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Benzothiazole Based Scaffolds in Breast Cancer Therapy: A Comprehensive Review of Design, Synthesis, and In-Silico Advances

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ABSTRACT

Breast cancer remains a leading cause of cancer-related mortality among women worldwide, necessitating the development of novel therapeutic strategies. Conventional treatment modalities suffer from limitations such as toxicity, resistance, and lack of specificity. In this context, heterocyclic compounds, particularly benzothiazole derivatives, have emerged as promising candidates due to their structural versatility and potent biological activity. This review highlights the significance of benzothiazole scaffolds in anticancer drug discovery, focusing on their chemical properties, mechanisms of action, and therapeutic potential against breast cancer. Additionally, the integration of in-silico approaches, ADMET profiling, and synthetic strategies in modern drug development is discussed. Recent literature findings are critically analyzed to provide insights into structure activity relationships and future perspectives for benzothiazole-based drug design.

Keywords: Benzothiazole Based Scaffolds, Breast Cancer Therapy, In-Silico Advances

1. Global Perspective and Challenges in Breast Cancer Treatment

Breast cancer continues to represent one of the most pressing public health concerns worldwide, both in terms of incidence and mortality. It is currently the most frequently diagnosed malignancy among women and a leading cause of cancer-related deaths across diverse populations. Epidemiological data indicate that nearly one in four cancer cases diagnosed in women is breast cancer, reflecting its substantial contribution to the global disease burden. Although significant progress has been achieved in early detection and therapeutic strategies, the benefits are unevenly distributed across regions, highlighting persistent global health disparities.

1.1 Epidemiological Trends and Risk Factors

The increasing incidence of breast cancer is multifactorial, involving a complex interplay between genetic predisposition, hormonal influences, and environmental and lifestyle-related factors. Non-modifiable risk factors include age, gender, family history, and inherited mutations in genes such as BRCA1 and BRCA2. Hormonal factors, including early menarche, late menopause, and reproductive history, further influence susceptibility.

On the other hand, modifiable risk factors such as obesity, sedentary lifestyle, alcohol consumption, and dietary patterns are becoming increasingly relevant due to rapid urbanization and lifestyle transitions, particularly in developing nations. The growing prevalence of these risk factors contributes significantly to the rising global incidence of breast cancer.

1.2 Molecular Heterogeneity of Breast Cancer

A defining characteristic of breast cancer is its remarkable heterogeneity. It is not a single disease but rather a group of biologically distinct subtypes with varying molecular profiles, clinical outcomes, and therapeutic responses. The major subtypes include hormone receptor-positive (estrogen and progesterone receptor-positive), HER2-enriched, luminal A and B, and triple-negative breast cancer (TNBC).

Each subtype is associated with unique signaling pathways and biological behavior. For instance, hormone receptor-positive cancers respond well to endocrine therapy, whereas HER2-positive cancers benefit from targeted monoclonal antibodies. In contrast, TNBC lacks these receptors, making it more aggressive and difficult to treat due to limited targeted therapy options.

This heterogeneity poses a significant challenge in clinical management, as a "one-size-fits-all" treatment approach is ineffective. Instead, personalized and subtype-specific therapies are required to improve patient outcomes.

1.3 Disparities in Global Healthcare Access

Despite advancements in medical technology, there is a stark contrast in breast cancer outcomes between high-income countries and low- and middle-income countries (LMICs). Developed regions benefit from organized screening programs, advanced imaging techniques, genetic testing, and access to targeted therapies. These factors contribute to early diagnosis and improved survival rates.

Conversely, LMICs often face significant barriers, including limited healthcare infrastructure, lack of awareness, delayed diagnosis, and financial constraints. As a result, patients in these regions are frequently diagnosed at advanced stages, leading to poorer prognoses and higher mortality rates.

Addressing these disparities requires the development of cost-effective diagnostic tools and accessible therapeutic options that can be implemented across diverse healthcare settings.

