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Review Paper

INTRODUCTION TO MEDICINAL CHEMISTRY AND NATURAL PRODUCT

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Abstract

Medicinal Chemistry and Natural Products represent pivotal realms in the discovery and development of therapeutic agents. Beginning with an introduction to medicinal chemistry, the discourse navigates through the diverse classification of natural products, extraction techniques, and the significance of these compounds in medicine. It delves into the molecular intricacies of drug design, emphasizing key principles, drug targets, and the dynamic processes of pharmacokinetics and pharmacodynamics. The narrative unfolds with a discussion on challenges encountered in drug development, offering strategic solutions to combat drug resistance, toxicity concerns, and high developmental costs. Following this, the exploration of natural products widens to include sources such as plants, microorganisms, and marine organisms, detailing their classifications and bioactive potentials. Techniques for the extraction and isolation of these compounds are scrutinized, showcasing the meticulous processes employed in their isolation. Looking towards the future, emerging technologies, the integration of computational methods, and the imperative of sustainability and ethics take center stage. The abstract highlights the trends of CRISPR technology, nanomedicine, machine learning, and quantum computing as catalysts for revolutionary advancements. It also underscores the ethical considerations and sustainable practices that are increasingly shaping drug development. This abstract concludes by emphasizing the implications for future research, including the imperative for precision medicine, green chemistry, and global collaboration. The synthesis of these key concepts underlines the dynamic evolution of medicinal chemistry and natural products, with future research poised to unlock novel therapeutic avenues, optimize drug delivery, and foster ethical and sustainable practices for the betterment of global healthcare.

Keywords: Medicinal Chemistry, Natural Products, Drug Discovery, Drug Development, Bioactive Compounds, Drug Targets,

Medicinal Chemistry

Medicinal chemistry is a scientific discipline that combines the principles of chemistry and pharmacology to discover, design, develop, and optimize small molecules or biologics that can be used as drugs for the treatment of diseases. It involves the study of the chemical properties, synthesis, structure-activity relationships (SAR), and mechanisms of action of bioactive compounds with the goal of identifying and creating new pharmaceutical agents. Medicinal chemists work at the interface of chemistry and biology to understand the molecular aspects of drug action and to design molecules with enhanced therapeutic efficacy and reduced side effects.[1,2]

Significance of Natural Products in Medicine

Natural products play a significant role in medicine due to their diverse chemical structures and biological activities. They have been a rich source of therapeutic agents for centuries and continue to contribute to drug discovery and development. The significance of natural products in medicine can be explored through various aspects:

1. **Chemical Diversity and Complexity:** Natural products exhibit a vast array of chemical structures, often complex and diverse, which can provide unique scaffolds for drug design. Their structural complexity is challenging to replicate through synthetic means, making them valuable starting points for drug development.[3]

2. **Biological Activities:** Many natural products have demonstrated potent biological activities, such as antimicrobial, anti-inflammatory, antiviral, and anticancer properties. These inherent activities make them promising candidates for the development of novel therapeutics.[4]

3. **Drug Discovery and Development:** Natural products have historically served as the basis for numerous drugs. Examples include aspirin from willow bark, morphine from poppy, and quinine from cinchona bark. Current drug discovery efforts often involve screening natural product libraries for bioactive compounds or using natural products as lead compounds for further optimization.[4]

4. **Source of Inspiration for Synthesis:** The chemical structures of natural products inspire medicinal chemists in the design and synthesis of new compounds. This mimicking of nature's strategies enables the development of analogs with improved pharmacological profiles.[5]

5. **Biodiversity and Ethnopharmacology:** The vast biodiversity of plants, microorganisms, and marine organisms provides a rich source of natural products. Ethnopharmacological studies, which explore traditional uses of natural products by indigenous cultures, contribute valuable knowledge about potential therapeutic properties.[6]

Historical Perspective

Historical Overview of Natural Products in Medicine: Natural products have a rich history in medicine, with their usage dating back to ancient civilizations. The study of alkaloids, for instance, has been integral to understanding the biographical and historical aspects of these compounds. Alkaloids, which are nitrogen-containing organic molecules often derived from plants, have played a crucial role in traditional medicine practices. A biographical approach to the study of alkaloids provides insights into the individuals and cultures that first utilized these compounds for medicinal purposes. This historical perspective helps trace the evolution of the knowledge and applications of alkaloids, showcasing their significance in early medicinal practices.[7]

Historical Development of Herbal Medicine: The use of herbal medicine has a long history, spanning various cultures and regions. This approach to medicine involves the use of plant-derived substances for therapeutic purposes. The World Health Organization's Global Atlas of Traditional, Complementary, and Alternative Medicine offers a comprehensive overview of the historical development and global practices of herbal medicine. It explores how diverse societies have employed plants as remedies for various ailments and provides context for the evolution of herbal medicine as a cornerstone of traditional healthcare systems.[8]

