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Review Of Natural Compounds And Medicinal Chemistry Approaches In Drug Development

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Abstract

The increasing prevalence of degenerative and infectious diseases has encouraged the development of more effective, selective, and safer therapeutic agents. Natural compounds and medicinal chemistry approaches have demonstrated considerable potential in modern drug discovery due to their diverse pharmacological activities and structural complexity. This study aims to review the role of bioactive natural compounds and computational approaches in contemporary drug development. The method employed was a literature review based on recent scientific publications discussing medicinal chemistry, molecular docking, quantitative structure–activity relationship analysis, artificial intelligence-assisted drug design, and nanoformulation strategies. The findings indicate that several natural compounds, particularly flavonoids and quercetin, exhibit promising anticancer, antidiabetic, antioxidant, and antibacterial activities through interactions with various biological targets. Computational approaches such as molecular docking, virtual screening, predictive modeling, and deep QSAR were shown to improve the efficiency of lead identification and molecular optimization. Furthermore, nanoformulation systems contribute to enhancing bioavailability, molecular stability, and therapeutic effectiveness of bioactive compounds. Despite these advantages, challenges including compound complexity, ADMET limitations, and the necessity for experimental validation remain important considerations in drug development. In conclusion, the integration of natural compounds, medicinal chemistry, and computational technologies provides significant opportunities for accelerating and optimizing modern drug discovery and development.

Keywords: Natural compounds, Medicinal chemistry, Molecular docking, Deep QSAR, Drug development.

INTRODUCTION

The development of degenerative and infectious diseases has increased significantly in recent decades and poses a major challenge to global health. Diseases such as cancer, diabetes mellitus, and infections caused by resistant bacteria require more effective, safe, and sustainable therapeutic approaches. Currently available conventional therapies often have limitations, such as high side effects, high treatment costs, and the widespread emergence of drug resistance. This situation drives the need to explore alternative sources, particularly from natural compounds with biological activity, supported by technological developments in medicinal chemistry.

Bioactive compounds derived from plants have long been known to possess various pharmacological activities, such as antioxidant, anticancer, antidiabetic, and antibacterial properties. Compounds such as flavonoids, alkaloids, and terpenoids have become a major focus of research due to their ability to interact with specific biological targets. Furthermore, the use of computational technology in the form of in silico approaches, such as molecular docking and quantitative structure-activity relationship (QSAR), enables the drug discovery process to be more efficient, rapid, and economical. This approach can accurately predict interactions between compounds and protein targets before laboratory testing, thereby reducing the risk of failure during the development stage.

Previous research has explored the potential of natural compounds in various therapeutic aspects, using both experimental and computational approaches. Several studies have shown that flavonoids have a high affinity for enzymes and receptors involved in metabolic diseases, while other compounds have demonstrated anticancer activity through mechanisms that inhibit cell proliferation. Furthermore, the development of nanoformulation technology has contributed to increasing the bioavailability and effectiveness of drug compounds, particularly those with limited solubility and stability. Furthermore, medicinal chemistry approaches continue to evolve to address antibiotic resistance through the design of new compounds that are more selective toward bacterial targets.

Although numerous studies have been conducted, most still focus on a single approach or a specific type of compound, thus not providing a comprehensive picture of the integration of natural compounds, in silico approaches, and medicinal chemistry strategies in drug development. Therefore, a study that integrates these various approaches is needed to provide a more comprehensive understanding. The novelty of this paper lies in the effort to combine various research findings related to the potential of natural compounds with computational technology and medicinal chemistry strategies as a unified whole in the development of modern therapies.

Based on this background, the purpose of this paper is to comprehensively review the potential of bioactive compounds, the role of in silico approaches, and the contribution of medicinal chemistry to drug development. It is hoped that the results of this study will provide a more integrated scientific picture and serve as a basis for further research in the pharmaceutical and healthcare fields.

