Indian Journal of Pharmaceutical Chemistry and Analytical Techniques (IJPCAT)
ISSN: 3049-3765 | Vol. 02, Issue-02, March-April, 2026, pp. 41-54
https://ijpcat.com/1

Natural Products as Lead Compounds in Medicinal Chemistry: Opportunities and Challenges

Pratiksha Bhaiyyasaheb Patil[1], Konda V. V. S. Krishna[2], Minakshi Ajamal Jadhav[3], Prajakta Jadhav[4], Hirkani Yuvraj Pawar[5], Mukesh Kumar Meena[6*]

[1]D.B. Patil College of Pharmacy, Parola, Kajgaon Road, Parola, Jalgaon, Pin: 425111
[2]Government Polytechnic for Women, Gujarathipeta, Srikakulam, Andhra Pradesh, India, Pin: 532005
[3]St. Wilfred Institute of Pharmacy, Panvel, Pin: 410206, Maharashtra, India
[4]AIMS College of Pharmacy, Dombivli, Maharashtra, Pin -421204, India
[5]Bharathi Vidyapeeth College of Pharmacy, Palus, Maharashtra, India
[6]Department of Pharmaceutical Sciences, Mohanlal Sukhadia University, Udaipur, Rajasthan 313001- India

*Corresponding Author E-mail: **mukesh_meena27@mlsu.ac.in**

Abstract:

Natural products have attracted significant attention as the important sources of lead compounds in medicinal chemistry by virtue of their extraordinary structural diversity, biological specificity, and capacity to react with a variety of molecular targets. The review focuses on evidence obtained solely based on animal-based preclinical studies to evaluate the therapeutic potential, mechanisms of action, pharmacokinetic behavior and safety profiles of natural compounds. Results in the animal models indicate that natural products have great pharmacological activities, such as anticancer effects via the induction of apoptosis and angiogenesis inhibition, anti-inflammatory effects via suppressing pro-inflammatory cytokines and oxidative stress, antimicrobial effects against resistant pathogens, and neuroprotective effects via the regulation of neuronal signaling and inhibition of toxic Although these are encouraging results, there are various limitations that are encountered, including low bioavailability, low solubility, rapid metabolism and variability in natural sources, which collectively limit their clinical uses. Moreover, physiological differences between animal models and humans also create translational challenges to predictability of preclinical findings. To overcome such limitations, new developments in drug delivery systems, such as nanoparticle-based drug delivery systems, liposomes, and polymeric formulations, as well as structural changes, such as prodrug development, have demonstrated the possibility of improving stability and therapeutic effectiveness. In general, although natural products still have enormous potential as lead compounds, pharmacokinetic and translational challenges are critical to their effective transition into clinically useful drugs.

Keywords: Natural Products, Medicinal Chemistry, Lead Compounds, Pharmacokinetics, Drug Discovery, Bioavailability, Toxicity Evaluation

Received: Jan. 28, 2026 **Revised: Feb. 18, 2026** **Accepted: March. 28, 2026** **Published: April 28, 2026**

DOI: https://doi.org/10.64062/IJPCAT.Vol2.Issue2.4

https://ijpcat.com/index.php/1/issue/archive

1. INTRODUCTION

Plants, microorganisms, and marine organisms have been used as a source of medicinal chemistry lead compounds, especially natural products, since ancient times, providing an extensive variety of structurally diverse and biologically active molecules. Their intricate chemical structures, such as a distinctive stereochemistry and a variety of functional groups, allow them to react well with various biological targets, such as enzymes, receptors, and signaling pathways[1]. This inherent versatility has seen natural products play a very significant role in the discovery of therapeutic agents to treat complex diseases, especially cancer, inflammation, infections, and neurodegenerative diseases. The utility of animal-based preclinical research has been important in confirming the pharmacological potential of these compounds, and showing them to have the ability to alter disease pathways, multitarget activity, and relatively favorable safety profiles relative to most synthetic drugs.

