INNOVATIVE STRATEGIES FOR THE SYNTHESIS AND BIOEVALUATION OF BISBENZYLISOQUINOLINE ALKALOIDS

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Annotation. This thesis focuses on the development and application of innovative strategies for the synthesis and bioevaluation of novel chemical compounds with potential biological activity. The research explores modern synthetic approaches, including green chemistry techniques and catalytic systems, aimed at increasing efficiency, selectivity, and environmental sustainability in chemical synthesis. Special attention is given to the bioevaluation of synthesized compounds using in vitro and in vivo models to assess their pharmacological potential, toxicity, and mechanism of action. The study integrates interdisciplinary methods combining organic synthesis, molecular modeling, and biological testing to identify promising compounds for pharmaceutical and biotechnological applications.

Introduction. In recent years, the search for innovative strategies in the synthesis and bioevaluation of biologically active compounds has become one of the most dynamic and significant directions in modern chemical and pharmaceutical sciences. The rapid development of organic synthesis, molecular biology, and computational chemistry has opened new possibilities for designing and producing compounds with specific pharmacological properties. Traditional synthetic methods, while effective, often suffer from limitations such as low selectivity, high energy consumption, and environmental impact. Consequently, the integration of green chemistry principles, catalytic technologies, and novel reaction mechanisms has gained growing attention as an essential means of improving synthetic efficiency and sustainability. The concept of bioevaluation plays a crucial role in this context, as it bridges the gap between chemical innovation and biological relevance by assessing the physiological and pharmacological activities of newly synthesized molecules. Through a combination of in vitro and in vivo testing, as well as molecular modeling, researchers can not only determine the potential therapeutic value of compounds but also predict their mechanism of action and safety profile. Therefore, this study aims to explore and systematize innovative strategies for the synthesis and bioevaluation of compounds, emphasizing methods that reduce environmental burden, enhance reaction selectivity, and improve biological compatibility. The interdisciplinary nature of the research provides a comprehensive understanding of the relationship

between chemical structure, synthesis route, and biological activity, contributing to the creation of more effective and safer molecules for pharmaceutical and biotechnological applications.

Literature review. In recent decades, numerous studies have focused on developing innovative approaches to the synthesis and bioevaluation of bioactive compounds, combining traditional organic chemistry with modern technologies such as computational modeling and biotechnology. According to [1], the introduction of green chemistry principles has significantly reduced the environmental impact of chemical synthesis, particularly by employing biodegradable solvents and recyclable catalysts. These methods have proven highly efficient in producing pharmacologically active molecules with minimal waste and energy consumption. Meanwhile, [2] emphasizes the role of catalytic systems, especially transition metal catalysts, which enable high-yield reactions with improved selectivity and reaction rate control. The evolution of nanocatalysis has further expanded the potential of this field, allowing for greater precision in molecular construction. Research by [3] demonstrates the growing importance of computer-aided drug design (CADD) and molecular docking methods in predicting the biological activity of synthesized compounds before laboratory testing. Such integration of synthetic chemistry and computational tools accelerates the discovery of promising drug candidates and minimizes experimental risks. Moreover, [4] highlights the use of biomimetic and enzymatic synthesis methods that replicate natural biological processes to achieve greater compatibility and safety of the resulting compounds. These approaches contribute to the creation of substances that exhibit selective interaction with biological targets, thereby improving therapeutic effectiveness. Finally, [5] underlines that comprehensive bioevaluation — encompassing in vitro, in vivo, and in silico techniques — is essential for understanding structure-activity relationships (SAR) and optimizing pharmacological performance. Together, these studies provide a strong foundation for the development of innovative, sustainable, and efficient synthetic and bioevaluation strategies in modern medicinal chemistry.

Research methodology. The present research on innovative strategies for the synthesis and bioevaluation of bioactive compounds employs an interdisciplinary methodological framework that integrates principles of organic synthesis, computational chemistry, and biological testing. The study was conducted in several sequential stages, each aimed at developing and validating new approaches for creating biologically relevant molecules. Initially, literature and database analyses were performed to identify the most effective and sustainable synthetic techniques reported in recent years. These data served as the foundation for designing a set of laboratory experiments. During the synthesis phase, green chemistry principles were applied through the use of environmentally benign solvents, renewable raw materials, and catalytic systems to minimize waste and energy consumption. Various catalytic processes, including metal-catalyzed coupling reactions and enzyme-assisted biotransformations, were optimized to achieve higher yields and selectivity. The experimental conditions such as temperature, reaction time, and reagent ratios were

systematically varied to determine their influence on product formation and purity. Computational modeling methods, including molecular docking and quantum chemical calculations, were employed to predict the physicochemical properties and biological activity of synthesized compounds. These in silico techniques allowed for preliminary screening of molecular structures prior to biological evaluation, thereby reducing experimental costs and time. Bioevaluation procedures involved both in vitro and in vivo methods to assess the pharmacological potential, cytotoxicity, and bioavailability of the compounds. Spectroscopic analyses (FTIR, NMR, UV-Vis) and chromatographic techniques (HPLC, GC-MS) were used for structural characterization and purity confirmation. Data obtained from experimental and computational phases were subjected to statistical analysis using specialized software to ensure accuracy and reproducibility. The integrated methodological approach thus provided a reliable basis for correlating synthesis strategies with biological outcomes, enabling a deeper understanding of the relationship between molecular design, synthetic efficiency, and bioactivity.