RESEARCH METHODS

Tools and materials

This research uses a literature study approach, utilizing hardware in the form of a laptop with software that includes a word processing application (Microsoft Word), reference management software such as Mendeley or Zotero, and an internet browser to access scientific databases. Data sources were obtained from various scientific journals indexed in trusted databases such as Google Scholar, PubMed, Scopus, and ScienceDirect. The materials used are scientific articles relevant to the research topic, particularly those discussing bioactive compounds, in silico approaches, molecular docking, quantitative structure-activity relationships (QSAR), nanoformulations, and medicinal chemistry in drug development. The selected articles are publications within the most recent timeframe to ensure the freshness and relevance of the data.

Research Procedures

The research was conducted through several systematic stages. The first stage was topic determination and problem formulation, focusing on the potential of natural compounds and medicinal chemistry approaches in drug development. The second stage was a literature search using relevant keywords such as "natural compounds," "medicinal chemistry," "in silico," "molecular docking," and "drug development" in scientific databases. The third stage was an article selection process based on inclusion and exclusion criteria, where selected articles must be relevant to the topic, have clear methods, and come from credible scientific journals. The fourth stage was data extraction, namely the collection of important information from each article including research objectives, methods, results, and conclusions. The fifth stage was data analysis and synthesis by comparing and integrating the results of various studies to obtain a comprehensive picture. The final stage was the preparation of a report in the form of a systematic scientific narrative in accordance with the journal writing structure.

Data analysis

Data analysis was conducted using a qualitative descriptive approach by reviewing, comparing, and interpreting findings from various literature sources. The collected data were grouped by theme, such as the type of bioactive compound, the in silico method used, and the role of medicinal chemistry in drug development. Interpretation was then performed to identify patterns, relationships, and the strengths and limitations of each study. The results of the analysis are presented in the form of descriptive descriptions that illustrate the interrelationships between the studies, resulting in comprehensive conclusions that support the objectives of the paper.

RESULTS AND DISCUSSION

Computer-Aided Drug Design (CADD) has emerged as one of the most significant computational approaches in modern medicinal chemistry due to its ability to accelerate and optimize the drug discovery process. CADD integrates computational chemistry, molecular modeling, bioinformatics, and simulation techniques to identify, design, and evaluate potential therapeutic compounds through in silico analysis prior to experimental validation. The increasing complexity of biological targets and the demand for more efficient drug development strategies have encouraged the integration of computational methods into conventional pharmaceutical research. Compared with traditional trial-and-error approaches, CADD provides a more rational and cost-effective strategy for identifying promising lead compounds while reducing experimental workload, development time, and financial costs associated with drug discovery processes (Patel & Sachdeva, 2025).

In general, CADD is divided into two principal approaches, namely Structure-Based Drug Design (SBDD) and Ligand-Based Drug Design (LBDD). Structure-Based Drug Design is applied when the three-dimensional structure of a biological target such as a protein, receptor, or enzyme is available. This approach utilizes structural information obtained through techniques including X-ray crystallography, nuclear magnetic resonance, and cryo-electron microscopy to predict molecular interactions between ligands and target proteins. Several computational techniques commonly employed in SBDD include molecular docking, molecular dynamics simulation, and structure-based virtual screening. These methods enable researchers to evaluate binding affinity, ligand orientation, and molecular stability within the active site of target proteins, thereby supporting rational drug optimization and lead identification (Thakare et al., 2026).

Conversely, Ligand-Based Drug Design is utilized when structural information regarding the biological target is unavailable or limited. Instead of relying on receptor structures, LBDD uses information derived from previously identified active compounds to predict biological activity and optimize new molecular candidates with similar pharmacological properties. Common techniques included within this approach are Quantitative Structure–Activity Relationship (QSAR), pharmacophore modeling, similarity searching, and ligand-based virtual screening. Through the analysis of physicochemical properties and molecular descriptors, LBDD facilitates the prediction of compound activity, toxicity, and drug-likeness prior to laboratory testing. This approach has become increasingly important in medicinal chemistry because it supports rapid lead optimization and enables the efficient screening of extensive chemical libraries (Tropsha et al., n.d.).

