docking, offering a more comprehensive understanding of drug-target interactions.

The shift from traditional empirical methods to modern CADD techniques, including the use of MD simulations, represents a fundamental transformation in cancer research and drug discovery. CADD offers the advantage of speed, cost-effectiveness, and the ability to make informed decisions in the early stages of drug development [9]. These capabilities are pivotal in expediting the creation of innovative cancer treatments and reducing the uncertainties that have characterized cancer research for centuries.

Two-dimensional quantitative structure-activity relationship (2D QSAR)

2D QSAR is a computational approach in cheminformatics that predicts the biological or chemical activity of compounds based on their 2D molecular structures. It relies on molecular descriptors to represent structural features, uses activity data to build quantitative relationships through statistical and machine learning models, validates predictions, and offers interpretability to identify influential molecular features [10]. This method finds applications in drug discovery, environmental risk assessment, chemical design, and agrochemical development, offering a versatile tool for optimizing compounds and saving resources in research and development [11].

3D QSAR for molecular insights

While 2D QSAR is efficient for screening, 3D QSAR takes molecular modeling to a higher level of detail. By accounting for the three-dimensional spatial arrangement of atoms within molecules, it provides a realistic representation of molecular interactions. This depth of understanding is invaluable in optimizing lead compounds. 3D QSAR can elucidate how specific molecular features influence a compound's interaction with its biological target, often revealing subtle nuances that are missed by 2D QSAR [12]. Practical implementation researchers have adopted a seamless workflow that integrates 2D and 3D QSAR techniques to streamline drug discovery processes.

Combining 2D and 3D QSAR for enhanced drug discovery

The integration of both 2D and 3D QSAR techniques in drug discovery has gained prominence as it offers a comprehensive and synergistic approach. These methods are not mutually exclusive; rather, they complement each other, allowing researchers to harness their respective strengths [13]. Efficiency of 2D QSAR in screening: In the initial stages of drug discovery, the focus is often on rapidly assessing a large number of compounds. 2D QSAR models excel at this task. These models consider molecular descriptors such as partition coefficient (logP), electronegativity, and molecular weight. They are computationally less demanding, making them well-suited for HTS. When processing large compound libraries, 2D QSAR models can quickly prioritize potential drug candidates, saving both time and resources [14].

Bridging history and innovation

The roots of QSAR can be traced back to the 19th century when early researchers began to correlate physicochemical properties with biological activities [15]. Traditional QSAR approaches were predominantly 2D and primarily focused on simple linear regression models. However, the transition to 3D QSAR, which incorporates the three-dimensional spatial arrangement of atoms, brought about a paradigm shift in the field [16]. This transition became prominent in the 1980s with the introduction of comparative molecular field analysis. Subsequent developments, including comparative molecular similarity indices analysis and advancements in software tools such as SYBYL and MOE, led to more accurate predictions [17]. The 21st century witnessed the integration of 3D QSAR with molecular modeling techniques, allowing for in-depth insights into molecular flexibility and dynamics. The integration of 2D and 3D QSAR techniques has redefined the landscape of drug discovery. These methods, while distinct in their approaches, work together harmoniously, resulting in more efficient and effective drug development processes. As cancer research and drug design continue to evolve, this combination of 2D and 3D QSAR approaches, inspired by the historical quest for understanding molecular interactions, is poised to yield further ground-breaking discoveries, offering new hope to patients with complex and life-threatening conditions.

Drug discovery often begins with HTS to identify lead compounds. 2D QSAR models rapidly analyze the structural and chemical properties of these compounds, narrowing down the list of potential candidates. Lead optimization: The leads selected from HTS undergo further refinement. Here, 3D QSAR models come into play. Researchers build detailed 3D molecular structures and study their interactions with target proteins. This step allows for a comprehensive assessment of a compound's potential to bind and modulate the biological target. The integration of 2D and 3D QSAR techniques has significantly advanced cancer research. When applied to oncology, the hybrid approach has led to the discovery of highly effective cancer therapies [18]. Case in point: Imatinib for chronic myeloid leukemia (CML) treatment: Imatinib, a breakthrough therapy for CML, represents the successful synergy of 2D and 3D QSAR. By initially screening a wide range of compounds using 2D QSAR, researchers identified potential inhibitors. Subsequently, they used 3D QSAR to meticulously design Imatinib, ensuring optimal binding and inhibition of the BCR-ABL kinase, the target implicated in CML [19].