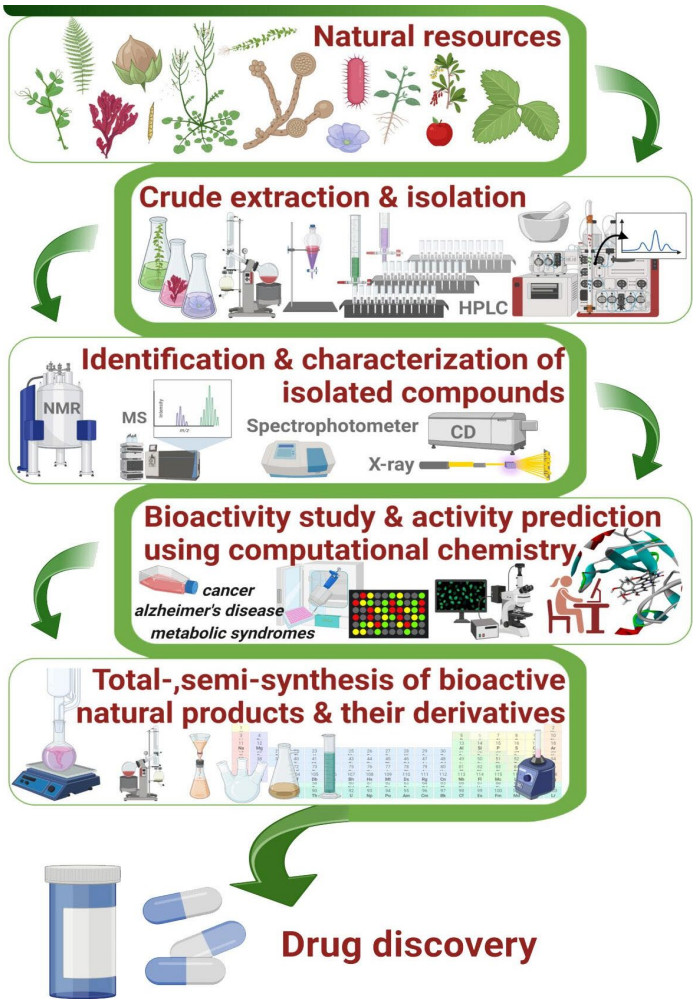

Figure 1: Natural Products as Lead Compounds in Medicinal Chemistry[2]

Although the use of natural products as lead compounds has a lot of promise, there are a few problems that need to be resolved in order to develop successful drugs. Their clinical applicability and reproducibility of results may be hampered by issues like poor bioavailability, low solubility, rapid metabolism, and variability of natural sources. Moreover, variations between animal models and human physiology pose translational constraints, making it difficult to advance preclinical results to clinical achievement. However, the development in drug delivery systems, structural modification methods and computational methods are

contributing to the elimination of these barriers. As such, it is necessary to comprehend the opportunities and challenges of natural products to maximize their contribution to medicinal chemistry and propel them to effective and clinically viable therapeutic agents[3].

1.1 Background and Context

Natural products have traditionally played a central role in drug discovery, providing them with a rich source of structurally diverse and biologically active natural products derived from plants, microorganisms and marine organisms. Evolutionary mechanisms have resulted in their complex chemical structures, which undergo complex stereochemistry and have a wide range of functional groups, making them more selective and effective in interacting with biological targets, including enzymes, receptors, and signaling molecules. This natural adaptability and specificity have made natural products valuable in medicinal chemistry, where they have played a key role in the discovery of therapeutic agents to a wide variety of diseases, such as cancer, inflammatory diseases, infectious diseases, and also neurological diseases. In addition, animal preclinical research have been an important element in confirming their pharmacological potential by expressed in vivo data of their effectiveness, their mechanism of action, and their safety and toxicity. These studies are not only useful in gaining insight into the behavior of natural compounds in complex biological systems, but also in their development as potential lead compounds in current drug design[4].

1.2 Objectives of the Review

The primary objective of this review is to:

- To determine the therapeutic potential of animal-derived natural products as lead compounds through preclinical animal models in diseases like cancer, inflammation, infections and neurodegeneration.
- To examine the action of natural compounds, such as apoptosis induction, anti-inflammatory effects, antioxidant, and regulation of signaling pathways, in animal models.
- To determine the pharmacokinetic characteristic and bioavailability issues of natural products and how these can be overcome to enhance their effects in vivo.
- To study the safety and toxicology of natural compounds using acute and chronic animal studies to identify their therapeutic index and adverse effects.
- To reveal the main opportunities and challenges, such as variability, standardization problems, and translational constraints, and present the sophisticated solutions to the optimization of drug development relying on natural products.

1.3 Importance of the Topic

The relevance of this subject is supported by the increasing demands across the world to have effective, safe, and multi-target therapeutic agents that can be used to treat complex and chronic illnesses like cancer, inflammatory diseases, infections and neuro degenerative diseases. Natural products in this respect have a clear advantage owing to their natural biological compatibility, structure diversity, and tendency to act on a wide variety of molecular targets simultaneously, which has elevated therapeutic effectiveness and minimized the chances of drug resistance[5]. Their broad spectrum of pharmacological activities renders them very encouraging candidates in contemporary medicinal chemistry. Nonetheless, these advantages

are faced with a number of challenges that restrict their complete therapeutic use, such as low bioavailability, insolubility, composition variability, and the inability to extrapolate animal test results to clinical use in humans. It is essential to address these issues by conducting a systematic investigation, especially by conducting preclinical studies using animals, to comprehend their pharmacokinetic behavior, safety profiles, and mechanism of action. These understandings are vital in maximizing natural compounds and ensure effective conversion into viable and effective therapeutic agents in clinical use[6].

2. PRECLINICAL EVALUATION OF NATURAL PRODUCTS IN ANIMAL MODELS

Natural products present considerable opportunities as lead compounds because of their various structures, multi-target activity, and promising therapeutic effects that they exhibit in animal models. Their potential is however hampered by issues like low bioavailability, variability, and translation of animal data into humans[7].