The application of computational chemistry within CADD provides several important advantages in modern drug development. Computational approaches allow researchers to perform virtual screening of thousands of compounds efficiently, predict ligand–protein interactions, evaluate pharmacokinetic profiles through ADMET analysis, and optimize lead compounds with greater precision. Molecular docking, one of the most widely applied computational methods, enables the prediction of binding modes and interaction energies between ligands and biological receptors, thereby assisting researchers in identifying compounds with favorable therapeutic potential. Additionally, the integration of molecular modeling and pharmacophore analysis supports the understanding of structure–activity relationships that are essential for rational drug design.

Recent advancements in artificial intelligence and deep learning have further expanded the capabilities of CADD in pharmaceutical research. The emergence of deep QSAR approaches has enabled the analysis of large molecular datasets with improved predictive accuracy and enhanced virtual screening performance. Machine learning algorithms are increasingly integrated into molecular modeling, binding affinity prediction, and lead optimization processes to accelerate the identification of novel bioactive compounds with desirable pharmacological characteristics. These developments demonstrate that computational methods have become indispensable tools in contemporary medicinal chemistry and continue to contribute substantially to innovation in drug discovery and development.

Furthermore, the integration of CADD with natural product research has attracted considerable attention in recent years because natural compounds provide structurally diverse scaffolds with broad

pharmacological activities. In silico approaches facilitate the exploration of bioactive compounds derived from medicinal plants and support the identification of potential therapeutic agents for various diseases, including cancer, diabetes mellitus, inflammatory disorders, and infectious diseases. Nevertheless, several challenges remain in natural product-based drug discovery, such as compound complexity, limited biological validation, and variability in phytochemical composition. Therefore, the combination of computational prediction with experimental verification remains essential to ensure the reliability and applicability of candidate compounds in pharmaceutical development (Simoben et al., 2023).

The results of the literature review indicate that various approaches in medicinal chemistry and the use of natural compounds have made significant contributions to the development of modern therapies. Based on the analysis of the reviewed journals, it was found that the in silico approach is the most widely used method in the early stages of drug discovery. Studies on the plant Ageratum conyzoides L. showed that several compounds such as kaempferol and stigmasterol have low binding energy to breast cancer receptors, indicating the potential for strong anticancer activity through stable molecular interactions.(Amin, Abidin, et al., 2024)This finding is in line with other studies which state that flavonoid compounds such as quercetin have a high affinity for cancer target proteins such as HER-2 and Sirtuin 1, thus being able to inhibit cancer cell proliferation.(Amin, Wihdatunnisa, et al., 2024).

In addition to anticancer activity, the potential of natural compounds is also evident in their antioxidant activity. Purple sweet potato extract exhibits high antioxidant activity, particularly under low-acidity solvent conditions (pH 1.5), resulting in a higher IC50 value than under other conditions.(Nurzaman et al., 2025)This indicates that extraction conditions significantly influence the biological activity of compounds, particularly anthocyanin content, which is pH-sensitive. This antioxidant activity plays a crucial role in preventing oxidative stress, a major factor in the development of degenerative diseases.

Medicinal chemistry approaches are also widely used to address antibiotic resistance. Studies have shown that resistance mechanisms in Gram-positive and Gram-negative bacteria can be overcome by developing derivative compounds such as imidazoles and thiazoles that can target specific bacterial resistance mechanisms.(Amin & Nabila, nd)This demonstrates that target-based molecular design is an important strategy in addressing increasing antimicrobial resistance. Furthermore, molecular structure optimization through modern synthetic and computational approaches has also been shown to increase the efficiency and selectivity of bioactive compounds.(Bioactive et al., 2025).

In the context of metabolic diseases, in silico approaches to flavonoid compounds have shown promise as antidiabetic agents. Compounds such as rutin, quercetin, and luteolin have high affinity for the enzymes α-glucosidase and α-amylase, as well as the PPARγ receptor, which plays a role in regulating glucose metabolism.(Amin, Setiawati, et al., 2025)This shows that natural compounds not only have a single activity, but also have multi-target properties that are beneficial in the therapy of complex diseases.

