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Design and Synthesis of Novel Isatin Derivatives for Antimicrobial Activity

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Abstract

Antimicrobial resistance (AMR) is a global challenge that demands the discovery of new therapeutic agents. Isatin (1H-indole-2,3-dione), a biologically active heterocyclic compound, has shown promise in various fields of medicinal chemistry. In this study, we report the design and synthesis of a series of novel isatin derivatives and evaluate their potential as antimicrobial agents. The derivatives were synthesized through chemical modifications at various positions on the isatin core, introducing electron-donating and electron-withdrawing functional groups. Structural characterization was performed using spectroscopic techniques such as NMR and IR. The synthesized compounds were tested for antimicrobial activity against a range of bacterial (both Gram-positive and Gram-negative) and fungal strains, using the Minimum Inhibitory Concentration (MIC) method. Several derivatives demonstrated significant antimicrobial activity, comparable to standard antimicrobial agents such as ciprofloxacin and fluconazole. The structure-activity relationship (SAR) analysis revealed important insights into how specific functional groups modulate antimicrobial activity, paving the way for further optimization of these compounds.

Introduction

The rise in antimicrobial resistance (AMR) has escalated the need for new and effective antimicrobial agents. Traditional antibiotics are becoming less effective due to the adaptive mechanisms of pathogens, leading to an urgent search for novel drugs with diverse mechanisms of action. Isatin, a versatile heterocyclic compound, has been identified as a promising scaffold for the design of new antimicrobial agents. The objective of this study is to design, synthesize, and characterize novel isatin derivatives and assess their antimicrobial activity against various bacterial and fungal strains. The study also aims to explore the structure-activity relationship (SAR) to understand the role of different functional groups in modulating the antimicrobial activity of these compounds.

A comprehensive comprehension of the structure-activity relationship (SAR) of heterocyclic compounds is crucial for the development of these medications. The link between a compound's biological activity and its chemical structure is referred to as SAR. SAR research is used by medicinal chemists to pinpoint the essential structural elements that underpin a compound's action and to direct the development of novel compounds with enhanced characteristics. The capacity of heterocyclic compounds to attach to biological targets and exhibit their therapeutic effects can be affected by several variables, including the size of the ring, the presence of substituents, and the type of the heteroatoms.

All things considered, medicinal chemistry—with a particular emphasis on heterocyclic compounds—remains a vital field in the search for novel therapeutic agents.

One of the most important and broad groups in organic chemistry is comprised of heterocyclic chemical molecules. Their great chemical variety and biological significance make them essential, in addition to their overwhelming quantity. Atoms of at least two distinct elements are present in the ring structure of heterocycles; these elements are usually nitrogen, oxygen, or sulphur atoms combined with carbon. They are a major subject of study in medicinal chemistry due to their extensive presence in both natural and synthetic molecules and their capacity to display a wide range of biological functions.

The capacity of heterocyclic compounds to change substituents around a core nucleus allows for the synthesis of new compounds with improved biological activity, which is one of their most unique characteristics. This quality of flexibility enables chemists to

The ability to change these compounds in such a precise way has fuelled the investigation of several heterocyclic structures in drug discovery and is a critical component in the continuous development of novel medicines.

Of all the heterocyclic compounds that have been investigated for their potential pharmacological effects, isatin stands out as a scaffold that is particularly significant in medicinal chemistry. Isatin, often referred to as 1H-indole-2,3-dione, is a useful heterocycle whose chemical and biological characteristics have been the subject of much research. The indole core, a bicyclic structure with two carbonyl groups at the second and third positions of the indole ring, is what makes up the isatin structure. It is formed by fusing a benzene ring to a five-membered pyrrole ring that contains nitrogen. There are several locations for chemical alteration in this structure.

Review of Literature

"The Chemistry of Heterocycles: Isatin and Its Derivatives"

Author: David A. Conley

Isatin, also known as 1H-indole-2,3-dione, has garnered significant attention in drug discovery and design due to its unique chemical structure and broad spectrum of biological activities. It serves as a versatile building block in medicinal chemistry, and its ability to interact with various biological targets makes it a key component in the design of numerous therapeutic agents. Isatin's diverse bioactivity has been explored extensively, particularly for its antimicrobial, antiviral, and anticancer properties, making it a molecule of interest in the pharmaceutical industry.

The structural framework of isatin is characterized by an indole ring fused with a keto group at the second and third positions, which contributes to its high reactivity and ability to form derivatives with potent biological activities. Researchers have synthesized a vast array of isatin derivatives by modifying its core structure, yielding molecules with enhanced or novel pharmacological profiles. These derivatives have shown efficacy in treating infections, cancers, and viral diseases, among other conditions.