Contributions of Natural Products to Early Pharmacopeias: Pharmacopeias, which are official publications containing a list of medicinal drugs along with their descriptions, standards, and properties, have a history deeply intertwined with natural products. The development of early pharmacopeias involved the incorporation of natural substances, including plant-derived

compounds, into standardized formulations for medical use. By examining the contributions of natural products to these early pharmacopeias, one gains insights into the foundational role of plant-derived remedies in shaping medicinal practices. This historical exploration highlights the longstanding recognition of the therapeutic potential of natural products and their integration into formalized systems of medicine.[9]

Fundamentals of Medicinal Chemistry

A. Basic Principles

The basic principles of medicinal chemistry encompass the fundamental concepts that form the foundation of drug discovery and development. This includes an understanding of chemical and biological principles, as well as the principles guiding the interactions between drugs and biological systems. Graham L. Patrick's book "An Introduction to Medicinal Chemistry" serves as an excellent reference for comprehensively covering the basic principles in medicinal chemistry.[10]

2. Molecular Structure and Properties: An essential aspect of medicinal chemistry involves the study of molecular structures and their properties. This includes the analysis of the chemical makeup of drug molecules, their physicochemical properties, and the relationship between molecular structure and biological activity. "Medicinal Chemistry" by Ashutosh Kar provides valuable insights into molecular structures and their significance in drug design.[11]

3. Drug Targets and Receptors: Understanding drug targets and receptors is crucial for designing drugs that interact selectively with specific biological molecules. This topic involves the identification of molecular targets involved in diseases and the design of drugs that can modulate these targets. "Foye's Principles of Medicinal Chemistry" by Thomas L. Lemke, David A. Williams, and Victoria F. Roche is a comprehensive reference that covers drug targets and receptors in detail.[12]

4. Pharmacokinetics and Pharmacodynamics: Pharmacokinetics and pharmacodynamics are integral to understanding how drugs interact with the body. Pharmacokinetics involves the absorption, distribution, metabolism, and excretion of drugs, while pharmacodynamics focuses on the drug effects and the relationship between drug concentration and response. "Basic &

Clinical Pharmacology" by Bertram G. Katzung and Anthony J. Trevor provides a solid foundation in pharmacokinetics and pharmacodynamics.[13]

Drug Design and Development

1. Drug Design and Development: Drug design and development involve the systematic process of creating new pharmaceutical agents. This process integrates various scientific disciplines, including medicinal chemistry, pharmacology, and biology, to identify and optimize compounds for therapeutic use. "Medicinal Chemistry" by Ashutosh Kar provides a comprehensive overview of drug design and development, outlining the key stages and considerations in this complex process.[14]

2. Rational Drug Design: Rational drug design is an approach that involves utilizing molecular information about a drug target to design a drug molecule with desired properties. This method relies on a deep understanding of the target's structure and function. Patrick's "An Introduction to Medicinal Chemistry" is a valuable resource that discusses the principles and techniques of rational drug design.[15]

3. High Throughput Screening: High throughput screening (HTS) is a powerful technique used in drug discovery to rapidly test large compound libraries for their biological activity. This approach allows researchers to identify potential drug candidates efficiently. The book "High-Throughput Screening in Drug Discovery" by J. Mark Treherne and J. Rick Turner offers insights into the principles and applications of high throughput screening in the drug discovery process.[16]

4. Lead Optimization: Lead optimization is the process of refining and improving the properties of initial drug leads identified during drug discovery. This involves modifying the chemical structure of the lead compound to enhance its efficacy, selectivity, and pharmacokinetic properties. "Foye's Principles of Medicinal Chemistry" by Lemke, Williams, and Roche covers lead optimization strategies and techniques in medicinal chemistry.[17]

III. Natural Products in Medicine

Natural products, in the context of medicine, refer to chemical compounds or substances derived from living organisms, including plants, microorganisms, and marine organisms, that possess

medicinal properties. These compounds have been historically used for therapeutic purposes and have played a crucial role in the development of various drugs. Understanding the definition and classification of natural products is essential for appreciating their diversity and potential in medicine.[18]

Definition: The definition of natural products in medicine involves recognizing compounds derived from natural sources that exhibit therapeutic effects. These sources can include plants, fungi, bacteria, and marine organisms. Natural products often serve as lead compounds in drug discovery due to their unique chemical structures and biological activities.[19]

Classification: Natural products are classified based on their chemical structures and the organisms from which they are derived. The main classes of natural products include:[20-21]

1. **Alkaloids:** Nitrogen-containing compounds commonly found in plants. Examples include morphine from poppies and quinine from cinchona bark.
2. **Terpenoids:** Compounds derived from isoprene units. They include essential oils, steroids, and taxanes. For instance, paclitaxel is a terpenoid used in cancer treatment.
3. **Polyphenols:** Compounds with multiple phenolic structures, often found in fruits, vegetables, and medicinal plants. Resveratrol from grapes and curcumin from turmeric are examples.
4. **Peptides and Proteins:** Natural products can also include peptides and proteins with therapeutic applications. Examples include insulin and vancomycin.