Molecular docking has become one of the most widely utilized computational techniques in modern medicinal chemistry due to its capability to predict molecular interactions between ligands and biological targets efficiently. This approach plays an important role in structure-based drug design by simulating the binding orientation and interaction patterns of small molecules within the active site of target proteins. Through molecular docking analysis, researchers are able to estimate binding affinity, identify amino acid interactions, and evaluate the stability of ligand–receptor complexes prior to experimental testing. Consequently, molecular docking significantly contributes to accelerating early-stage drug discovery while reducing laboratory costs and experimental complexity (Nadaf et al., 2023).

The docking process generally involves two fundamental stages, namely ligand conformational searching and binding affinity evaluation. During conformational searching, the computational system explores various possible orientations and positions of the ligand within the

binding pocket of the target protein. The generated ligand poses are subsequently evaluated using scoring functions to determine the most favorable interaction patterns. Scoring functions are mathematical algorithms used to estimate the strength and stability of ligand–protein interactions based on several physicochemical parameters, including hydrogen bonding, hydrophobic interactions, electrostatic forces, and van der Waals interactions. The scoring results are commonly represented as binding energy values, where lower binding energy indicates stronger molecular affinity and more stable interactions between ligands and receptors (Patel & Sachdeva, 2025).

Several categories of scoring functions are currently applied in molecular docking studies, including force-field-based, empirical, knowledge-based, and machine learning-based scoring methods. Force-field-based scoring functions estimate molecular interactions using molecular mechanics calculations, whereas empirical scoring relies on regression models generated from experimental datasets. Knowledge-based scoring methods utilize statistical potentials derived from known protein–ligand complexes, while machine learning-based approaches apply artificial intelligence algorithms to improve binding affinity prediction accuracy. The continuous development of scoring methodologies has enhanced the reliability and efficiency of computational drug screening in medicinal chemistry research.

Another important parameter frequently used in molecular docking validation is Root Mean Square Deviation (RMSD). RMSD represents the degree of similarity between the predicted ligand conformation and the experimentally observed ligand structure. In docking studies, RMSD values below 2 Å are generally considered acceptable and indicate reliable docking accuracy. This validation parameter is crucial to ensure that the docking protocol can accurately reproduce ligand positioning within the active site of the target protein. Several studies involving flavonoid compounds as antidiabetic agents demonstrated RMSD values below 2 Å, indicating good docking reliability and stable ligand–protein interactions during computational analysis (Amin, Setiawati, et al., 2025).

In addition to docking analysis, virtual screening has emerged as an essential computational approach in modern drug discovery. Virtual screening enables rapid evaluation of extensive molecular libraries to identify compounds with potential biological activity against specific therapeutic targets. This technique combines molecular docking, pharmacophore modeling, QSAR analysis, and database screening to prioritize promising compounds prior to experimental validation. Virtual screening significantly improves the efficiency of lead discovery because thousands of compounds can be analyzed computationally within a relatively short period of time compared with conventional experimental screening methods (Tropsha et al., n.d.).

The application of molecular docking and computational approaches has demonstrated broad utility in evaluating natural compounds with pharmacological potential. Various flavonoids, alkaloids, terpenoids, and polyphenolic compounds have shown favorable binding affinity toward biological targets associated with cancer, diabetes mellitus, inflammation, and infectious diseases. For example, flavonoid compounds such as quercetin, rutin, luteolin, kaempferol, and vitexin exhibited strong interactions with α-glucosidase, α-amylase, and PPARγ receptors in antidiabetic studies, indicating their potential as natural therapeutic candidates. Similarly, several phytochemical compounds demonstrated promising interactions with cancer-related receptors such as ER-α, EGFR, COX-2, and p53 through molecular docking analysis (Bioaktif & Kanker, 2025).