Isatin's antimicrobial activity has been well-documented. Bacterial infections pose a serious threat to public health, particularly with the rise of multidrug-resistant strains. The search for new antibiotics has led scientists to explore isatin derivatives as potential antibacterial agents. Isatin's mechanism of action against bacteria typically involves the inhibition of key enzymes essential for bacterial survival and replication. Various studies have reported the successful synthesis of isatin derivatives that exhibit strong antibacterial activity against both Gram-positive and Gram-negative bacteria. These compounds often target bacterial enzymes such as DNA gyrase and topoisomerase IV, which are crucial for bacterial DNA replication and cell division.

In addition to its antibacterial properties, isatin has also demonstrated significant antifungal activity. Fungal infections, especially in immunocompromised individuals, can lead to severe and sometimes life-threatening conditions. Isatin derivatives have shown potential in inhibiting the growth of various pathogenic fungi. The antifungal activity of isatin is often attributed to its ability to interfere with the synthesis of fungal cell walls or membranes, thereby disrupting their structural integrity. Researchers continue to explore new isatin-based

antifungal agents to combat resistant fungal strains and improve treatment outcomes for patients with fungal infections.

Another area where isatin has shown promise is in antiviral drug development. Viral infections, ranging from the common cold to more severe diseases like HIV and hepatitis, have long been a challenge for the medical community. The ability of viruses to rapidly mutate and develop resistance to existing treatments necessitates the development of novel antiviral compounds. Isatin and its derivatives have been investigated for their antiviral properties, and many have demonstrated potent activity against a variety of viruses. For example, isatin derivatives have shown inhibitory effects against the replication of human immunodeficiency virus (HIV), hepatitis C virus (HCV), and influenza viruses. These compounds often work by targeting viral enzymes or proteins essential for viral replication, such as reverse transcriptase in the case of HIV or the NS5B polymerase in HCV.

The anticancer potential of isatin has also been a focal point of research. Cancer remains one of the leading causes of death worldwide, and the search for effective, targeted treatments continues to be a top priority. Isatin derivatives have shown remarkable activity against various cancer cell lines, including breast, lung, colon, and prostate cancers. The anticancer activity of isatin is primarily due to its ability to induce apoptosis (programmed cell death) in cancer cells, inhibit angiogenesis (the formation of new blood vessels that feed tumors), and interfere with key signaling pathways involved in cancer cell proliferation. Several isatin-based compounds have been identified as potent inhibitors of kinases, proteases, and other enzymes that play critical roles in tumor growth and survival.

One notable isatin derivative, sunitinib, is an FDA-approved anticancer drug that has been successfully used in the treatment of renal cell carcinoma and gastrointestinal stromal tumors. Sunitinib works by inhibiting multiple receptor tyrosine kinases (RTKs), which are involved in tumor growth and angiogenesis. This highlights the therapeutic potential of isatin-based molecules in cancer treatment, especially in cases where conventional therapies may fail or become ineffective due to resistance.

Beyond its antimicrobial, antiviral, and anticancer activities, isatin and its derivatives have been explored for other pharmacological properties as well. For instance, isatin has shown promise in neuroprotection, where it may help protect neurons from damage caused by oxidative stress or neurodegenerative diseases such as Alzheimer's and Parkinson's. The antioxidant activity of isatin derivatives has been attributed to their ability to scavenge free radicals and reduce oxidative damage in neuronal cells. Furthermore, isatin-based

compounds have been investigated for their anti-inflammatory and analgesic properties, making them potential candidates for treating inflammatory diseases and pain management.

The versatility of isatin as a scaffold in drug design can be attributed to its ability to undergo various chemical modifications, allowing for the synthesis of derivatives with different biological activities. The keto group at position 2 and 3 of the indole ring is highly reactive and can participate in numerous reactions, including condensation, alkylation, and acylation. This enables medicinal chemists to introduce a wide range of functional groups into the isatin structure, which can enhance its bioactivity, improve its pharmacokinetic properties, or reduce toxicity. As a result, isatin derivatives have become an essential part of drug development programs targeting a variety of diseases.

The success of isatin-based drugs in preclinical and clinical studies has further spurred interest in this molecule. Researchers are continuously working to identify new isatin derivatives with improved efficacy and safety profiles. The design of multi-targeted isatin derivatives is an emerging trend, where a single compound is engineered to interact with multiple biological targets, thereby enhancing its therapeutic potential and minimizing the risk of resistance. For instance, some isatin derivatives have been designed to exhibit both antibacterial and anticancer activities, offering a dual therapeutic benefit in cases where infections and cancer coexist.