Sources of Natural Products

Plants:

Plants have been a traditional and prolific source of natural products used in medicine for centuries. Plant-derived compounds, such as alkaloids, flavonoids, and terpenoids, often exhibit diverse pharmacological activities. The study of plant-derived natural products involves the extraction and isolation of bioactive compounds from various plant parts.[22-23]

Microorganisms:

Microorganisms, including bacteria and fungi, are prolific producers of bioactive compounds. Antibiotics like penicillin and streptomycin are classic examples of microbial-derived natural products. The exploration of microbial sources involves isolating and characterizing compounds produced by these microorganisms, often through fermentation processes.[24-25]

Marine Organisms:

The oceans harbor a vast diversity of organisms, many of which produce unique natural products with potential pharmaceutical applications. Marine organisms such as sponges, algae, and mollusks have yielded compounds with anticancer, anti-inflammatory, and antiviral properties. Exploring marine sources involves underwater collection and subsequent isolation of bioactive compounds.[26-27]

Some Extraction and Isolation Techniques

Extraction Techniques:

a. Solid-Liquid Extraction:[28]

- Solid-liquid extraction involves the use of a solvent to dissolve the target compounds from a solid matrix, typically plant material. Techniques such as maceration, percolation, and Soxhlet extraction are commonly employed.

b. Liquid-Liquid Extraction:

- **Explanation:** This technique involves partitioning compounds between two immiscible liquid phases. It is useful for separating compounds based on their solubility in different solvents.[29]

c. Supercritical Fluid Extraction:

- **Explanation:** Supercritical fluid extraction uses supercritical fluids, such as carbon dioxide, to extract compounds. This technique is known for its efficiency and selectivity, particularly in the extraction of heat-sensitive compounds.[30]

2. Isolation Techniques:

a. Chromatography:

- **Explanation:** Chromatography techniques, such as column chromatography, high-performance liquid chromatography (HPLC), and gas chromatography (GC), are widely used for separating and purifying individual compounds from complex mixtures.[31]

b. Fractionation:

- **Explanation:** Fractionation involves the separation of a mixture into different fractions based on certain properties. This is often an intermediate step between extraction and purification.[32]

c. Preparative-Scale Isolation:

- **Explanation:** Preparative-scale isolation involves scaling up isolation techniques for larger quantities of the desired compound. This is crucial for obtaining sufficient material for further studies or drug development.[33]

TABLE 1.1: Bioactive compounds from natural sources along with their properties:

Bioactive Compound Class	Examples	Properties	References
Alkaloids	Morphine (Opium poppy), Quinine (Cinchona bark)	Analgesic, anti-inflammatory, antimalarial	Cordell et al.,(2011)[34]
Terpenoids	Paclitaxel (Yew trees), Artemisinin (Artemisia annua)	Anticancer, anti-inflammatory, antimalarial	Dewick et al.,(2009)[35]
Polyphenols	Resveratrol (Grapes), Curcumin (Turmeric)	Antioxidant, anti-inflammatory, anticancer	Scalbert et al.,(2005)[36]
Peptides and Proteins	Insulin, Vancomycin	Hormonal regulation, antimicrobial	Chakrabarti et al.,(1996)[37]

IV. Medicinal Chemistry Approaches to Natural Product Derivatives

A. Structural Modifications:

- **Explanation:** Structural modifications involve making changes to the chemical structure of a natural product to improve its pharmacological properties. Medicinal chemists modify functional groups, stereochemistry, or overall molecular architecture to enhance

potency, selectivity, or bioavailability. This approach aims to optimize the compound for therapeutic use while retaining the essential pharmacophoric elements.[38]

B. Semi-synthesis:

- **Explanation:** Semi-synthesis involves the modification of a natural product by chemically manipulating its existing structure, often using readily available starting materials. This approach allows for the synthesis of analogs or derivatives with improved biological activities or pharmacokinetic profiles. Semi-synthesis is particularly valuable when the isolation of a sufficient quantity of a natural product is challenging.[39]

C. Total Synthesis:

- **Explanation:** Total synthesis involves the complete chemical construction of a natural product from simple starting materials. This approach allows for the creation of natural product derivatives with diverse structural variations. Total synthesis provides a powerful tool for exploring the structure-activity relationship (SAR) and developing analogs with improved biological properties.[40]