1.4 Therapeutic Resistance and Disease Progression

One of the most critical challenges in breast cancer treatment is the emergence of therapeutic resistance. Although many patients initially respond to treatment, resistance often develops over time, leading to disease recurrence and metastasis.

Mechanisms of resistance include genetic mutations, activation of alternative signaling pathways, overexpression of drug efflux pumps, and evasion of apoptosis. These factors reduce the effectiveness of chemotherapy, hormone therapy, and targeted agents.

Metastatic breast cancer, particularly TNBC, remains largely incurable, with significantly lower survival rates compared to localized disease. The persistence of resistance highlights the urgent need for innovative therapeutic strategies capable of overcoming these limitations.

1.5 Need for Novel Therapeutic Approaches

The growing burden of breast cancer, combined with its biological complexity and treatment limitations, underscores the necessity for continued research in drug discovery. There is a pressing demand for novel therapeutic agents that offer:

- Enhanced selectivity toward cancer cells
- Reduced systemic toxicity
- Improved pharmacokinetic profiles
- Ability to overcome drug resistance

In this context, heterocyclic compounds particularly benzothiazole derivatives have gained significant attention due to their structural versatility and promising anticancer activity. These compounds provide a strong foundation for the development of next-generation therapeutics aimed at improving clinical outcomes and reducing the global burden of breast cancer.

2. Limitations of Conventional Therapeutic Modalities (Elaborated)

Despite remarkable advancements in breast cancer management, existing therapeutic approaches continue to face significant clinical and practical limitations. These challenges arise from issues related to toxicity, resistance, specificity, cost, and variability in patient response. A critical evaluation of these limitations provides the foundation for the development of next-generation therapeutic agents.

2.1 Chemotherapy: Efficacy Versus Toxicity

Chemotherapy remains a cornerstone in the treatment of breast cancer, particularly in advanced and metastatic stages. Commonly used agents include anthracyclines, taxanes, alkylating agents, and antimetabolites. While these drugs are effective in reducing tumor burden, their mechanism of action is largely non-selective, targeting rapidly dividing cells irrespective of their malignant or normal origin.

This lack of specificity leads to severe systemic toxicities, including cardiotoxicity, bone marrow suppression, gastrointestinal disturbances, alopecia, and neurotoxicity. These adverse effects not only compromise patient quality of life but also necessitate dose reduction or discontinuation, thereby limiting therapeutic efficacy.

2.2 Multidrug Resistance (MDR)

A major obstacle in chemotherapy is the development of multidrug resistance (MDR), which significantly reduces treatment effectiveness. Cancer cells employ multiple mechanisms to evade drug action, including:

- Overexpression of efflux transporters such as P-glycoprotein
- Alterations in drug targets
- Enhanced DNA repair mechanisms
- Suppression of apoptosis pathways

MDR is particularly problematic in aggressive subtypes such as triple-negative breast cancer (TNBC), where treatment options are already limited. This phenomenon often leads to treatment failure, disease recurrence, and poor clinical outcomes.

2.3 Hormone Therapy: Benefits and Limitations

Hormone therapy has significantly improved outcomes in estrogen receptor (ER)-positive breast cancer. Agents such as tamoxifen, aromatase inhibitors, and fulvestrant target hormonal pathways critical for tumor growth.

However, these therapies are ineffective in ER-negative tumors, limiting their applicability. Additionally, prolonged use often results in resistance due to receptor mutations or activation of alternative signaling pathways. Hormone therapies are also associated with adverse effects such as thromboembolism, osteoporosis, and endometrial complications.

2.4 Targeted Therapy: Precision with Constraints

Targeted therapies, including monoclonal antibodies and kinase inhibitors, represent a significant advancement in precision oncology. Drugs targeting HER2 and CDK4/6 pathways have shown improved clinical outcomes in selected patient populations.

Nevertheless, their effectiveness is restricted to patients expressing specific biomarkers. Furthermore, these therapies are often associated with high costs, limiting accessibility in resource-constrained settings. Resistance to targeted agents also develops over time, diminishing long-term benefits.