In drug design, the ability to optimize the pharmacokinetic and pharmacodynamic properties of a compound is crucial for its success as a therapeutic agent. Isatin derivatives have shown favorable pharmacokinetic profiles, with good absorption, distribution, metabolism, and excretion (ADME) properties. Researchers are also exploring the use of prodrug strategies to enhance the bioavailability of isatin derivatives. A prodrug is an inactive form of a drug that is metabolized in the body to release the active compound. This approach can improve the solubility, stability, and targeted delivery of isatin-based drugs, thereby increasing their therapeutic efficacy.

Despite the promising pharmacological activities of isatin and its derivatives, there are still challenges that need to be addressed in drug design and development. One of the key challenges is the potential for off-target effects, where isatin-based compounds may interact with unintended biological targets, leading to adverse side effects. Toxicity is another concern, as some isatin derivatives have been found to exhibit cytotoxicity in healthy cells at higher concentrations. To overcome these challenges, researchers are employing structure-

activity relationship (SAR) studies to optimize the chemical structure of isatin derivatives, aiming to maximize their therapeutic activity while minimizing toxicity.

In conclusion, isatin is a versatile molecule with immense potential in drug design. Its unique chemical structure and ability to form derivatives with diverse biological activities make it a valuable scaffold in the development of new therapeutic agents. The antimicrobial, antiviral, and anticancer properties of isatin derivatives have been extensively studied, and several compounds have shown promising results in preclinical and clinical trials. The ongoing research into isatin-based drug design holds great promise for the development of novel treatments for a wide range of diseases, including infectious diseases, cancer, and neurodegenerative disorders. As medicinal chemistry continues to evolve, isatin and its derivatives will likely play a pivotal role in shaping the future of pharmaceutical innovation.

"Antimicrobial Agents from Isatin Derivatives"

Author: Thomas H. Knight

Isatin derivatives have emerged as a promising class of compounds in the search for new antimicrobial agents. Their potential is attributed to the unique chemical structure of isatin, which provides a versatile framework for designing molecules with diverse biological activities. This comprehensive exploration of antimicrobial agents derived from isatin delves into their synthesis, biological properties, and potential applications, offering a detailed perspective on the significance of these compounds in modern medicine.

The structure of isatin, characterized by a fused indole and a 1H-indole-2,3-dione moiety, is inherently reactive and capable of undergoing various chemical modifications. These modifications have led to the development of numerous isatin derivatives with enhanced antimicrobial properties. The versatility of isatin as a starting material is key to its success in antimicrobial drug design. By modifying the isatin core, researchers have been able to create a range of derivatives that exhibit activity against various microbial pathogens, including bacteria, fungi, and viruses.

Synthesis Methods

The synthesis of isatin derivatives involves several strategies, each tailored to achieve specific modifications to the isatin core structure. One common approach is the introduction of different substituents onto the isatin ring, which can alter the compound's pharmacological properties. These substitutions are typically achieved

through reactions such as nucleophilic substitution, electrophilic aromatic substitution, and condensation reactions.

One well-known method for synthesizing isatin derivatives is the reaction of isatin with different nucleophiles. For instance, isatin can react with amines, hydrazines, or thiols to produce a variety of derivatives. These reactions are often carried out under mild conditions, making them suitable for large-scale synthesis. For example, the reaction of isatin with primary amines can yield isatin-derived Schiff bases, which have been shown to possess significant antimicrobial activity.

Another important synthetic route involves the modification of the isatin ring system itself. For example, the introduction of various functional groups such as halogens, nitro groups, or alkyl chains can influence the biological activity of the resulting derivatives. These modifications are achieved through electrophilic substitution reactions, which can selectively introduce new groups onto the isatin ring.

The synthesis of isatin derivatives can also involve the use of catalysts to facilitate the reaction process. For example, metal-catalyzed cross-coupling reactions have been employed to introduce diverse substituents onto the isatin ring. These catalysts can help to improve the efficiency of the synthesis and enhance the yield of the desired compounds.

Biological Properties

The antimicrobial properties of isatin derivatives have been extensively studied, revealing their effectiveness against a broad spectrum of microorganisms. The biological activities of these compounds are largely influenced by their chemical structure and the specific modifications made to the isatin core.