TABLE: 2 Some Success Stories in Drug Development

Drug	Properties	Indication/Use	Year of Approval	Reference
Aspirin	Analgesic, anti-inflammatory, antipyretic	Pain relief, inflammation, fever	1899	Vane et al.,(2003) [41]
Penicillin	Antibiotic, inhibits bacterial cell wall synthesis	Bacterial infections	1942	Abraham et al.,(1940) [42]
Statins (e.g., Atorvastatin)	Cholesterol-lowering, cardiovascular protection	Hypercholesterolemia, cardiovascular risk reduction	1987 (lovastatin)	Endo et al.,(1992)[43]
Imatinib (Gleevec)	Tyrosine kinase inhibitor, used in leukemia treatment	Chronic myeloid leukemia (CML)	2001	Druker et al.,(1996)[44]
Metformin	Antidiabetic, reduces blood glucose levels	Type 2 diabetes mellitus	1995	Bailey et al.,(1996)[45]
Rituximab	Monoclonal antibody,	Non-Hodgkin	1997 (non-	Maloney et

(Rituxan)	used in non-Hodgkin lymphoma treatment	lymphoma, rheumatoid arthritis	Hodgkin lymphoma)	al.,(1997)[46]
Enalapril	ACE inhibitor, used in hypertension	Hypertension, heart failure	1985	Cushman et al.,(1981)[47]
Paclitaxel (Taxol)	Anticancer, microtubule stabilizer	Ovarian, breast, and lung cancers	1992	Sciff et al.,(1979)[48]
Sildenafil (Viagra)	PDE5 inhibitor, used in erectile dysfunction	Erectile dysfunction	1998	Boolell et al.,(1996)[49]
Clopidogrel (Plavix)	Antiplatelet agent, used in preventing blood clots	Prevention of thrombosis, cardiovascular events	1997	Savi et al.,(2000) [50]
Warfarin	Anticoagulant, vitamin K antagonist	Thrombosis prevention, atrial fibrillation	1954	Link et al.,(1954][51]
Omeprazole (Prilosec)	Proton pump inhibitor	Gastroesophageal reflux disease (GERD), ulcers	1989	Shin et al.,(2008)[52]

Clozapine	Atypical antipsychotic	Schizophrenia	1975	Meltzer et al.,(1976)[53]
Zidovudine (AZT)	Antiretroviral, reverse transcriptase inhibitor	HIV/AIDS	1987	Mitsuya e al.,(1990)[54]
Levothyroxine	Thyroid hormone replacement	Hypothyroidism	1950	Braverman et al.,(1996)[55]
Cisplatin	Platinum-based chemotherapy	Various cancers, including testicular cancer	1978	Rosenberg et al.,(1965)[56]
Infliximab (Remicade)	Monoclonal antibody, tumor necrosis factor (TNF) inhibitor	Rheumatoid arthritis, Crohn's disease	1998	Present et al.,(1999)[57]
Donepezil (Aricept)	Acetylcholinesterase inhibitor	Alzheimer's disease	1996	Burn et al.,(1999)[58]

Oseltamivir (Tamiflu)	Neuraminidase inhibitor	Influenza	1999	Hayden et al.,(1997)[59]
Albuterol (Ventolin)	Beta-2 adrenergic agonist	Asthma, chronic obstructive pulmonary disease	1981	Murphy et al.,(2011)[60]

Challenges:

1. **Drug Resistance:**
    - **Challenge:** Pathogens and cancer cells can develop resistance to existing drugs.
    - **Solution:** Continuous research for novel drug targets, combination therapies, and understanding the molecular basis of resistance mechanisms.
2. **Safety and Toxicity:**
    - **Challenge:** Some drugs may have unexpected side effects or toxicities.
    - **Solution:** Comprehensive preclinical testing, advanced predictive models, and thorough safety assessments during clinical trials.
3. **High Development Costs:**
    - **Challenge:** Drug development is resource-intensive, with high costs and a lengthy timeline.
    - **Solution:** Increased collaboration, utilization of computational methods, and advancements in technology for more efficient drug discovery.
4. **Limited Target Specificity:**

- **Challenge:** Many drugs affect non-target tissues, leading to side effects.
- **Solution:** Targeted drug delivery systems, precision medicine approaches, and identifying more selective drug targets.

5. **Biological Complexity:**
    - **Challenge:** Understanding the intricate biological processes and interactions within the human body.
    - **Solution:** Systems biology approaches, advancements in omics technologies, and integration of big data for a holistic understanding.
6. **Regulatory Hurdles:**
    - **Challenge:** Stringent regulatory requirements can slow down drug approval processes.
    - **Solution:** Improved communication between regulators and researchers, streamlining regulatory pathways, and embracing innovative trial designs.
7. **Limited Oral Bioavailability:**
    - **Challenge:** Some drugs face challenges in reaching their target site in an active form.
    - **Solution:** Development of prodrugs, nanotechnology-based delivery systems, and formulation optimization for improved bioavailability.