2.1 Overview of Animal-Based Research Studies

Recent preclinical investigations have shown great progress on the use of natural products as lead compounds:

- **Anticancer activity:** Natural compounds like flavonoids, alkaloids and terpenoids have demonstrated incredible tumor growth inhibitory effect in xenograft mouse models. The action of these bioactive molecules is manifested in a variety of ways: by induction of apoptosis through mitochondrial pathways, angiogenesis inhibition by suppression of vascular endothelial growth factors (VEGF), and by regulation of important oncogenic signaling pathways, including PI3K/Akt and MAPK. Moreover, some of the studies have also reported decreased metastasis and better survival rates in the treated animals, which could serve as safer alternatives or as adjunct to the traditional chemotherapy[8].
- **Anti-inflammatory effects:** Plant products such as curcumin and resveratrol have been shown to have potent anti-inflammatory effects in rodent models. These compounds can inhibit pro-inflammatory cytokines including TNF-α, IL-1B and IL-6, and improve anti-inflammatory mediators. They also control the oxidative stress scavenging free radicals and enhancing antioxidant enzyme activity, such as superoxide dismutase (SOD) and catalase. Moreover, their capability to suppress major inflammatory cascades like NF-KB and COX-2 has been linked to a decrease in tissue injury, and better physiological outcomes.
- **Antimicrobial activity:** Natural extracts that have been tested in infected animal systems have been found to be promising with regard to their efficacy against a variety of pathogenic microorganisms including antibiotic-resistant bacterial strains. These substances have antimicrobial effects that affect the cell membranes of microbes by disrupting protein and nucleic acid synthesis, quorum sensing, and biofilm formation. They have also shown in vivo that they improve immune responses in the host organisms, decrease the microbial load, and increase healing in the infection site as potential alternatives to synthetic antibiotics[9].
- **Neuroprotective effects:** Experiments in rat models of neurodegenerative diseases have shown that natural products have considerable neuroprotective effects. These compounds promote memory and cognitive functions by alleviating oxidative stress,

preventing neuronal apoptosis, and stimulating neurogenesis. Mechanistically, they regulate the levels of neurotransmitters, enhance the functioning of mitochondria, and lower the deposition of toxic proteins including 2 -amyloid plaques. Antioxidant and anti-inflammatory effects of them also lead to the preservation of neuronal integrity and disease progression in diseases like Alzheimer and Parkinson disease.

2.2 Methodologies Used in Animal Studies

Common methodologies include:

- **Xenograft tumor models:** The models were commonly employed to determine the anticancer efficacy by inoculating human or murine tumor cells into immunocompromised mice. They enable researchers to test the tumor growth inhibitory effects, metastasis and drug responsiveness in a controlled in vivo setup. Orthotopic xenografts offer more realistic tumor microenvironment and allow improved insights into tumor-host interactions, angiogenesis, and penetration of natural compounds in therapy[10].
- **Chemically induced disease models:** These models are used to model the pathological states of human beings like inflammation, neurodegenerative diseases and metabolic diseases. Animals are treated with chemical agents such as carcinogens, neurotoxins, or inducing agents of inflammation to simulate progression of the disease. These models are what can be used specifically to assess the preventive and therapeutic actions of natural products, and the mechanisms and progression of diseases under controlled experimental conditions.
- **Knockout and transgenic animal models:** Transgenic animals are utilized to study particular molecular processes and interactions of genes in disease pathways. The deletion of certain genes is done in knockout models, whereas the introduction or overexpression of genes is done in transgenic models[11]. These models offer useful information about the contribution of genetic factors to disease development and aids in discovering molecular targets of natural products as a source of drugs.
- **Dose-response and toxicity studies:** These researches are critical in the establishment of therapeutic index, optimum dosage range and safety margins of bioactive compounds. Through the application of different doses of natural products, the researchers are able to evaluate efficacy, monitor adverse effects and determine the maximum tolerated dose (MTD). Acute and chronic toxicity tests are performed in order to investigate short-term and long-term safety profiles, which is necessary to be suitable to proceed to further clinical development[12].
- **Histopathological and biochemical analyses:** These are analyses conducted to assess the organ-specific effects and biomarker alterations after treatment. Histopathological analysis is a microscopic study of tissue fragments to identify structural and cellular changes, and biochemical analysis of parameters like enzyme activity, oxidative stress indicators, and inflammatory mediators. A combination of these techniques gives a complete picture of the physiological and molecular action of natural compounds in animal models.