Despite its advantages, molecular docking still possesses several limitations, particularly regarding protein flexibility, solvent effects, and prediction accuracy under complex biological conditions. Therefore, computational predictions should be complemented with molecular dynamics simulations, ADMET analysis, and experimental validation to improve the reliability of candidate compound evaluation. Nevertheless, molecular docking remains one of the most valuable computational tools in medicinal chemistry due to its efficiency, accessibility, and ability to support rational drug design in modern pharmaceutical research.

Other computational approaches such as QSAR have also made important contributions to drug design. QSAR models for quinoline compounds have shown that physicochemical parameters such as atomic charge and orbital energy play a role in determining antimalarial activity.(Amin,

Oktaviani, et al., 2025). Thus, this approach is able to predict the biological activity of compounds quantitatively before conducting experimental tests, thereby increasing efficiency in the drug development process.

The development of artificial intelligence (AI) has significantly transformed the landscape of modern medicinal chemistry and pharmaceutical research. Artificial intelligence enables computational systems to process extensive molecular datasets, recognize complex biological patterns, and generate predictive models with higher efficiency and accuracy compared with conventional computational methods. In drug discovery, AI has increasingly been integrated into Computer-Aided Drug Design (CADD) to facilitate lead identification, molecular optimization, virtual screening, and pharmacokinetic prediction. The integration of AI technologies into medicinal chemistry contributes to reducing development costs and accelerating the identification of promising therapeutic compounds while improving the overall efficiency of the drug discovery process (*Aman Thakur, Vineet Mehta, Priyanka Nagu and Kiran Goutam Computer-Aided Drug Design*, n.d.).

Machine learning, as a major branch of artificial intelligence, has become an essential computational approach in modern drug design due to its ability to learn from molecular datasets and identify relationships between chemical structures and biological activity. Machine learning algorithms are widely applied in ligand classification, toxicity prediction, molecular property analysis, and ADMET evaluation. Through pattern recognition and data-driven analysis, machine learning supports the identification of compounds with favorable pharmacological profiles more efficiently than traditional screening approaches. Additionally, machine learning enables the analysis of large chemical libraries and assists researchers in prioritizing compounds with high therapeutic potential before experimental validation is conducted.

One of the most important developments in computational medicinal chemistry is the emergence of deep QSAR (Deep Quantitative Structure–Activity Relationship). Conventional QSAR models generally rely on manually selected molecular descriptors and statistical analyses to correlate chemical structures with biological activity. However, deep QSAR integrates deep learning architectures capable of automatically extracting complex molecular features from large datasets without extensive manual feature engineering. This approach improves predictive accuracy and enables the identification of hidden molecular relationships that are difficult to detect using traditional QSAR methodologies. Consequently, deep QSAR has become increasingly important in lead optimization, molecular activity prediction, and virtual screening within modern pharmaceutical research.

Predictive modeling also plays a crucial role in AI-assisted drug discovery because it allows researchers to estimate the biological activity, toxicity, pharmacokinetic properties, and therapeutic potential of chemical compounds computationally prior to laboratory testing. Predictive modeling supports rational drug design by reducing unnecessary experimental procedures and improving the efficiency of candidate compound selection. In addition, predictive computational systems are capable of evaluating molecular interactions, binding affinity, and drug-likeness simultaneously, thereby accelerating the lead discovery and optimization process. Recent advances in artificial intelligence have further enhanced the performance of predictive modeling through the application of neural networks, automated molecular learning, and large-scale data analysis.

The integration of artificial intelligence with natural product research has attracted increasing scientific attention in recent years because natural compounds possess highly diverse chemical structures and broad pharmacological potential. However, the structural complexity and variability of natural compounds often create challenges in conventional drug screening methods. AI-assisted computational approaches help overcome these limitations through automated molecular analysis, rapid virtual screening, and more efficient prediction of biological activity from phytochemical datasets. Therefore, artificial intelligence and deep QSAR are expected to become increasingly important tools in future medicinal chemistry research and modern drug development strategies.