Solutions:

1. **Personalized Medicine:**
    - **Solution:** Tailoring treatments based on individual patient characteristics, genetic makeup, and response patterns.
2. **Drug Repurposing:**

- **Solution:** Identifying new uses for existing drugs, accelerating development timelines, and reducing costs.

3. **Big Data and AI Integration:**

    - **Solution:** Utilizing artificial intelligence and machine learning for data analysis, pattern recognition, and predicting drug interactions.

4. **Collaborative Research Models:**

    - **Solution:** Encouraging collaboration between academia, pharmaceutical companies, and government institutions to pool resources and expertise.

5. **Patient-Centric Drug Development:**

    - **Solution:** Involving patients in the drug development process, considering patient preferences, and enhancing the patient experience during clinical trials.

6. **Advancements in Drug Delivery:**

    - **Solution:** Developing innovative drug delivery systems such as nanoparticles, liposomes, and implantable devices to enhance drug efficacy and reduce side effects.

7. **Digital Health Technologies:**

    - **Solution:** Incorporating digital tools, wearables, and remote monitoring to collect real-time patient data, improving clinical trial efficiency.

Future Trends in Medicinal Chemistry and Natural Products

Emerging Technologies:

- **Overview:** The convergence of various cutting-edge technologies is shaping the future of medicinal chemistry.
- **Trends:**

    1. **CRISPR Technology:** Precise genome editing for target validation and personalized medicine.[61]

2. **Nanomedicine:** Utilizing nanoscale materials for targeted drug delivery and imaging.[62]
3. **3D Printing:** Customized drug formulations and scaffolds for tissue engineering.[63]
4. **Machine Learning and AI:** Accelerating drug discovery, predicting drug interactions, and optimizing lead compounds.[64]

B. Integration of Computational Methods:

- **Overview:** Computational methods are increasingly integral in drug discovery and design.
- **Trends:**
    1. **Virtual Screening:** High-throughput computational screening of compound libraries.[65]
    2. **Structure-Based Drug Design:** Rational drug design based on molecular structures and interactions.[66]
    3. **Machine Learning:** Predicting biological activities, optimizing lead compounds, and identifying drug-target interactions.[67]
    4. **Quantum Computing:** Potential for solving complex problems in drug discovery with unparalleled computational power.[68]

C. Sustainability and Ethical Considerations:

- **Overview:** Increasing emphasis on sustainable and ethically sourced drug development.
- **Trends:**
    1. **Green Chemistry:** Minimizing environmental impact through eco-friendly synthesis methods.[69]
    2. **Ethical Sourcing of Natural Products:** Ensuring fair practices in obtaining raw materials.[70]
    3. **Social Responsibility:** Addressing healthcare disparities and focusing on neglected diseases.[71]
    4. **Circular Economy:** Integrating principles of recycling and waste reduction in the drug development process.[72]

Summary of Key Concepts:

- **Medicinal Chemistry Overview:** Medicinal chemistry plays a crucial role in drug discovery, involving the design, synthesis, and optimization of compounds for therapeutic use. It integrates principles from chemistry, biology, and pharmacology.
- **Natural Products in Medicine:** Natural products, derived from plants, microorganisms, and marine organisms, continue to be valuable sources of bioactive compounds. Their diverse chemical structures contribute to the development of novel drugs.
- **Basic Principles:** Understanding molecular structures, drug targets, pharmacokinetics, and pharmacodynamics is fundamental to medicinal chemistry. These principles guide the rational design and development of drugs.
- **Drug Design and Development:** The drug development process involves rational drug design, high-throughput screening, lead optimization, and extensive preclinical and clinical testing to ensure safety and efficacy.
- **Challenges and Solutions:** Drug development faces challenges such as resistance, safety concerns, and high costs. Solutions include personalized medicine, drug repurposing, and the integration of emerging technologies.
- **Natural Products Classification:** Natural products, including alkaloids, terpenoids, polyphenols, peptides, and proteins, exhibit diverse biological activities and are classified based on their chemical structures.
- **Extraction and Isolation Techniques:** Techniques such as chromatography, distillation, and extraction are employed to isolate bioactive compounds from natural sources.
- **Emerging Technologies:** Future trends in medicinal chemistry involve emerging technologies like CRISPR, nanomedicine, 3D printing, and advanced computational methods, shaping the landscape of drug discovery.
- **Integration of Computational Methods:** Computational approaches, including virtual screening, machine learning, and quantum computing, are becoming integral in drug discovery, enabling faster and more efficient processes.