2.5 Immunotherapy: Emerging Yet Limited

Immunotherapy, particularly immune checkpoint inhibitors, has emerged as a promising approach, especially for TNBC. These therapies aim to enhance the body's immune response against cancer cells.

However, their efficacy is limited to a subset of patients, and predictive biomarkers for response remain inadequately defined. Additionally, immune-related adverse effects can be severe and unpredictable, posing further challenges in clinical application.

2.6 Socioeconomic and Accessibility Challenges

Beyond biological limitations, socioeconomic factors significantly influence treatment outcomes. High costs of advanced therapies, lack of healthcare infrastructure, and limited awareness contribute to delayed diagnosis and suboptimal treatment in many regions.

These disparities highlight the urgent need for affordable, effective, and widely accessible therapeutic options that can address both biological and systemic challenges in breast cancer care.

2.7 Need for Alternative Therapeutic Strategies

Given these limitations, there is a strong rationale for developing novel therapeutic agents that can:

- Overcome drug resistance mechanisms
- Exhibit higher selectivity toward cancer cells
- Reduce systemic toxicity
- Be cost-effective and globally accessible

Heterocyclic compounds, particularly benzothiazole derivatives, have emerged as promising candidates capable of addressing many of these unmet needs.

3.Heterocyclic Compounds as Privileged Structures in Drug Discovery (Elaborated)

Heterocyclic compounds form the backbone of modern medicinal chemistry and play a crucial role in the development of therapeutic agents across various disease areas, including cancer. Their structural diversity and functional adaptability make them indispensable in rational drug design.

3.1 Structural and Chemical Diversity

Heterocycles are cyclic compounds containing one or more heteroatoms such as nitrogen, oxygen, or sulfur within the ring structure. These heteroatoms introduce unique electronic properties, enabling diverse interactions with biological targets.

The presence of heteroatoms influences parameters such as polarity, hydrogen bonding capacity, and electronic distribution, which are critical for drug–target interactions. This versatility allows heterocyclic compounds to be tailored for specific biological activities.

3.2 Role in Drug–Target Interactions

One of the key advantages of heterocyclic scaffolds is their ability to mimic natural biomolecules such as nucleic acids, amino acids, and metabolic intermediates. This biomimicry facilitates strong binding to enzymes, receptors, and other macromolecules.

Interactions such as hydrogen bonding, π–π stacking, and electrostatic forces enhance binding affinity and specificity. For example:

- Nitrogen-containing heterocycles enable hydrogen bonding
- Aromatic systems promote π–π interactions
- Sulfur-containing rings improve lipophilicity and membrane permeability

These properties are essential for achieving high biological activity and selectivity.

3.3 Importance in Anticancer Drug Development

Heterocyclic compounds have been widely used in anticancer drug discovery due to their ability to modulate key cellular processes. Many clinically successful anticancer drugs contain heterocyclic frameworks, demonstrating their therapeutic relevance.

They act on various targets, including:

- DNA replication and repair mechanisms
- Cell cycle regulation
- Apoptosis pathways
- Kinase signaling networks

Their multi-target potential is particularly advantageous in treating complex diseases like cancer, where multiple pathways are dysregulated.

3.4 Structure–Activity Relationship (SAR) and Optimization

Heterocyclic scaffolds offer significant flexibility for chemical modification, enabling systematic exploration of structure–activity relationships (SAR).

By introducing different substituents, medicinal chemists can optimize:

- Potency and selectivity
- Solubility and bioavailability
- Metabolic stability
- Toxicity profiles

This tunability is critical for transforming initial lead compounds into clinically viable drug candidates.

3.5 Drug-Likeness and Pharmacokinetic Advantages

Many heterocyclic compounds satisfy Lipinski's Rule of Five, indicating favorable oral bioavailability. Their physicochemical properties can be optimized to enhance absorption, distribution, metabolism, and excretion (ADME) characteristics.