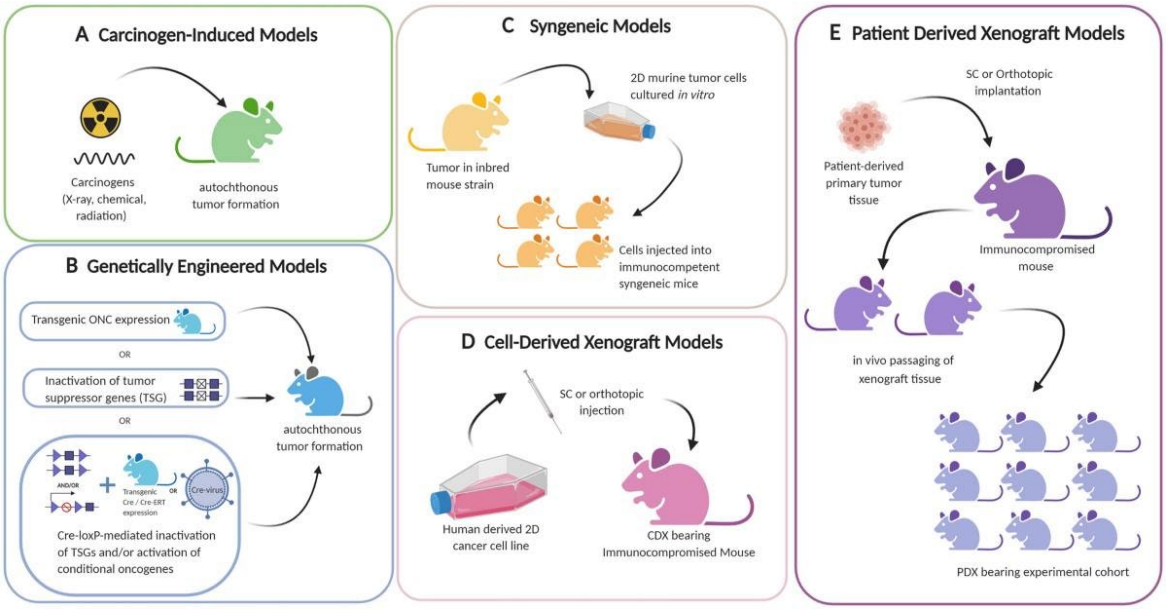

Figure 2: Types of Animal Models Used in Preclinical Cancer Research[13]

2.3 Critical Evaluation

Strengths

Research studies on animals have a number of significant advantages in the testing of natural products as possible therapies. Major benefits include the fact that they can offer in vivo confirmation of pharmacological effects, where researchers can observe the behavior of compounds in a living biological system as opposed to isolated conditions. Such studies also help in the in-depth knowledge of pharmacokinetics and pharmacodynamics, such as absorption, distribution, metabolism, and excretion, dose-response relationships[14]. Moreover, animal models can be used to investigate systemic toxicity and organ-specific response to determine the possible adverse effect and safety concern at an early phase of drug development. The other important advantage is the controlled experiment environment where genetics, diet and exposure conditions have been under strict control to produce reliable, reproducible and scientifically valid results.

Limitations

Although animal studies have these benefits, there are a number of constraints that should be taken into account when using their results. The differences between animals and humans in terms of species may limit the ability to directly extrapolate results, because physiological and metabolic differences can affect the efficacy and safety of drugs. Also, the scope, construction, and magnitude of animal research may be restricted because of the ethical issues and legal restrictions regarding animal testing[15]. The other major problem is that the composition of natural products varies, and the differences in the origin of the plant, environmental factors, and extraction methods can cause a variation in results. Finally, insufficient standardization of experimental procedures in various studies may pose challenges in comparative research, reproducibility and generalizability of results, and, by implication, the overall validity of the conclusions made based on preclinical studies.

3. NATURAL PRODUCTS IN DRUG DESIGN AND PRECLINICAL EVALUATION

Natural-products offer structurally diverse and biologically potent scaffolds capable of multi-target therapeutic effects in animal models and thus used as valuable in drug design and lead optimization. Nevertheless, issues like low bioavailability, high metabolism, and possible toxicity would necessitate enhanced delivery models and stringent preclinical safety testing[16].

3.1 Structural Diversity and Drug Design

The complex and unique chemical scaffolds of natural product are challenging to synthesize synthetically because of complex stereochemistry, variety of functional groups and elevated degree of molecular complexity. Such structural diversity facilitates more specific and powerful interactions with biological targets like enzymes, receptors and proteins[17]. Consequently, natural compounds are frequently highly target specific with strong biological activity. These attributes render them good starting points when it comes to the optimization of lead where structural alteration and semi-synthetic techniques are applied to increase efficacy, decrease toxicity and enhance pharmacokinetic characteristics. Moreover, natural scaffolds have led to the development of many clinically successful drugs, proving their enduring relevance in the current drug design.