- **Sustainability and Ethics:** There is a growing emphasis on sustainable practices, ethical sourcing of natural products, and addressing social responsibility in drug development to minimize environmental impact and promote fairness.

Implications for Future Research:

- **Advanced Drug Delivery Systems:** Research into innovative drug delivery systems, such as nanoparticles and targeted delivery, is critical for enhancing drug efficacy and reducing side effects.
- **Precision Medicine:** Future research should focus on advancing precision medicine approaches, tailoring treatments based on individual patient characteristics, genetics, and responses.
- **Green Chemistry and Circular Economy:** The incorporation of green chemistry principles and a circular economy in drug development will contribute to environmental sustainability and reduced waste.
- **Exploration of Untapped Natural Sources:** Future research should explore untapped natural sources for novel bioactive compounds, potentially uncovering new therapeutic agents.
- **Integration of AI and Quantum Computing:** Continued research into the integration of artificial intelligence and quantum computing holds promise for accelerating drug discovery and solving complex computational challenges.
- **Ethical Frameworks in Drug Development:** Research should delve into the establishment and implementation of ethical frameworks in drug development, ensuring fair practices and social responsibility.
- **Addressing Antibiotic Resistance:** Ongoing research is crucial for addressing antibiotic resistance by discovering new antibacterial agents and developing strategies to combat resistance mechanisms.

- **Inclusion of Patient Perspectives:** Future studies should actively involve patient perspectives in drug development, ensuring that treatments align with patient preferences and needs.

- **Global Collaboration:** Encouraging global collaboration among researchers, pharmaceutical companies, and regulatory bodies will facilitate knowledge sharing and accelerate the development of new drugs.

In conclusion, the dynamic field of medicinal chemistry and natural products continues to evolve, driven by advancements in technology, a growing emphasis on sustainability, and a commitment to addressing global health challenges. Future research holds the key to unlocking novel therapeutic agents, improving drug delivery systems, and fostering ethical and sustainable practices in the pursuit of enhanced healthcare outcomes.

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Conflict of interest

Authors declare no conflict of interest

References

1. Patrick, Graham L. (2009). "An Introduction to Medicinal Chemistry." Oxford University Press.
2. Thomas L. Lemke, David A. Williams, and Victoria F. Roche. (2017). "Foye's Principles of Medicinal Chemistry." Wolters Kluwer.
3. Newman, D. J., & Cragg, G. M. (2016). Natural Products as Sources of New Drugs from 1981 to 2014. Journal of Natural Products, 79(3), 629–661.
4. Butler, M. S., & Cooper, M. A. (2011). Antibiotics in the clinical pipeline at the end of 2011. The Journal of Antibiotics, 64(6), 413–425.
5. Koehn, F. E., & Carter, G. T. (2005). The evolving role of natural products in drug discovery. Nature Reviews Drug Discovery, 4(3), 206–220
6. Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. Environmental Health Perspectives, 109(Suppl 1), 69–75

7. Cordell, G. A. (2011). Introduction to Alkaloids: A Biographical Approach. In The Alkaloids: Chemistry and Biology (Vol. 68, pp. 1–37). Academic Press
8. Bodeker, G., & Ong, C. K. (2005). WHO Global Atlas of Traditional, Complementary and Alternative Medicine. World Health Organization
9. Mann, J. (2002). Secondary Metabolism and Medicinal Chemistry. In Natural Products: Their Chemistry and Biological Significance (pp. 369–412). Longman
10. Patrick, G. L. (2009). An Introduction to Medicinal Chemistry. Oxford University Press
11. Kar, A. (2017). Medicinal Chemistry. New Age International
12. Lemke, T. L., Williams, D. A., & Roche, V. F. (2017). Foye's Principles of Medicinal Chemistry. Wolters Kluwer
13. Katzung, B. G., & Trevor, A. J. (Eds.). (2018). Basic & Clinical Pharmacology. McGraw-Hill Education
14. Kar, A. (2017). Medicinal Chemistry. New Age International.
15. Patrick, G. L. (2009). An Introduction to Medicinal Chemistry. Oxford University Press
16. Treherne, J. M., & Turner, J. R. (Eds.). (2006). High-Throughput Screening in Drug Discovery. John Wiley & Sons
17. Lemke, T. L., Williams, D. A., & Roche, V. F. (2017). Foye's Principles of Medicinal Chemistry. Wolters Kluwer
18. Cordell, G. A. (2006). Introduction to Alkaloids. In Alkaloids: Chemistry and Biology (Vol. 63, pp. 1–44). Elsevier
19. Newman, D. J., & Cragg, G. M. (2020). Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. Journal of Natural Products, 83(3), 770–803.
20. Dewick, P. M. (2009). Medicinal Natural Products: A Biosynthetic Approach. John Wiley & Sons.
21. Butler, M. S., Robertson, A. A. B., & Cooper, M. A. (2014). Natural product and natural product derived drugs in clinical trials. Natural Product Reports, 31(11), 1612–1661
22. Atanasov, A. G., Waltenberger, B., Pferschy-Wenzig, E. M., Linder, T., Wawrosch, C., Uhrin, P., ... & Dirsch, V. M. (2015). Discovery and resupply of pharmacologically active plant-derived natural products: A review. Biotechnology Advances, 33(8), 1582–1614.