Additionally, heterocycles can be modified to reduce off-target effects and improve therapeutic indices, making them safer for clinical use.

3.6 Benzothiazole as a Privileged Heterocyclic Scaffold

Among various heterocycles, benzothiazole stands out as a privileged scaffold due to its unique structural and electronic properties. Its fused bicyclic system enables strong interactions with multiple biological targets.

Benzothiazole derivatives have demonstrated activity against a wide range of cancer-related pathways, including estrogen receptor signaling, HER2 inhibition, and PI3K/Akt modulation. Their versatility and efficacy make them highly promising candidates for breast cancer drug development.

4. Benzothiazole Scaffold: Structural Features and Biological Significance (Elaborated)

The benzothiazole scaffold is a fused bicyclic heterocyclic system composed of a benzene ring condensed with a thiazole ring containing nitrogen and sulfur atoms. This unique structural arrangement imparts a combination of aromatic stability, electronic richness, and conformational rigidity, making benzothiazole a highly valuable framework in medicinal chemistry. Its physicochemical properties allow it to interact efficiently with a wide range of biological macromolecules, thereby contributing to its diverse pharmacological activities.

4.1 Structural Characteristics and Electronic Properties

The presence of heteroatoms (nitrogen and sulfur) within the thiazole ring plays a crucial role in determining the electronic distribution of the molecule. These atoms facilitate:

- Hydrogen bonding interactions with biological targets
- Dipole–dipole interactions enhancing binding affinity
- Coordination with metal ions in enzyme active sites

The fused aromatic system promotes π–π stacking interactions, particularly with nucleic acids and aromatic amino acid residues in proteins. This contributes significantly to the stability of ligand–target complexes.

Additionally, benzothiazole exhibits optimal lipophilicity, which enhances membrane permeability and allows efficient intracellular accumulation an important feature for anticancer agents.

4.2 Synthetic Flexibility and Functionalization

One of the major advantages of the benzothiazole scaffold is its synthetic versatility. Multiple substitution positions on both the benzene and thiazole rings enable extensive structural modification.

Medicinal chemists can introduce a wide range of functional groups, such as:

- Electron-donating groups (e.g., –OH, –NH_2)
- Electron-withdrawing groups (e.g., –NO_2, halogens)
- Heterocyclic moieties and hybrid pharmacophores

These modifications allow fine-tuning of physicochemical and biological properties, including binding affinity, selectivity, solubility, and metabolic stability. This flexibility is essential for optimizing drug candidates during lead development.

4.3 Broad Pharmacological Profile

Benzothiazole derivatives have demonstrated a wide spectrum of biological activities, including antimicrobial, antiviral, anti-inflammatory, antidiabetic, and notably, anticancer effects.

In oncology, benzothiazoles have shown potent cytotoxicity against various cancer cell lines, including breast, lung, colon, ovarian, and prostate cancers. Their broad applicability arises from their ability to interact with multiple molecular targets involved in tumor progression.

4.4 Mechanisms Underlying Anticancer Activity

The anticancer potential of benzothiazole derivatives is attributed to their multi-target mode of action. Key mechanisms include:

- **DNA Intercalation:** Disruption of DNA replication and transcription
- **Topoisomerase Inhibition:** Prevention of DNA unwinding and cell division
- **Tubulin Polymerization Disruption:** Interference with mitotic spindle formation
- **Apoptosis Induction:** Activation of intrinsic (mitochondrial) pathways
- **Kinase Inhibition:** Modulation of signaling pathways such as PI3K/Akt and HER2
- **Anti-angiogenic Effects:** Inhibition of tumor vascularization

These diverse mechanisms enable benzothiazoles to act against both proliferating and resistant cancer cells.