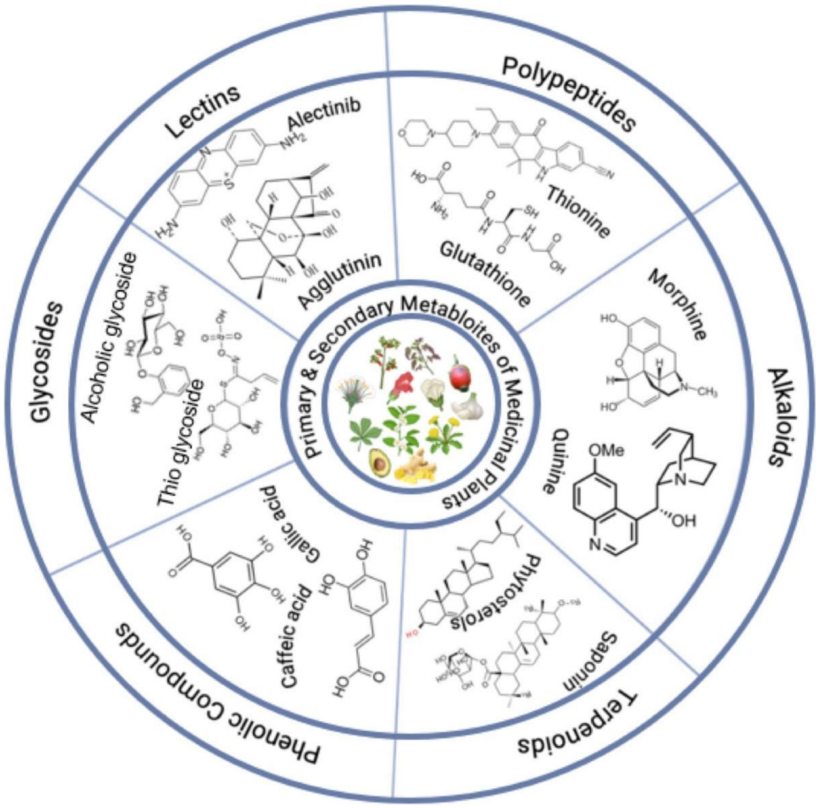

Figure 3: Structural Diversity of Natural Products[18]

3.2 Mechanisms of Action in Animal Models

The animal researches have indicated various ways in which natural products have a therapeutic effect:

- **Induction of apoptosis via mitochondrial pathways:** Natural compounds may induce programmed cell death by impairing the mitochondrial membrane potential, releasing cytochrome c and caspases, destroying damaged or cancerous cells.

- **Inhibition of inflammatory mediators (e.g., TNF-α, IL-6):** Numerous natural products inhibit pro-inflammatory cytokines and signal transduction including NF-κB, which results in fewer inflammation and tissue injury in different disease models[19].
- **Modulation of oxidative stress and free radical scavenging:** Natural antioxidants neutralize reactive oxygen species (ROS), improve endogenous antioxidant defenses, and prevent oxidative damage of cells in chronic diseases.
- **Regulation of enzyme activity and signal transduction pathways:** These compounds are able to prevent or stimulate important enzymes and pathways, such as kinases, cyclooxygenases and transcription factors, and thereby affect cellular processes, including proliferation, differentiation, and immune responses.

Together, these processes emphasize the multi-target aspect of natural products that is especially beneficial with regard to treating complicated illnesses[20].

3.3 Pharmacokinetics and Bioavailability Challenges

Although they have good efficacy, most natural compounds are limited by a number of pharmacokinetic constraints which impede their clinical use:

- **Poor solubility and absorption:** Most natural products used as bio-actives are hydrophobic, which leads to low solubility and low absorption in the gastrointestinal tract.
- **Rapid metabolism and elimination:** These substances are commonly rapidly broken down in the liver and excreted lowering the efficacy and existence period of the treatment.
- **Low systemic availability:** This is because very low proportion of the dose that is administered reaches the target site due to poor absorption and fast clearance.

To overcome these issues, some of the strategies that have been investigated in animal studies involve the application of nanoparticle-based delivery systems, liposomes and polymeric carriers to improve solubility and stability[21]. To enhance therapeutic potential, structural modification has been used to enhance pharmacokinetic profiles and bioavailability as well as prodrug formation and derivatization.

3.4 Safety and Toxicological Evaluation

In vivo preclinical toxicity animal studies have demonstrated that natural products tend to be less toxic than many synthetic drugs, essentially because of their natural origin and their capacity to interact with physiological systems. Nevertheless, safety assessment is essential, because it may cause adverse effects like hepatotoxicity, nephrotoxicity, and immunological disruptions with high doses or long-term exposure[22].

The toxicological tests that are normally involved are the acute, sub-acute and chronic toxicity tests, the hematological, biochemical and histopathological tests. These experiments assist to establish safe dosage levels, target organ toxicity, and the therapeutic index. Also, reproductive toxicity, genotoxicity and carcinogenicity studies are occasionally done to guarantee the safety in the long-term. Dose optimization and stringent preclinical testing must therefore be done prior to the advancement of natural compounds to clinical trials[23].