Molecular docking

Molecular docking is a pivotal technique in structural biology and drug discovery. It plays a central role in computer-aided drug design (CADD). It serves the purpose of predicting the orientation and binding affinity of one molecule to another, often involving a receptor or target molecule, typically a protein or nucleic acid. Before discussing its relevance in CADD, it's essential to understand the methodology.

Methodology of molecular docking

In molecular docking, a series of preparatory steps are followed to set the stage for the interaction between ligands and target molecules. Typically, water molecules, ions, and other non-essential components are removed from the receptor molecule to create a clean and simplified structure. Furthermore, hydrogen atoms are added, and sometimes the energy of the molecule is minimized to ensure stability.

Scoring functions play a critical role in analyzing and evaluating binding interactions during molecular docking. These scoring functions take into account various aspects of the interaction, such as steric hindrances, hydrogen bonding, electrostatic interactions, and more [20].

Multiple docking simulations are performed, generating a range of potential binding configurations. Subsequently, the results are thoroughly analyzed, and the most favorable interactions are identified. Notably, molecular docking is not a one-size-fits-all approach, and various software tools are available for these simulations.

Use of molecular docking in cancer research

Cancer, a complex and heterogeneous group of diseases, continues to pose a significant global health challenge. Molecular docking, with

Table 1: Software tools for molecular docking

Software name	Founding year	Developer	Place	Application
AutoDock	1982	Arthur J. Olson and colleagues	The Scripps Research Institute, USA	Predicts small molecule binding affinities and modes, which are critical for drug discovery, with respect to protein targets
AutoDock Vina	2010	Dr. Oleg Trott	The Scripps Research Institute, USA	Carries out molecular docking with efficiency and accuracy, supporting drug design and lead compound identification
DOCK	1982	Irwin D. Kuntz *et al*.	University of California, USA	Predicts ligand binding modes and interactions within protein binding sites, which helps with structure-based drug design
MOE	Late 1980s	Dr. Paul Czodrowski	Montreal, Canada	Provides a full range of molecular modeling services, such as structure-based design, drug discovery, and simulations
Glide	2004	Schrodinger	New York, USA	Used in structure-based drug design, which makes it possible to create new compounds with higher binding affinities
GOLD	1995	Cambridge Crystallographic Data Centre	Cambridge Crystallographic Data Centre, UK	Predicts the energetics and ligand binding positions within protein structures, which is useful for the development and improvement of drugs
PyRx	2008	Sargis Dallakyan and Ruben Abagyan	The Scripps Research Institute, USA	Enables lead identification by providing a user-friendly interface for molecular docking and virtual screening

its ability to predict molecular interactions and binding affinities, has emerged as a valuable tool in cancer research. Its applications in this field extend across various domains, providing insights that aid in understanding cancer mechanisms and developing novel therapeutic strategies [21].

Influence on radiation response

One area where molecular docking is making a profound impact in cancer research is in understanding radiation response. By assessing molecules that influence radiation response, such as DNA repair proteins, molecular docking can identify chemicals that increase the susceptibility of cancer cells to radiation therapy. This knowledge has the potential to enhance the effectiveness of radiation-based cancer treatments [22].

Personalized treatment recommendations

Cancer is inherently heterogeneous, with genetic variations contributing to the complexity of the disease. Molecular docking can be employed to evaluate how a patient's unique genetic profile influences the binding of drugs to target molecules. This personalized approach to cancer research can lead to more tailored treatment recommendations based on an individual's genetic characteristics [23].

Angiogenesis inhibition

In cancer treatment, angiogenesis, the growth of new blood vessels, is often inhibited to curb the supply of nutrients to tumors. Molecular docking plays a crucial role in identifying substances that can bind to angiogenesis-related proteins, potentially halting the development of tumor-induced blood vessels. This strategy offers a promising avenue for cancer therapy [24].

Drug repurposing

Drug repurposing is a cost-effective strategy to identify new therapeutic uses for existing drugs. Molecular docking assesses the ability of drugs to bind to cancer-related proteins, offering insights into the potential repurposing of FDA-approved medications for cancer treatment. This approach not only accelerates drug development but also conserves resources [25].

Understanding drug resistance

Drug resistance is a significant challenge in cancer treatment. Molecular docking is employed to mimic how medications interact with mutant or altered target proteins, shedding light on how cancer cells develop resistance to treatment. This knowledge informs the development of new therapeutics designed to overcome drug resistance [26].

Advancements in cancer drug discovery

With advancements in computational methods, the application of molecular docking has transformed cancer drug discovery. It serves as a powerful tool to identify new drug candidates, evaluate their interactions with cancer-related targets, and assess their potential efficacy. Researchers can now rapidly screen vast chemical libraries to pinpoint promising compounds for cancer therapy.