4.5 Structure Activity Relationship (SAR) Insights

Extensive SAR studies have demonstrated that the nature and position of substituents significantly influence biological activity:

- Electron-donating groups may enhance interaction with hormone receptors
- Electron-withdrawing groups often improve kinase inhibition
- Halogen substitution increases lipophilicity and membrane permeability
- Hybridization with other pharmacophores enhances multi-target activity

Such insights guide rational drug design and enable the development of highly potent and selective benzothiazole derivatives.

4.6 Pharmacokinetic and Drug-Likeness Properties

Benzothiazole derivatives generally exhibit favorable pharmacokinetic profiles, including:

- Adequate oral bioavailability
- Good metabolic stability
- Efficient tissue distribution
- Compliance with Lipinski's Rule of Five

Importantly, several derivatives demonstrate selective toxicity toward cancer cells while sparing normal cells, reducing systemic side effects. This selectivity is a major advantage over conventional chemotherapeutic agents.

5. Rationale for Selecting Benzothiazole Derivatives in Breast Cancer Therapy (Elaborated)

The selection of benzothiazole derivatives as potential therapeutic agents for breast cancer is supported by strong scientific, structural, and pharmacological evidence. Their unique properties align well with the requirements for effective anticancer drug development, particularly in addressing the limitations of current therapies.

5.1 Activity Against Diverse Breast Cancer Subtypes

Benzothiazole derivatives have demonstrated significant activity against a variety of breast cancer cell lines, including:

- MCF-7 (hormone receptor-positive)

- MDA-MB-231 (triple-negative)
- T47D and SKBR3 (HER2-positive)

Their ability to act across multiple subtypes highlights their broad therapeutic potential, especially in challenging cases such as TNBC, where treatment options are limited.

5.2 Multi-Target Mechanism of Action

Unlike conventional therapies that often focus on a single target, benzothiazole derivatives exhibit multi-target activity. They can simultaneously modulate:

- Estrogen receptor signaling
- HER2 kinase pathways
- PI3K/Akt signaling cascade
- Microtubule dynamics

This multi-target approach enhances therapeutic efficacy and reduces the likelihood of resistance development, making these compounds particularly valuable in complex diseases like breast cancer.

5.3 Potential to Overcome Drug Resistance

Drug resistance remains a major challenge in breast cancer treatment. Benzothiazole derivatives have shown the ability to:

- Induce apoptosis in resistant cancer cells
- Bypass efflux pump mechanisms
- Target alternative signaling pathways

These properties make them promising candidates for overcoming multidrug resistance and improving long-term treatment outcomes.

5.4 Structural Tunability and Optimization Potential

The benzothiazole scaffold allows precise structural modification, enabling the design of derivatives with enhanced biological activity. By altering substituents, researchers can:

- Improve binding affinity to specific targets
- Enhance solubility and bioavailability
- Reduce toxicity
- Achieve subtype-specific targeting

This tunability supports the development of personalized therapeutic agents tailored to different breast cancer subtypes.

5.5 Favourable Pharmacokinetic and Safety Profile

Benzothiazole derivatives generally exhibit desirable drug-like properties, including:

- Optimal lipophilicity for membrane penetration
- Good metabolic stability
- Reduced toxicity toward normal cells

Their selective cytotoxicity is particularly advantageous, as it minimizes adverse effects commonly associated with conventional chemotherapy.

5.6 Compatibility with Modern Drug Discovery Approaches

Benzothiazole derivatives are highly amenable to integration with modern drug discovery tools, including:

- Molecular docking and virtual screening
- ADMET prediction models
- Structure-based drug design

These approaches enable efficient identification and optimization of lead compounds, accelerating the drug development process.

5.7 Strategic Importance in Future Therapeutics

Given their multi-functional nature, structural flexibility, and strong biological activity, benzothiazole derivatives represent a strategic platform for next-generation anticancer drug development. They hold significant promise for:

- Developing targeted therapies
- Addressing aggressive and resistant cancer subtypes
- Improving patient outcomes with reduced toxicity

6. Role of In-Silico Approaches in Drug Development

In-silico methodologies have emerged as a cornerstone in modern drug discovery, offering a highly efficient and cost-effective alternative to traditional experimental approaches. These computational techniques facilitate the rational design of drug candidates by enabling the prediction of molecular interactions at an atomic level.