4. OPPORTUNITIES AND CHALLENGES IN UTILIZING NATURAL PRODUCTS AS LEAD COMPOUNDS

Natural products provide extraordinary possibilities in medicinal chemistry due to their enormous structural variety, biological selectivity and evolutionary fine-tuning to interact with sophisticated biological targets[24]. The animal experimental research has always indicated that these compounds have immense therapeutic potential in a broad range of illnesses, such as cancer, inflammation, microbial infections and neurodegenerative illnesses. The fact that they can act on several molecular targets concurrently increases the effectiveness of treatment and minimizes drug resistance, especially in the treatment of multifactorial diseases. In addition, preclinical investigations tend to have relatively lower toxicity and higher biocompatibility of natural compounds, which further increases the presence of natural compounds as potential lead candidates in drug development[25].

Although these benefits exist, there are a number of obstacles that restrict the further use of natural products. Their low solubility, low absorption and rapid metabolism are one of the primary issues that lower their overall bioavailability and therapeutic efficacy in vivo because of their poor pharmacokinetic profile[26]. Moreover, natural products tend to be variable in composition with changes in environmental conditions, geographical locations, and modes of extractions, causing problems with reproducibility and standardization of experimental results. Isolating and purifying active compounds in large quantities is also complicated, which presents a considerable challenge technologically and economically[27].

Moreover, the limitations of translation may occur because of the variations between animal models and human physiology, which will impact the predictive validity of preclinical discoveries[28]. The ethical aspects with regards to large scale animal experimentation are also not without concern. To alleviate these problems, further studies are required to develop better drug delivery systems like nanoparticles and liposomal carriers to increase bioavailability, better methods of standardization and quality control. The combination of novel strategies, such as computational modeling, artificial intelligence, and nanotechnology, can further speed up the discovery, optimization, and successful development of natural product-based lead compounds into effective therapeutic agents[29].

Table 1: Summary of Key Literature on Natural Products in Medicinal Chemistry[30]

Author(s) & Year	Study Focus	Methodology/Approach	Key Findings
Shultz (2018)[31]	Evolution of drug properties and Rule of Five	Analysis of physicochemical properties of approved oral drugs	Natural products often exceed traditional drug-likeness criteria but still show strong therapeutic potential
Ivasiv et al. (2019)[32]	Molecular hybridization for multitarget drugs	Design and synthesis of hybrid pharmacophores	Hybrid molecules showed enhanced efficacy and multi-target activity with reduced drug resistance

Zhang et al. (2020)[33]	Drug discovery strategies from natural products	Bioactivity-guided isolation, HTS, structure-based design	Advanced technologies improved identification and optimization of natural leads
Liu et al. (2018)[34]	Natural deep eutectic solvents (NADES)	Evaluation of extraction efficiency and solvent properties	NADES improved solubility, stability, and bioavailability of natural compounds
Lautié et al. (2020)[35]	Chemical diversity of plant natural products	Use of metabolomics, cheminformatics, bioinformatics	Plant metabolites provide vast chemical diversity for drug discovery

5. DISCUSSION

Natural products are promising lead compounds because of their multi-target therapeutic action and good safety profiles in animal experiments, and hence useful in the development of drugs. However, limitations such as poor pharmacokinetics, variability, and translational gaps require advanced delivery systems, standardization, and innovative research approaches to enhance their clinical applicability[36].

5.1 Interpretation and Analysis of Findings

The review shows that natural products are very effective lead compounds in medicinal chemistry especially when animal-based studies have validated them. Their structural diversity and ability to act on multiple biological targets enable them to modulate complex disease pathways such as cancer progression, inflammation, microbial infections, and neurodegeneration. Their therapeutic effectiveness, such as tumor inhibition, decreasing inflammatory mediators, and neuroprotective effects, has been presented in animal models with a high level of evidence[37]. These results support the fact that natural products have great potential in pharmacological aspects and could be powerful candidates to further drug development.

5.2 Implications and Significance

These findings have significant implications on drug discovery and development. The multi-target mechanisms of natural products provide a strategic benefit in the treatment of multifactorial diseases as they enhance treatment outcomes and reduce drug resistance. They are also relatively low toxicity profiles in preclinical models, which increases their capacity to be lead compounds. Moreover, natural scaffolds remain a source of inspiration of the creation of semi-synthetic analogues and the creation of new drug design strategies, which underpin their role in the further development of modern medicinal chemistry[38].

5.3 Research Gaps and Limitations

In spite of their potential, there are a number of gaps and limitations. Their applicability to clinical use is severely limited by poor pharmacokinetic characteristics such as low levels of solubility, low absorption, and rapid metabolic rates. Natural variability and absence of

standard methods of extraction and characterization pose a challenge to reproducibility and consistency of findings. Moreover, the differences between animal models and humans in terms of interspecies also restrain the direct translation of preclinical results[39]. There are also ethical issues and governmental limitations that pertain to animal research.

5.4 Future Research Directions

The future studies need to be directed towards overcoming these limitations by using innovative and multidisciplinary ways. Bioavailability and targeted delivery can be increased with the creation of new drug delivery systems like nanoparticles, liposomes and polymeric carriers. Extraction, isolation, and characterization procedures should be standardized to enhance reproducibility[40]. Computational modeling, artificial intelligence and systems biology may be integrated to speed up lead optimization and drug design. Furthermore, the advancement of more predictive and human-relevant animal models will enhance translational accuracy and make the successful translation of natural products to clinically viable drugs possible.