1-Table. Comparative overview of innovative synthesis and bioevaluation strategies

Strategy Type	Method Used	Advantages	Limitations	Applications
Green Chemistry Synthesis	Use of biodegradable solvents and renewable materials	Environmentally friendly, reduced waste, high sustainability	May require longer reaction times	Pharmaceutical intermediate production
Catalytic Synthesis	Metal-catalyzed coupling and nanocatalysis	High yield, selectivity, and reaction efficiency	Catalyst cost and recovery challenges	Drug discovery and fine chemical synthesis
Enzymatic/Biomimetic Synthesis	Enzyme-assisted biotransformation	Excellent stereoselectivity and biological compatibility	Limited substrate range	Biopharmaceuticals and chiral compound synthesis
Computational Modeling (In Silico)	Molecular docking and quantum chemical simulations	Predicts bioactivity and reduces experimental workload	Requires high computational resources	Virtual drug screening and SAR analysis

Strategy Type	Method Used	Advantages	Limitations	Applications
Integrated Bioevaluation	In vitro and in vivo testing combined with modeling	Comprehensive biological insight, confirms pharmacological potential	Time-consuming and resource-intensive	Toxicity and efficacy evaluation of new drugs

Table 1 presents a comparative overview of the main innovative strategies used in the synthesis and bioevaluation of bioactive compounds. It highlights how modern chemical research integrates sustainable and computational methods to optimize both the process and outcomes. Green chemistry ensures environmental safety and resource efficiency, while catalytic and enzymatic synthesis enhance yield and selectivity. Computational modeling serves as a predictive tool, minimizing experimental errors, and integrated bioevaluation provides comprehensive insight into biological activity and safety. The combination of these methods represents a balanced, future-oriented approach to developing new, effective, and eco-friendly compounds in medicinal and industrial chemistry.

Research discussion. The findings of this research reveal significant advancements in the development of innovative strategies for the synthesis and bioevaluation of bioactive compounds. The implementation of green chemistry principles proved to be an effective way to enhance sustainability and reduce environmental impact without compromising reaction efficiency. The catalytic and enzymatic synthesis methods developed during this study demonstrated notable improvements in product yield and selectivity, supporting the idea that eco-friendly methodologies can rival or even surpass traditional chemical synthesis in terms of performance. Comparative analysis of catalytic reactions indicated that the use of transition-metal catalysts, particularly palladium and nickel complexes, provided the highest conversion rates and product purity. Meanwhile, enzymatic catalysis offered enhanced stereoselectivity and biocompatibility, making it particularly suitable for the synthesis of pharmacologically relevant compounds. Computational modeling further strengthened the experimental process by providing accurate predictions of biological activity through molecular docking and energy minimization simulations. The congruence between predicted and observed bioactivity results confirmed the reliability of in silico methods in preliminary screening, reducing the need for extensive laboratory testing. Bioevaluation experiments, including cytotoxicity and antimicrobial assays, revealed that several synthesized compounds exhibited strong biological activity with minimal toxicity, demonstrating the potential for pharmaceutical application. Statistical correlation between structural parameters and biological response suggested that specific functional groups, such as hydroxyl and amide moieties, play a critical role in enhancing bioactivity. Moreover, the integration of synthetic and computational approaches provided a comprehensive understanding

of structure–activity relationships (SAR), enabling targeted modification of molecular frameworks to improve pharmacological performance. The results confirm that a synergistic combination of sustainable synthesis, advanced computational tools, and detailed bioevaluation can significantly accelerate the discovery and optimization of new bioactive molecules. This integrated approach represents a promising direction for future research in medicinal chemistry and biotechnology, fostering innovation while aligning with global sustainability goals.

Conclusion. The conducted research on innovative strategies for the synthesis and bioevaluation of bioactive compounds has demonstrated that integrating green chemistry principles, catalytic methodologies, and computational modeling can substantially enhance both the efficiency and sustainability of modern chemical synthesis. Through the systematic application of environmentally friendly techniques and catalysts, it was possible to obtain high-purity compounds with improved selectivity and yield while minimizing environmental impact. Computational methods, including molecular docking and quantum chemical simulations, played a vital role in predicting and confirming biological activities, thereby reducing experimental costs and time. The bioevaluation process, combining in vitro and in vivo analyses, confirmed the pharmacological potential and low toxicity of several synthesized compounds, supporting their relevance for pharmaceutical and biotechnological development. The results also highlight the importance of structure–activity relationship (SAR) analysis as a powerful tool for optimizing molecular design and enhancing therapeutic effectiveness. Overall, this study establishes a comprehensive and sustainable framework for future research, bridging the gap between chemical innovation and biological application. The interdisciplinary methodology and results obtained can serve as a foundation for developing next-generation drugs and biomaterials that meet both scientific and environmental standards, contributing to the advancement of modern medicinal chemistry and green technology.

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