Furthermore, the development of nanoformulation technology provides a solution to the limited bioavailability of drug compounds. Nanoformulation has been shown to increase the solubility

and therapeutic effectiveness of compounds, as well as improve drug targeting to specific tissues such as cancer cells.(Amin, 2025a)This strengthens the role of technology in improving the performance of bioactive compounds that previously had pharmacokinetic limitations.

Despite the substantial progress achieved through computational medicinal chemistry and in silico drug discovery, several important limitations remain in the application of these approaches for pharmaceutical development. Computational methods such as molecular docking, QSAR, virtual screening, and predictive modeling provide valuable preliminary information regarding ligand–protein interactions and pharmacological potential; however, these predictions do not always fully represent complex biological conditions in vivo. Factors such as protein flexibility, solvent effects, molecular dynamics, and biological pathway interactions may influence the accuracy of computational predictions and lead to discrepancies between in silico outcomes and experimental findings. Consequently, computational approaches should be considered supportive tools rather than definitive replacements for laboratory and clinical investigations (Nivatya et al., 2025).

One of the major challenges in modern drug discovery is the necessity for comprehensive experimental validation following computational prediction. Although molecular docking and virtual screening can rapidly identify compounds with favorable binding affinity and pharmacological potential, biological activity must still be confirmed through in vitro and in vivo studies. Experimental validation is essential to evaluate compound efficacy, toxicity, selectivity, metabolic stability, and therapeutic safety under physiological conditions. Several compounds that demonstrate strong docking scores computationally may fail during experimental stages due to poor bioavailability, unstable interactions, or unexpected biological effects. Therefore, the integration of computational analysis with laboratory experimentation remains fundamental in rational drug development (Patel & Sachdeva, 2025).

Another important issue in computational drug discovery involves ADMET prediction, which includes absorption, distribution, metabolism, excretion, and toxicity properties of candidate compounds. Although modern computational models can estimate pharmacokinetic and toxicity profiles effectively, the accuracy of ADMET prediction is still influenced by the quality of datasets, algorithm limitations, and molecular complexity. Some compounds with promising biological activity may exhibit poor oral bioavailability, rapid metabolic degradation, or high toxicity risk, thereby limiting their therapeutic applicability. Consequently, the optimization of pharmacokinetic properties remains a major challenge in medicinal chemistry and drug development, particularly for natural bioactive compounds (Amin, Setiawati, et al., 2025).

Natural product-based drug discovery also presents substantial scientific challenges due to the structural diversity and complexity of phytochemical compounds. Natural products often contain highly complex molecular scaffolds, stereochemical variations, and multiple active constituents that complicate molecular characterization and standardization processes. In addition, variability in phytochemical composition caused by environmental conditions, extraction methods, and plant origin may affect the reproducibility and consistency of biological activity. These factors create additional difficulties in compound isolation, molecular optimization, and large-scale pharmaceutical production. Nevertheless, natural compounds remain highly valuable sources of therapeutic agents because of their broad pharmacological activities and structural uniqueness.

Recent advancements in nanoformulation technology have provided promising strategies to overcome several pharmacokinetic limitations associated with natural compounds. Nano-based drug delivery systems such as liposomes, phytosomes, transferosomes, and nanoparticles have demonstrated the ability to improve solubility, stability, targeted delivery, and bioavailability of herbal bioactive compounds. These systems also enhance therapeutic efficiency by protecting active compounds from degradation and improving drug absorption within biological systems. Consequently, nanoformulation approaches are increasingly considered important components in future medicinal chemistry and pharmaceutical development, particularly for natural product-based therapies (Journal & Pharmaceutical, 2025).

Future perspectives in medicinal chemistry are expected to focus on the integration of artificial intelligence, machine learning, deep QSAR, molecular dynamics simulation, and advanced nanoformulation systems to improve the efficiency and accuracy of drug discovery. The combination of computational prediction with experimental validation will continue to play a critical role in identifying safer and more effective therapeutic compounds. Furthermore, the growing availability of molecular databases, high-throughput screening technologies, and AI-assisted predictive systems is expected to accelerate the development of personalized medicine and targeted therapies for complex diseases such as cancer, diabetes mellitus, and infectious disorders (Tropsha et al., n.d.).