6. CONCLUSION

Natural products remain a very important and essential source of lead compounds in medical chemistry, especially as illustrated by a plethora of animal-based preclinical trials. Their outstanding structural diversity, biological specificity and modulation of numerous molecular targets are particularly beneficial in treating complex and multifactorial diseases like cancer, inflammation, infections, and neurodegenerative disorders. The pharmacological potential of animal models has continued to propound their great potential in tumor suppression, anti-inflammatory and antimicrobial effects, and neuroprotection, as well as acceptable safety profiles in most cases relative to most synthetic drugs. Nevertheless, even with these potential beneficial properties, a number of obstacles restrict their complete therapeutic use, such as low bioavailability, low solubility, high metabolic rate, inconsistencies in natural sources, and translational disparities between animal models and human physiology. The above restrictions emphasize the necessity of further development of drug delivery systems, structural modification approaches and standardization methods to enhance their pharmacokinetic characteristics and reproducibility. In general, natural products have great potential as lead compounds but to achieve success in translating their potential into safe, effective and clinically viable drugs, existing challenges need to be overcome by multidisciplinary research methods.

REFERENCES

1. Bharate, S. B., & Lindsley, C. W. (2024). Natural products driven medicinal chemistry. Journal of Medicinal Chemistry, 67(23), 20723-20730.
2. Atanasov, A. G., Zotchev, S. B., Dirsch, V. M., & Supuran, C. T. (2021). Natural products in drug discovery: advances and opportunities. Nature reviews Drug discovery, 20(3), 200-216.
3. Chopra, B., & Dhingra, A. K. (2021). Natural products: A lead for drug discovery and development. Phytotherapy Research, 35(9), 4660-4702.
4. Blakemore, D. C., Castro, L., Churcher, I., Rees, D. C., Thomas, A. W., Wilson, D. M., & Wood, A. (2018). Organic synthesis provides opportunities to transform drug discovery. Nature chemistry, 10(4), 383-394.

5. Boström, J., Brown, D. G., Young, R. J., & Keserü, G. M. (2018). Expanding the medicinal chemistry synthetic toolbox. Nature Reviews Drug Discovery, 17(10), 709-727.
6. Thomford, N. E., Senthebane, D. A., Rowe, A., Munro, D., Seele, P., Maroyi, A., & Dzobo, K. (2018). Natural products for drug discovery in the 21st century: innovations for novel drug discovery. International journal of molecular sciences, 19(6), 1578.
7. Gerry, C. J., & Schreiber, S. L. (2018). Chemical probes and drug leads from advances in synthetic planning and methodology. Nature Reviews Drug Discovery, 17(5), 333-352.
8. Najmi, A., Javed, S. A., Al Bratty, M., & Alhazmi, H. A. (2022). Modern approaches in the discovery and development of plant-based natural products and their analogues as potential therapeutic agents. Molecules, 27(2), 349.
9. Schneider, G. (2018). Automating drug discovery. Nature reviews drug discovery, 17(2), 97-113.
10. Li, G., & Lou, H. X. (2018). Strategies to diversify natural products for drug discovery. Medicinal research reviews, 38(4), 1255-1294.
11. Devine, P. N., Howard, R. M., Kumar, R., Thompson, M. P., Truppo, M. D., & Turner, N. J. (2018). Extending the application of biocatalysis to meet the challenges of drug development. Nature Reviews Chemistry, 2(12), 409-421.
12. Berdigaliyev, N., & Aljofan, M. (2020). An overview of drug discovery and development. Future medicinal chemistry, 12(10), 939-947.
13. Han, B., He, X. H., Liu, Y. Q., He, G., Peng, C., & Li, J. L. (2021). Asymmetric organocatalysis: an enabling technology for medicinal chemistry. Chemical Society Reviews, 50(3), 1522-1586.
14. Abouelhassan, Y., Garrison, A. T., Yang, H., Chavez-Riveros, A., Burch, G. M., & Huigens III, R. W. (2019). Recent progress in natural-product-inspired programs aimed to address antibiotic resistance and tolerance. Journal of medicinal chemistry, 62(17), 7618-7642.
15. Dzobo, K. (2022). The role of natural products as sources of therapeutic agents for innovative drug discovery. Comprehensive pharmacology, 408.
16. Henninot, A., Collins, J. C., & Nuss, J. M. (2018). The current state of peptide drug discovery: back to the future?. Journal of medicinal chemistry, 61(4), 1382-1414.
17. Fuchter, M. J. (2020). On the promise of photopharmacology using photoswitches: a medicinal chemist's perspective. Journal of Medicinal Chemistry, 63(20), 11436-11447.
18. Hou, W., & Xu, H. (2022). Incorporating selenium into heterocycles and natural products─ from chemical properties to pharmacological activities. Journal of Medicinal Chemistry, 65(6), 4436-4456.
19. Mak, K. K., & Pichika, M. R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug discovery today, 24(3), 773-780.
20. Miethke, M., Pieroni, M., Weber, T., Brönstrup, M., Hammann, P., Halby, L., ... & Müller, R. (2021). Towards the sustainable discovery and development of new antibiotics. Nature Reviews Chemistry, 5(10), 726-749.