MDs simulation

MDs simulation is a computational technique employed across various scientific disciplines, including chemistry, biochemistry, and material science, to model and analyze the dynamic behavior of molecules and atoms over time [27]. This powerful method provides valuable insights into the dynamic properties and behaviors of molecular systems at the atomic and molecular levels, allowing scientists to understand how molecules interact with one another. It plays a significant role in unraveling the intricate world of complex systems, such as proteins, DNA, and materials, at the atomic and molecular scales.

The roots of MDs simulation can be traced back to the mid-20th century. In the 1950s and 1960s, pioneers such as Alder and Wainwright ventured into early computer simulations to study the motion of particles in simple gases. The framework of modern MDs simulations began taking shape in the 1970s when computational technology made significant strides. Researchers like Nobel laureate Martin Karplus, alongside his collaborators, developed essential algorithms and techniques for simulating molecular systems. These ground-breaking methodologies allowed scientists to model the interactions between atoms and molecules by calculating forces, positions, and velocities over short time intervals. The evolution of MDs simulation has been closely linked to advancements in computer hardware and algorithms. Force fields, which describe the interactions between atoms and molecules, have become more accurate and sophisticated. Present-day MDs simulations can effectively model complex biomolecules, such as proteins, nucleic acids, and biological membranes, as well as materials and chemical reactions [28]. The field continues to expand as computational resources become more powerful, enabling scientists to delve deeper into the dynamic behavior of various systems.

MDs simulation in CADD

MDs simulation is a potent tool in cancer research, offering deep insights into the behavior of biomolecules central to cancer development and therapeutic strategies. It plays a pivotal role in unraveling the intricacies of cancer-related proteins, notably kinases and receptors, facilitating the design of targeted therapies. By employing MD simulations, researchers can glean invaluable insights into the structural dynamics of cancer-

associated proteins, thus paving the way for the development of drugs tailored to specific cancer types. For instance, the study of the BRAF kinase in melanoma is a prime example of MD simulations guiding the development of vemurafenib, an effective drug for melanoma patients with specific BRAF mutations [29]. MD simulations are equally vital in elucidating mechanisms of drug resistance in cancer treatment, a fundamental aspect that leads to the design of second-generation drugs aimed at combating resistance [30]. A striking illustration is the influence of MD simulations in the development of tyrosine kinase inhibitors such as osimertinib for lung cancer. Furthermore, MD simulations play a crucial role in comprehending the interactions between potential anti-cancer drugs and their target proteins, thereby facilitating the discovery of novel drug candidates. In the realm of cancer immunotherapy, MD simulations have proven to be indispensable in understanding binding mechanisms and optimizing drug candidates. Moreover, MD simulations are extensively employed to model the interactions between drugs and membrane proteins, with direct implications for cancer therapy and drug delivery. This has been particularly significant in the context of HER2-positive breast cancer, where MD simulations have been used to explore how drug-loaded nanoparticles interact with HER2 receptors on cancer cells, enabling precise and targeted therapy [31]. The application of MDs simulation in cancer research is continually expanding, offering new and innovative avenues for comprehending cancer at the molecular level and advancing therapeutic approaches.

Applications of MDs simulations in cancer research

MDs simulations have emerged as a pivotal tool within the domain of CADD for investigating and understanding molecular interactions at an atomic level. In the context of cancer research, MD simulations offer an array of applications that significantly contribute to the identification, design, and optimization of potential anticancer agents. Some prominent uses of MD simulations in this field include:

1. Elucidating protein-ligand interactions: MD simulations enable the exploration of the dynamic behaviour and binding mechanisms of small molecule ligands with target proteins implicated in cancer pathways. These simulations provide insights into the stability of protein-ligand complexes, revealing crucial information about binding affinities, specific binding sites, and conformational changes, facilitating the rational design of novel drugs or inhibitors [32].
2. Prediction of drug resistance mechanisms: Cancer cells often develop resistance to chemotherapy drugs, posing a significant challenge in treatment. MD simulations aid in elucidating the molecular basis of drug resistance by analyzing the structural changes in drug-target complexes over time. Understanding these mechanisms allows researchers to devise strategies to overcome resistance and design more effective therapeutic agents.
3. Investigation of biomolecular dynamics: MD simulations offer the ability to study the dynamics and behavior of biomolecules such as proteins and nucleic acids associated with cancer progression. These simulations help in understanding protein folding, conformational changes, and interactions within complex biological systems, providing valuable insights into disease mechanisms and potential drug targets.
4. Optimization of drug candidates: By simulating the behavior of various drug candidates within the biological environment, MD simulations aid in refining molecular structures for enhanced efficacy, specificity, and reduced off-target effects. This iterative process assists in selecting promising lead compounds for further experimental validation.
5. Exploration of protein mutations and structural variations: Cancer often arises due to mutations in key proteins. MD simulations allow the exploration of how these mutations affect protein structure, dynamics, and interactions. This knowledge helps in designing personalized therapies targeting specific mutations or structural variations present in individual cancer cases [33].
6. Understanding drug delivery mechanisms: MD simulations contribute to understanding drug delivery mechanisms, such as interactions between nanoparticles or drug carriers and biological systems. This insight is crucial for developing targeted drug delivery systems that improve drug efficacy and minimize side effects in cancer treatment [34].