23. Newman, D. J., & Cragg, G. M. (2012). Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010. Journal of Natural Products, 75(3), 311–335
24. Berdy, J. (2005). Bioactive microbial metabolites. The Journal of Antibiotics, 58(1), 1–26.
25. Demain, A. L., & Sanchez, S. (2009). Microbial drug discovery: 80 years of progress. Journal of Antibiotics, 62(1), 5–16.
26. Blunt, J. W., Copp, B. R., Keyzers, R. A., Munro, M. H., & Prinsep, M. R. (2015). Marine natural products. Natural Product Reports, 32(2), 116–211.
27. Mayer, A. M. S., & Rodríguez, A. D. (2019). Marine pharmacology in 2016–2017: Marine compounds with antibacterial, antidiabetic, antifungal, anti-inflammatory, antiprotozoal, antituberculosis, antiviral, and anthelmintic activities; affecting the immune and nervous systems, and other miscellaneous mechanisms of action. Marine Drugs, 17(5), 310.
28. Stahl, E. (2013). Thin-Layer Chromatography: A Laboratory Handbook (Vol. 1). Springer Science & Business Media.
29. Sarker, S. D., & Nahar, L. (2012). An Introduction to Natural Products Isolation (2nd ed.). Springer
30. Hawthorne, S. B., & Miller, D. J. (1994). Supercritical fluid extraction: An overview. Analytical Chemistry, 66(7), 210A–217A
31. Snyder, L. R., Kirkland, J. J., & Dolan, J. W. (2010). Introduction to Modern Liquid Chromatography (3rd ed.). John Wiley & Sons
32. Winter, R., & Herzig, A. (1996). Fractionation of natural products. Journal of Chromatography A, 754(1-2), 279–285
33. Sarker, S. D., & Nahar, L. (2012). An Introduction to Natural Products Isolation (2nd ed.). Springer
34. Cordell, G. A. (2011). Introduction to Alkaloids: A Biographical Approach. In The Alkaloids: Chemistry and Biology (Vol. 68, pp. 1–37). Academic Press
35. Dewick, P. M. (2009). Medicinal Natural Products: A Biosynthetic Approach. John Wiley & Sons

36. Scalbert, A., Manach, C., Morand, C., Rémésy, C., & Jiménez, L. (2005). Dietary polyphenols and the prevention of diseases. Critical Reviews in Food Science and Nutrition, 45(4), 287–306
37. Chakrabarti, S., & Blundell, T. L. (1996). Bacterial Collagenase and Proteinase-Inhibitors—Structure-Function Relationships and Development of Novel Inhibitors. Philosophical Transactions of the Royal Society B: Biological Sciences, 351(1349), 147–161
38. Newman, D. J., & Cragg, G. M. (2012). Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010. Journal of Natural Products, 75(3), 311–335
39. Nicolaou, K. C., & Montagnon, T. (2008). Molecules That Changed the World. Wiley-VCH
40. Corey, E. J., & Cheng, X.-M. (1989). The Logic of Chemical Synthesis. John Wiley & Sons
41. Vane, J. R., & Botting, R. M. (2003). The mechanism of action of aspirin. Thrombosis Research, 110(5-6), 255–258
42. Abraham, E. P., Chain, E., Fletcher, C. M., et al. (1940). Further observations on penicillin. The Lancet, 236(6104), 177–189
43. Endo, A. (1992). The discovery and development of HMG-CoA reductase inhibitors. Journal of Lipid Research, 33(11), 1569–1582
44. Druker, B. J., Tamura, S., Buchdunger, E., et al. (1996). Effects of a selective inhibitor of the Abl tyrosine kinase on the growth of Bcr-Abl positive cells. Nature Medicine, 2(5), 561–566
45. Bailey, C. J., & Turner, R. C. (1996). Metformin. New England Journal of Medicine, 334(9), 574–579.
46. Maloney, D. G., Grillo-López, A. J., White, C. A., et al. (1997). IDEC-C2B8 (Rituximab) anti-CD20 monoclonal antibody therapy in patients with relapsed low-grade non-Hodgkin's lymphoma. Blood, 90(6), 2188–2195
47. Cushman, D. W., & Ondetti, M. A. (1981). History of the design of captopril and related inhibitors of angiotensin converting enzyme. Hypertension, 3(2), 2–8
48. Schiff, P. B., Fant, J., & Horwitz, S. B. (1979). Promotion of microtubule assembly in vitro by taxol. Nature, 277(5698), 665–667.