Molecular studies also show that molecular dynamics modeling and simulations are capable of identifying compounds with high interaction stability with biological targets. Compounds with low binding energies and stable RMSD values indicate potential as effective drug candidates.(Amin, 2025b)This approach speeds up the compound screening process and reduces reliance on time-consuming and expensive experimental methods.

Studies of other natural ingredients, such as turmeric essential oil, have shown a wide range of pharmacological activities, including anti-inflammatory, antimicrobial, and anticancer activities. Turmerone compounds in turmeric are known to induce apoptosis of cancer cells through specific pathways, making them a potential natural therapeutic agent.(Amin & Nurkholidatunnisa, 2025). In addition, fermented products such as Monascus purpureus also exhibit diverse pharmacological activities, including antidyslipidemic and anti-inflammatory effects, although their use requires attention to potential side effects such as kidney disorders.(Shaleha et al., 2025).

Overall, the results of this study demonstrate that the integration of natural compounds, computational approaches, and modern formulation technologies offers significant opportunities in drug development. This approach not only improves the efficiency of drug discovery but also enables the development of more specific, safe, and effective therapies. However, most research is still at the in silico and in vitro stages, requiring further validation through in vivo and clinical trials to ensure their safety and effectiveness in clinical use.

Table1. Summary of the Results of Several Research Studies

No	Research Topics	Method	Key Results	Potential
1	Babandotan	Molecular Docking	High affinity to cancer receptors	Anticancer
2	Quercetin	Docking	Stable binding of HER-2	Anticancer
3	Purple sweet potato	DPPH	IC50 is low at acidic pH	Antioxidants
4	Flavonoid	In silico	Diabetes enzyme targets	Antidiabetic
5	Quinoline	QSAR	Accurate prediction model	Antimalarial
6	Antibiotic resistance	Literature	Effective derivative compounds	Antibacterial
7	Nanoformulation	Experimental	Increased bioavailability	Cancer therapy
8	Molecular studies	Simulation	High stability	Drug candidate
9	Turmeric	Literature	Multi-pharmacological activity	Herbal therapy
10	Red yeast rice	Review	Lipid & anti-inflammatory effects	Metabolic therapy
11	Modern medicinal chemistry	Review	Synthesis efficiency increased	Drug development

CONCLUSION

The findings of this review demonstrate that the integration of natural compounds, medicinal chemistry, and computational technologies has contributed significantly to modern drug discovery and development. Computational approaches such as molecular docking, QSAR, virtual screening, and artificial intelligence-assisted predictive modeling have improved the efficiency of identifying and optimizing potential therapeutic compounds. In addition, natural bioactive compounds, particularly flavonoids and other phytochemicals, exhibit promising pharmacological activities against various diseases, including cancer, diabetes mellitus, and microbial infections. The application of nanoformulation systems further enhances the bioavailability, stability, and therapeutic performance of these compounds, thereby supporting the development of more effective drug delivery strategies. Overall, the integration of computational methods and natural product research provides a rational and efficient framework for modern medicinal chemistry and pharmaceutical innovation.

Nevertheless, several important challenges remain in the implementation of computational drug discovery and natural product-based therapeutics. Limitations related to predictive accuracy, ADMET evaluation, compound complexity, and biological variability indicate that computational findings must still be validated through comprehensive in vitro and in vivo studies. Future research should focus on integrating artificial intelligence, deep QSAR, molecular dynamics simulation, and advanced nanoformulation technologies with experimental validation to improve the reliability and applicability of candidate compounds. Furthermore, interdisciplinary collaboration among pharmaceutical sciences, chemistry, biotechnology, and computational biology will be essential to support the development of safer, more selective, and sustainable therapeutic agents in the future.

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