FUTURE PROSPECTS AND CHALLENGES

The integration of 3D QSAR and molecular docking in CADD has significantly advanced the field of pharmaceutical development, including cancer research. These computational techniques have played a crucial role in exploring molecular interactions and designing effective drugs with reduced side effects. Notable successes, such as the development of targeted cancer therapies like "Imatinib," underscore the pivotal role of these methods in drug discovery. However, as the field progresses, future prospects and challenges are apparent. MDs simulations have also emerged as a valuable tool in drug design, offering insights into the dynamic behaviour of molecules. Challenges persist, including computational demands and force field accuracy, which impact the reliability of these simulations.

Recent advancements, like the CHARMM general force field, have improved the accuracy of MDs for drug-like molecules, further enhancing CADD methodologies [35]. In addition, a diverse computational toolbox, which includes quantum mechanics and dynamics, is being explored to address the evolving needs of drug discovery. The future of computational cancer research and drug discovery holds immense promise, and a synergy of both MD and QSAR techniques will be instrumental. These methods, alongside advancements in multi-omics data integration and innovative drug screening, will continue to shape the field and bring us closer to personalized, effective cancer treatments. Interdisciplinary collaboration between computational scientists, biologists, and chemists remains vital for driving innovation and addressing the complexities of modern drug discovery.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

The conception and design of this study were initiated by Mr. Archit Sharma. Ketan Chandra, Saransh, Monika Ahlawat, and Sunidhi Chauhan contributed to data collection, literature review, and manuscript writing. All authors contributed to manuscript revisions and approved the final version.

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REFERENCES

1. Del Carmen Quintal Bojórquez N, Campos MR. Traditional and novel computer-aided drug design (CADD) approaches in the anticancer drug discovery process. Curr Cancer Drug Targets 2023;23:333-45.
2. Sliwoski G, Kothiwale S, Meiler J, Lowe EW Jr. Computational methods in drug discovery. Pharmacol Rev 2013;66:334-95.
3. Baig MH, Ahmad K, Rabbani G, Danishuddin M, Choi I. Computer aided drug design and its application to the development of potential drugs for neurodegenerative disorders. Curr Neuropharmacol 2018;16:740-8.
4. Yu W, MacKerell AD Jr. Computer-aided drug design methods. Methods Mol Biol 2017;1520:85-106.
5. Rahman MM, Islam MR, Rahman F, Rahaman MS, Khan MS, Abrar S, *et al*. Emerging promise of computational techniques in anti-cancer research: At a glance. Bioengineering (Basel) 2022;9:335.
6. Mak IW, Evaniew N, Ghert M. Lost in translation: Animal models and clinical trials in cancer treatment. Am J Transl Res 2014;6:114-8.
7. Ekins S, Mestres J, Testa B. *In silico* pharmacology for drug discovery: Methods for virtual ligand screening and profiling. Br J Pharmacol 2007;152:9-20.
8. Torres PH, Sodero AC, Jofily P, Silva-Jr FP. Key topics in molecular docking for drug design. Int J Mol Sci 2019;20:4574.
9. Dara S, Dhamercherla S, Jadav SS, Babu CM, Ahsan MJ. Machine