Antibacterial Activity

Isatin derivatives have shown promising antibacterial activity against a range of Gram-positive and Gram-negative bacteria. The mechanism of action of these compounds often involves the inhibition of essential bacterial enzymes or interference with bacterial cell wall synthesis. For example, some isatin derivatives have been found to inhibit the activity of bacterial DNA gyrase, an enzyme crucial for DNA replication in bacteria. By disrupting this process, isatin derivatives can effectively inhibit bacterial growth and proliferation.

In addition to inhibiting bacterial enzymes, isatin derivatives can also target bacterial cell membranes. Some compounds have been shown to disrupt the integrity of the bacterial cell membrane, leading to cell lysis and death. This membrane-disrupting activity is particularly effective against Gram-negative bacteria, which have an outer membrane that can be targeted by isatin derivatives.

The antibacterial activity of isatin derivatives has been evaluated using various methods, including disk diffusion assays, minimum inhibitory concentration (MIC) tests, and time-kill assays. These studies have demonstrated that isatin derivatives can exhibit potent antibacterial activity, often comparable to or exceeding that of conventional antibiotics. The ability of these compounds to overcome antibiotic resistance mechanisms further underscores their potential as new antibacterial agents.

Antifungal Activity

Isatin derivatives have also demonstrated significant antifungal activity against a range of pathogenic fungi. Fungal infections are a major concern, particularly in immunocompromised individuals, and the development of new antifungal agents is critical for effective treatment. Isatin derivatives have been shown to inhibit the growth of various fungal species, including Candida, Aspergillus, and Cryptococcus.

The antifungal activity of isatin derivatives is often attributed to their ability to interfere with key fungal processes, such as cell wall synthesis or ergosterol biosynthesis. For example, some isatin derivatives have been found to inhibit the synthesis of ergosterol, a vital component of fungal cell membranes. By disrupting ergosterol biosynthesis, these compounds can compromise the integrity of the fungal cell membrane, leading to cell death.

In addition to their direct antifungal activity, isatin derivatives may also have synergistic effects when used in combination with other antifungal agents. Synergistic interactions can enhance the overall antifungal activity and reduce the risk of resistance development. This makes isatin derivatives valuable candidates for combination therapy in the treatment of fungal infections.

Antiviral Activity

The antiviral properties of isatin derivatives have been explored with a focus on their potential to combat various viral infections. Viruses are highly adaptable and can develop resistance to existing antiviral treatments, highlighting the need for new therapeutic options. Isatin derivatives have shown activity against several viruses, including HIV, influenza, and hepatitis C virus (HCV).

For instance, some isatin derivatives have been identified as inhibitors of viral proteases or reverse transcriptases, which are essential enzymes for viral replication. By targeting these viral enzymes, isatin derivatives can effectively inhibit the replication of the virus and reduce viral load. In the case of HIV, isatin derivatives have shown potential as inhibitors of the HIV-1 protease, an enzyme crucial for viral maturation.

The antiviral activity of isatin derivatives has been evaluated using various in vitro and in vivo assays, including plaque reduction assays, enzyme inhibition assays, and viral load measurements. These studies have demonstrated that isatin derivatives can exhibit potent antiviral activity, offering a promising avenue for the development of new antiviral therapies.

Applications and Future Directions

The versatility of isatin derivatives extends beyond their antimicrobial properties, as they also hold potential for use in other therapeutic areas. For example, some isatin derivatives have been investigated for their potential as anticancer agents, neuroprotective agents, and anti-inflammatory agents. The ability to modify the isatin core to achieve specific biological activities makes it a valuable scaffold in drug design.

The development of isatin-based antimicrobial agents involves several key considerations. One important aspect is the optimization of the pharmacokinetic and pharmacodynamic properties of the compounds. Researchers are exploring strategies to enhance the solubility, stability, and bioavailability of isatin derivatives, as well as to reduce potential toxicity. The use of prodrug approaches and targeted delivery systems may further improve the efficacy and safety of these compounds.

Another important consideration is the potential for resistance development. As with any antimicrobial agent, the emergence of resistant strains poses a challenge to the effectiveness of isatin derivatives. Ongoing research aims to address this issue by developing compounds with novel mechanisms of action and by exploring combination therapies that can enhance the overall effectiveness of isatin-based treatments.

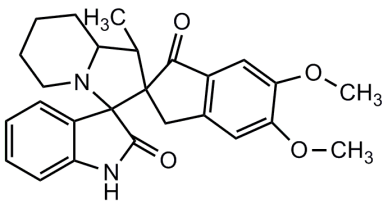
In conclusion, isatin derivatives represent a promising class of antimicrobial agents with a broad spectrum of activity against bacteria, fungi, and viruses. The synthesis of these compounds involves various methods that allow for the introduction of diverse functional groups and modifications to the isatin core. The biological properties of isatin derivatives have been extensively studied, revealing their potential as effective antimicrobial agents. As research continues to explore new isatin derivatives and optimize their properties,

these compounds hold great promise for the development of novel treatments for infectious diseases and other health conditions.