21. Nelson, K. M., Bisson, J., Singh, G., Graham, J. G., Chen, S. N., Friesen, J. B., ... & Pauli, G. F. (2020). The essential medicinal chemistry of cannabidiol (CBD). Journal of medicinal chemistry, 63(21), 12137-12155.

22. Campos, K. R., Coleman, P. J., Alvarez, J. C., Dreher, S. D., Garbaccio, R. M., Terrett, N. K., ... & Parmee, E. R. (2019). The importance of synthetic chemistry in the pharmaceutical industry. Science, 363(6424), eaat0805.

23. Chaachouay, N., & Zidane, L. (2024). Plant-derived natural products: a source for drug discovery and development. Drugs and Drug Candidates, 3(1), 184-20

24. Guillemard, L., Kaplaneris, N., Ackermann, L., & Johansson, M. J. (2021). Late-stage C–H functionalization offers new opportunities in drug discovery. Nature Reviews Chemistry, 5(8), 522-545.

25. Muttenthaler, M., King, G. F., Adams, D. J., & Alewood, P. F. (2021). Trends in peptide drug discovery. Nature reviews Drug discovery, 20(4), 309-325.

26. Huang, M., Lu, J. J., & Ding, J. (2021). Natural products in cancer therapy: past, present and future. Natural products and bioprospecting, 11(1), 5-13.

27. Nasim, N., Sandeep, I. S., & Mohanty, S. (2022). Plant-derived natural products for drug discovery: current approaches and prospects. The Nucleus, 65(3), 399-411.

28. Schneider, P., Walters, W. P., Plowright, A. T., Sieroka, N., Listgarten, J., Goodnow Jr, R. A., ... & Schneider, G. (2020). Rethinking drug design in the artificial intelligence era. Nature reviews drug discovery, 19(5), 353-364.

29. Koparde, A. A., Doijad, R. C., & Magdum, C. S. (2019). Natural products in drug discovery. Pharmacognosy-medicinal plants, 8.

30. Patton, E. E., Zon, L. I., & Langenau, D. M. (2021). Zebrafish disease models in drug discovery: from preclinical modelling to clinical trials. Nature reviews Drug discovery, 20(8), 611-628.

31. Shultz, M. D. (2018). Two decades under the influence of the rule of five and the changing properties of approved oral drugs: miniperspective. Journal of Medicinal Chemistry, 62(4), 1701-1714.

32. Ivasiv, V., Albertini, C., Gonçalves, A. E., Rossi, M., & Bolognesi, M. L. (2019). Molecular hybridization as a tool for designing multitarget drug candidates for complex diseases. Current Topics in Medicinal Chemistry, 19(19), 1694-1711.

33. Zhang, L., Song, J., Kong, L., Yuan, T., Li, W., Zhang, W., ... & Du, G. (2020). The strategies and techniques of drug discovery from natural products. Pharmacology & Therapeutics, 216, 107686.

34. Liu, Y., Friesen, J. B., McAlpine, J. B., Lankin, D. C., Chen, S. N., & Pauli, G. F. (2018). Natural deep eutectic solvents: properties, applications, and perspectives. Journal of natural products, 81(3), 679-690.

35. Lautié, E., Russo, O., Ducrot, P., & Boutin, J. A. (2020). Unraveling plant natural chemical diversity for drug discovery purposes. Frontiers in pharmacology, 11, 397.

36. Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D. P., Acosta-Torres, L. S., ... & Shin, H. S. (2018). Nano based drug delivery systems: recent developments and future prospects. Journal of nanobiotechnology, 16(1), 71.

37. Docherty, J. H., Lister, T. M., Mcarthur, G., Findlay, M. T., Domingo-Legarda, P., Kenyon, J., ... & Larrosa, I. (2023). Transition-metal-catalyzed C–H bond activation for

the formation of C–C bonds in complex molecules. Chemical Reviews, 123(12), 7692-7760.

38. Naeem, A., Hu, P., Yang, M., Zhang, J., Liu, Y., Zhu, W., & Zheng, Q. (2022). Natural products as anticancer agents: current status and future perspectives. Molecules, 27(23), 8367.

39. Heinrich, M., Appendino, G., Efferth, T., Fürst, R., Izzo, A. A., Kayser, O., ... & Viljoen, A. (2020). Best practice in research–overcoming common challenges in phytopharmacological research. Journal of ethnopharmacology, 246, 112230.

40. Vinogradov, A. A., Yin, Y., & Suga, H. (2019). Macrocyclic peptides as drug candidates: recent progress and remaining challenges. Journal of the American Chemical Society, 141(10), 4167-4181.