learning in drug discovery: A review. Artif Intell Rev 2022;55:1947-99.
10. Niazi SK, Mariam Z. Recent advances in machine-learning-based chemoinformatics: A comprehensive review. Int J Mol Sci 2023;24:11488.
11. Batool M, Ahmad B, Choi S. A structure-based drug discovery paradigm. Int J Mol Sci 2019;20:2783.
12. Rasulev B. Recent developments in 3D QSAR and molecular docking studies of organic and nanostructures. In: Handbook of Computational Chemistry. Vol. 9. Berlin, Germany: Springer International Publishing; 2016. p. 2133-61.
13. Singh V, Kumar A, Gupta S. Mental health prevention and promotion-a narrative review. Front Psychiatry 2022;13:898009.
14. Szymański P, Markowicz M, Mikiciuk-Olasik E. Adaptation of high-throughput screening in drug discovery-toxicological screening tests. Int J Mol Sci 2012;13:427-52.
15. Debnath AK. Quantitative structure-activity relationship (QSAR) paradigm--Hansch era to new millennium. Mini Rev Med Chem 2001;1:187-95.
16. Cherkasov A, Muratov EN, Fourches D, Varnek A, Baskin II, Cronin M, *et al*. QSAR modeling: Where have you been? Where are you going to? J Med Chem 2014;57:4977-5010.
17. Zhao X, Chen M, Huang B, Ji H, Yuan M. Comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA) studies on α(1A)-adrenergic receptor antagonists based on pharmacophore molecular alignment. Int J Mol Sci 2011;12:7022-37.
18. Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, *et al*. New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Med 2021;9:20503121211034366. doi: 10.1177/20503121211034366
19. Iqbal N, Iqbal N. Imatinib: A breakthrough of targeted therapy in cancer. Chemother Res Pract 2014;2014:357027.
20. Meng XY, Zhang HX, Mezei M, Cui M. Molecular docking: A powerful approach for structure-based drug discovery. Curr Comput Aided Drug Des 2011;7:146-57.
21. Arjmand B, Hamidpour SK, Alavi-Moghadam S, Yavari H, Shahbazbadr A, Tavirani MR, *et al*. Molecular docking as a therapeutic approach for targeting cancer stem cell metabolic processes. Front Pharmacol 2022;13:768556. Erratum in: Front Pharmacol 2022;13:892656.
22. Bravatà V, Cava C, Minafra L, Cammarata FP, Russo G, Gilardi MC, *et al*. Radiation-induced gene expression changes in high and low grade breast cancer cell types. Int J Mol Sci 2018;19:1084.
23. Urbach D, Lupien M, Karagas MR, Moore JH. Cancer heterogeneity: Origins and implications for genetic association studies. Trends Genet 2012;28:538-43.
24. Rajabi M, Mousa SA. The role of angiogenesis in cancer treatment. Biomedicines 2017;5:34.
25. Fu L, Jin W, Zhang J, Zhu L, Lu J, Zhen Y, *et al*. Repurposing non-oncology small-molecule drugs to improve cancer therapy: Current situation and future directions. Acta Pharm Sin B 2022;12:532-57.
26. Mansoori B, Mohammadi A, Davudian S, Shirjang S, Baradaran B. The different mechanisms of cancer drug resistance: A brief review. Adv Pharm Bull 2017;7:339-48.
27. Hollingsworth SA, Dror RO. Molecular dynamics simulation for all. Neuron 2018;99:1129-43.
28. Hospital A, Goñi JR, Orozco M, Gelpí JL. Molecular dynamics simulations: Advances and applications. Adv Appl Bioinform Chem 2015;8:37-47.
29. Castellani G, Buccarelli M, Arasi MB, Rossi S, Pisanu ME, Bellenghi M, *et al*. BRAF mutations in melanoma: Biological aspects, therapeutic implications, and circulating biomarkers. Cancers (Basel) 2023;15:4026.
30. Emran TB, Shahriar A, Mahmud AR, Rahman T, Abir MH, Siddiquee MF, *et al*. Multidrug resistance in cancer: Understanding molecular mechanisms, immunoprevention and therapeutic approaches. Front Oncol 2022;12:891652.
31. Sitia L, Sevieri M, Signati L, Bonizzi A, Chesi A, Mainini F, *et al*. HER-2-targeted nanoparticles for breast cancer diagnosis and treatment. Cancers (Basel) 2022;14:2424.
32. Agu PC, Afiukwa CA, Orji OU, Ezeh EM, Ofoke IH, Ogbu CO, *et al*. Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. Sci Rep 2023;13:13398.
33. Pandurangan AP, Blundell TL. Prediction of impacts of mutations on protein structure and interactions: SDM, a statistical approach, and mCSM, using machine learning. Protein Sci 2020;29:247-57.
34. Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, *et al*. Advances in drug delivery systems, challenges and future directions. Heliyon 2023;9:e17488.
35. Zhu X, Lopes PE, Mackerell AD Jr. Recent developments and applications of the CHARMM force fields. Wiley Interdiscip Rev Comput Mol Sci 2012;2:167-85.