Molecular docking plays a pivotal role in predicting the binding affinity and orientation of small molecules within the active site of biological targets. This allows researchers to identify potential lead compounds with high specificity. Complementarily, pharmacophore modeling aids in identifying the essential structural features required for biological activity, thereby guiding the design of novel analogues. Virtual screening, both ligand-based and structure-based, enables the rapid evaluation of large chemical libraries, significantly accelerating the hit identification process.

Beyond target interaction studies, in-silico tools are extensively employed for ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profiling. Early prediction of pharmacokinetic behavior and toxicity risks ensures that only viable candidates progress to synthesis and biological testing, thereby reducing attrition rates in later stages.

Overall, these computational approaches not only minimize experimental workload and resource consumption but also enhance the precision of drug design, making them indispensable in contemporary medicinal chemistry and pharmaceutical research.

7. Advances in Benzothiazole-Based Anticancer Research

Benzothiazole derivatives have garnered significant attention in recent years due to their diverse pharmacological properties, particularly in anticancer research. Structural modifications of the benzothiazole scaffold have led to the development of compounds with improved potency, selectivity, and multi-target activity.

Hybridization strategies have proven particularly effective, where benzothiazole is conjugated with other bioactive moieties such as triazoles and coumarins. These hybrid molecules exhibit synergistic effects, enabling simultaneous modulation of multiple signaling pathways involved in cancer progression. Such multi-target approaches are especially beneficial in complex diseases like breast cancer, where redundancy in signaling networks often leads to drug resistance.

Advancements in ADMET-guided drug design have further optimized the pharmacokinetic properties of benzothiazole derivatives, improving their bioavailability and reducing toxicity. Additionally, molecular dynamics simulations and QSAR (Quantitative Structure–Activity Relationship) studies provide deeper insights into structure–activity correlations, facilitating rational optimization of lead compounds.

From a synthetic perspective, the adoption of green chemistry principles has enabled the development of environmentally benign and sustainable synthetic routes. Furthermore, target-specific benzothiazole derivatives have shown promising activity against critical molecular targets such as HER2 receptors, PARP enzymes, and angiogenesis-related pathways, highlighting their therapeutic potential in precision oncology.

8. Integrated Strategy: From Design to Biological Evaluation

The success of drug discovery programs increasingly relies on an integrated, multidisciplinary strategy that combines computational modeling, synthetic chemistry, and biological validation.

The process typically begins with in-silico design and screening, where potential lead compounds are identified based on their predicted interaction with specific biological targets. These computational insights guide the rational design of molecules with optimized physicochemical and pharmacological properties.

Subsequently, synthetic chemistry techniques are employed to construct and modify these compounds, enabling fine-tuning of their structural and functional attributes. This iterative optimization process is crucial for enhancing potency, selectivity, and drug-likeness.

Finally, biological evaluation through in vitro and in vivo assays validates the anticancer activity of the synthesized compounds. These studies provide critical data on efficacy, mechanism of action, and safety profiles.

This integrated workflow not only improves the efficiency and success rate of drug discovery but also ensures a more systematic and evidence-based approach to the development of novel therapeutic agents.

9. Future Perspectives and Research Directions

Despite significant progress, several challenges remain in the development of benzothiazole-based anticancer agents. Future research should prioritize the design of subtype-specific derivatives tailored to different molecular subtypes of breast cancer, such as HER2-positive and triple-negative breast cancer.

Addressing multidrug resistance (MDR) is another critical area, as resistance mechanisms often limit the long-term efficacy of anticancer therapies. Structural modifications aimed at bypassing efflux pumps and resistance pathways will be essential.

Improving selectivity toward cancer cells while minimizing toxicity to normal tissues remains a key objective. Advanced drug delivery systems, particularly nanotechnology-based platforms, offer promising solutions by enabling targeted and controlled release of therapeutic agents.