49. Boolell, M., Allen, M. J., Ballard, S. A., et al. (1996). Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. International Journal of Impotence Research, 8(2), 47–52
50. Savi, P., Pereillo, J. M., Uzabiaga, M. F., et al. (2000). Identification and biological activity of the active metabolite of clopidogrel. Thrombosis and Haemostasis, 84(05), 891–896
51. Link, K. P. (1954). The discovery of dicumarol and its sequels. Circulation, 9(1), 97–107
52. Shin, J. M., & Sachs, G. (2008). Pharmacology of proton pump inhibitors. Current Gastroenterology Reports, 10(6), 528–534
53. Meltzer, H. Y., & Stahl, S. M. (1976). The dopamine hypothesis of schizophrenia: a review. Schizophrenia Bulletin, 2(1), 19–76.
54. Mitsuya, H., Broder, S., & Yarchoan, R. (1990). Pathogenesis of HIV and therapy. In Progress in Drug Research/Fortschritte der Arzneimittelforschung/Progrès des recherches pharmaceutiques (Vol. 34, pp. 151–185).
55. Braverman, L. E., & Utiger, R. D. (1996). The Thyroid. A Fundamental and Clinical Text. Lippincott Williams & Wilkins
56. Rosenberg, B., VanCamp, L., & Krigas, T. (1965). Inhibition of cell division in Escherichia coli by electrolysis products from a platinum electrode. Nature, 205(4972), 698–699
57. Present, D. H., Rutgeerts, P., Targan, S., et al. (1999). Infliximab for the treatment of fistulas in patients with Crohn's disease. New England Journal of Medicine, 340(18), 1398–1405
58. Burns, A., Rossor, M., Hecker, J., Gauthier, S., Petit, H., Möller, H. J., & Rogers, S. L. (1999). The effects of donepezil in Alzheimer's disease—results from a multinational trial. Dementia and Geriatric Cognitive Disorders, 10(3), 237–244
59. Hayden, F. G., Osterhaus, A. D., Treanor, J. J., et al. (1997). Efficacy and safety of the neuraminidase inhibitor zanamivir in the treatment of influenzavirus infections. New England Journal of Medicine, 337(13), 874–880
60. Murphy, K. R., & Meltzer, E. O. (2011). Blinded, randomized, crossover study to investigate potential effects of inhaled formoterol/budesonide and salmeterol/fluticasone on cardiovascular function in healthy subjects. Clinical Therapeutics, 33(3), 371–387

61. Makarova, K. S., Haft, D. H., Barrangou, R., et al. (2011). Evolution and classification of the CRISPR-Cas systems. Nature Reviews Microbiology, 9(6), 467–477.
62. Ventola, C. L. (2017). Progress in Nanomedicine: Approved and Investigational Nanodrugs. P&T: A Peer-Reviewed Journal for Formulary Management, 42(12), 742–755.
63. Ozbolat, I. T., & Hospodiuk, M. (2016). Current advances and future perspectives in extrusion-based bioprinting. Biomaterials, 76, 321–343.
64. Schneider, P., Walters, W. P., & Plowright, A. T. (2019). SWEETLEAD: an in silico database of approved drugs, regulated chemicals, and herbal isolates for computer-aided drug discovery. PLoS ONE, 14(11), e0225507
65. Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J. (2004). Docking and scoring in virtual screening for drug discovery: methods and applications. Nature Reviews Drug Discovery, 3(11), 935–949.
66. Leach, A. R., & Gillet, V. J. (2007). An Introduction to Chemoinformatics. Springer Science & Business Media.
67. Ching, T., Himmelstein, D. S., Beaulieu-Jones, B. K., et al. (2018). Opportunities and obstacles for deep learning in biology and medicine. Journal of The Royal Society Interface, 15(141), 20170387.
68. Cao, Y., & Gao, X. (2018). Quantum machine learning for quantum chemistry. Physical Chemistry Chemical Physics, 20(41), 26220–26228
69. Anastas, P. T., & Warner, J. C. (1998). Green Chemistry: Theory and Practice. Oxford University Press.
70. Newman, D. J., & Cragg, G. M. (2020). Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. Journal of Natural Products, 83(3), 770–803.
71. Pammolli, F., Magazzini, L., & Riccaboni, M. (2011). The productivity crisis in pharmaceutical R&D. Nature Reviews Drug Discovery, 10(6), 428–438.
72. Guzman, D., Brase, S., & Grepioni, F. (2019). Green Chemistry Metrics beyond Reaction Performance: A Perspective. Molecules, 24(3), 526