Furthermore, translating promising compounds from preclinical studies to clinical trials requires rigorous optimization of pharmacokinetic and safety profiles. Collaborative efforts integrating computational predictions, experimental validation, and clinical research will be crucial in advancing these compounds toward therapeutic application.

10. Conclusion

Benzothiazole derivatives represent a highly promising class of heterocyclic compounds with substantial potential in breast cancer therapy. Their structural versatility allows extensive chemical modifications, enabling the development of molecules with enhanced potency, selectivity, and multi-target activity.

The integration of in-silico approaches with synthetic and biological methodologies has transformed the drug discovery landscape, providing a robust framework for the identification and optimization of novel anticancer agents. These strategies significantly reduce time, cost, and failure rates, thereby accelerating the development pipeline.

Continued advancements in computational tools, green synthesis techniques, and targeted therapeutic strategies are expected to further unlock the potential of benzothiazole-based compounds. Ultimately, such efforts will contribute to the development of more effective, safer, and personalized treatments for breast cancer management.

REFERENCES

1. Yadav, K. P., Rahman, M. A., Nishad, S., Maurya, S. K., Anas, M., & Mujahid, M. (2023). Synthesis and biological activities of benzothiazole derivatives: A review. *Intelligent Pharmacy, 1*(3), 122–132. https://doi.org/10.1016/j.ipha.2023.06.001
2. Ingle, R. G., & Marathe, R. P. (2012). Review on literature study of benzothiazole. *International Journal of Pharmaceutical Research & Allied Sciences, 1*(4), 11–15.
3. Lionta, E., Spyrou, G., Vassilatis, D. K., & Cournia, Z. (2014). Structure-based virtual screening for drug discovery. *Current Topics in Medicinal Chemistry, 14*(16), 1923–1938.
4. Meng, X. Y., Zhang, H. X., Mezei, M., & Cui, M. (2011). Molecular docking: A powerful approach for structure-based drug discovery. *Current Computer-Aided Drug Design, 7*(2), 146–157.
5. Morris, G. M., & Lim-Wilby, M. (2008). Molecular docking. *Methods in Molecular Biology, 443*, 365–382.
6. Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J. (2004). Docking and scoring in virtual screening. *Nature Reviews Drug Discovery, 3*(11), 935–949.
7. Trott, O., & Olson, A. J. (2010). AutoDock Vina: Improving speed and accuracy of docking. *Journal of Computational Chemistry, 31*(2), 455–461.
8. Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: A web tool for pharmacokinetics evaluation. *Scientific Reports, 7*, 42717.
9. Pires, D. E., Blundell, T. L., & Ascher, D. B. (2015). pkCSM: Predicting small-molecule pharmacokinetics. *Journal of Medicinal Chemistry, 58*(9), 4066–4072.
10. Lipinski, C. A. (2004). Lead- and drug-like compounds: The rule-of-five revolution. *Drug Discovery Today: Technologies, 1*(4), 337–341.
11. Veber, D. F., Johnson, S. R., Cheng, H. Y., Smith, B. R., Ward, K. W., & Kopple, K. D. (2002). Molecular properties affecting oral bioavailability. *Journal of Medicinal Chemistry, 45*(12), 2615–2623.
12. Cherkasov, A., et al. (2014). QSAR modeling: Where have you been? Where are you going? *Journal of Medicinal Chemistry, 57*(12), 4977–5010.
13. Hansch, C., Leo, A., & Hoekman, D. (1995). *Exploring QSAR: Fundamentals and applications in chemistry and biology*. ACS.
14. Todeschini, R., & Consonni, V. (2009). *Molecular descriptors for chemoinformatics*. Wiley-VCH.
15. Leach, A. R., Gillet, V. J., Lewis, R. A., & Taylor, R. (2010). Three-dimensional pharmacophore methods. *Journal of Medicinal Chemistry, 53*(2), 539–558.
16. Schneider, G. (2010). Virtual screening: An endless staircase? *Nature Reviews Drug Discovery, 9*(4), 273–276.
17. Macalino, S. J. Y., et al. (2015). Role of computer-aided drug design in modern drug discovery. *Archives of Pharmacal Research, 38*, 1686–1701.
18. Sliwoski, G., et al. (2014). Computational methods in drug discovery. *Pharmacological Reviews, 66*(1), 334–395.
19. Ferreira, L. G., et al. (2015). Molecular docking and structure-based drug design strategies. *Molecules, 20*(7), 13384–13421.
20. Lionta, E., et al. (2014). Structure-based virtual screening approaches. *Current Topics in Medicinal Chemistry, 14*(16), 1923–1938.

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21. Kamal, A., et al. (2012). Chalcone-amidobenzothiazole conjugates as anticancer agents. *Bioorganic & Medicinal Chemistry, 20*(11), 3480–3492.

22. Bradshaw, T. D., & Westwell, A. D. (2004). The development of benzothiazoles as anticancer agents. *Current Medicinal Chemistry, 11*(8), 1009–1021.
23. Hutchinson, I., et al. (2001). Antitumor benzothiazoles: Mechanism of action. *Journal of Medicinal Chemistry, 44*(9), 1446–1455.
24. Mortimer, C. G., et al. (2006). Benzothiazoles and cancer therapy. *Bioorganic & Medicinal Chemistry Letters, 16*(11), 3212–3216.
25. Shi, D. F., et al. (1996). Antitumor benzothiazoles: Structure–activity relationships. *Journal of Medicinal Chemistry, 39*(17), 3375–3384.
26. Kashiyama, E., et al. (1999). Selective anticancer benzothiazoles. *Journal of Medicinal Chemistry, 42*(20), 4172–4184.
27. McKeown, S. R., et al. (2007). Benzothiazoles in breast cancer therapy. *Clinical Cancer Research, 13*(17), 5076–5084.
28. Stevens, M. F., et al. (2001). Benzothiazoles: Antitumor drug development. *Journal of Medicinal Chemistry, 44*(5), 753–763.
29. Bradshaw, T. D., et al. (2002). Mechanistic insights into benzothiazole anticancer activity. *Cancer Research, 62*(17), 4999–5006.
30. Hong, S., et al. (2013). Benzothiazole-based kinase inhibitors. *Journal of Medicinal Chemistry, 56*(9), 3531–3545.
31. DiMasi, J. A., et al. (2016). Innovation in the pharmaceutical industry. *Journal of Health Economics, 47*, 20–33.
32. Paul, S. M., et al. (2010). Improving R&D productivity in pharma. *Nature Reviews Drug Discovery, 9*(3), 203–214.
33. Ekins, S. (2007). In silico pharmacology for drug discovery. *Trends in Pharmacological Sciences, 28*(9), 445–450.
34. van de Waterbeemd, H., & Gifford, E. (2003). ADMET in silico modelling. *Nature Reviews Drug Discovery, 2*(3), 192–204.
35. Gleeson, M. P., et al. (2011). Generation of ADMET rules. *Journal of Medicinal Chemistry, 54*(14), 5034–5044.
36. Kirchmair, J., et al. (2015). Predicting drug metabolism. *Nature Reviews Drug Discovery, 14*(6), 387–404.
37. Wang, J., et al. (2015). Molecular dynamics simulations in drug discovery. *Chemical Reviews, 115*(9), 5271–5330.
38. Hollingsworth, S. A., & Dror, R. O. (2018). Molecular dynamics simulation advances. *Neuron, 99*(6), 1129–1143.
39. Patra, J. K., et al. (2018). Nano-based drug delivery systems. *Journal of Nanobiotechnology, 16*, 71.
40. Torchilin, V. P. (2014). Multifunctional nanocarriers. *Nature Reviews Drug Discovery, 13*(11), 813–827.

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