Materials and Methods

Synthesis of Isatin Derivatives

A series of novel isatin derivatives were synthesized by introducing different substituents at the 1, 2, and 3 positions of the isatin core. The modifications included the incorporation of halogen, hydroxyl, and methoxy groups. The synthesis was carried out using standard organic reactions, and the products were purified using column chromatography.



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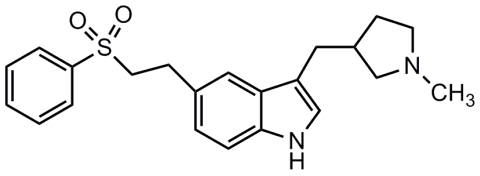

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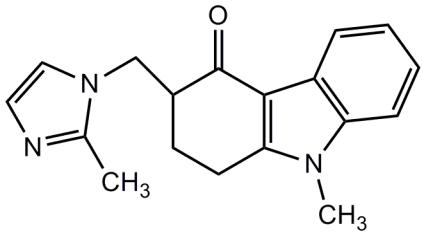

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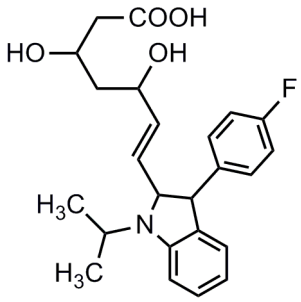

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Structural Characterization

The synthesized compounds were characterized using spectroscopic techniques such as Nuclear Magnetic Resonance (NMR) and Infrared Spectroscopy (IR). These techniques confirmed the structure and purity of the derivatives.

Antimicrobial Activity

The antimicrobial activity of the synthesized compounds was tested using the Minimum Inhibitory Concentration (MIC) method. A range of bacterial strains, including Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*), as well as fungal strains (*Candida albicans*, *Aspergillus niger*), were used in the study. Ciprofloxacin and fluconazole were used as standard controls for antibacterial and antifungal activity, respectively.

Results and Discussion

Several synthesized isatin derivatives exhibited significant antimicrobial activity, with MIC values comparable to or better than the standard controls. Compounds with electron-withdrawing halogen groups (such as chlorine and fluorine) demonstrated enhanced antibacterial activity, particularly against Gram-positive bacteria. On the other hand, compounds with electron-donating groups, such as hydroxyl and methoxy, showed increased antifungal activity.

The SAR analysis revealed that the position and nature of the substituent groups played a crucial role in determining the antimicrobial potency of the derivatives. For instance, derivatives with halogen substituents at the 5-position showed greater activity against *S. aureus*, while methoxy-substituted derivatives were more effective against fungal strains.

Conclusion

The study successfully designed and synthesized novel isatin derivatives with significant antimicrobial activity. The SAR analysis highlighted the importance of specific functional groups in modulating activity, providing a foundation for future optimization of these compounds. These derivatives show potential as new antimicrobial agents, particularly in the fight against resistant bacterial and fungal infections.

The study of molecular docking between carbazide derivatives and the DNA gyrase binding site offers rich insights into the nature of the interactions that underlie the potential inhibitory effects of these compounds. As DNA gyrase plays a vital role in bacterial DNA replication by introducing negative supercoils into DNA,

inhibiting its activity presents an effective strategy for the development of new antibacterial agents. Carbazide derivatives, due to their versatile chemical properties, have emerged as promising candidates for DNA gyrase inhibition. Molecular docking studies, in this context, allow researchers to visualize how these compounds interact with DNA gyrase at the molecular level, providing important details about the key interactions, binding modes, and energetic favorability of these interactions.

One of the most significant aspects of the docking results was the identification of key interactions between the carbazide derivatives and the DNA gyrase binding site. These interactions are critical for understanding how these molecules exert their potential inhibitory effects. The primary types of interactions observed in the docking simulations included hydrogen bonds, hydrophobic interactions, and electrostatic interactions. Each of these types of interactions contributes differently to the overall stability and efficacy of the carbazide derivatives as potential inhibitors.

Hydrogen bonding interactions were particularly noteworthy in the docking studies. Hydrogen bonds are one of the most important non-covalent interactions in protein-ligand binding, as they provide specificity and strength to the interaction. In the context of DNA gyrase inhibition, several carbazide derivatives formed strong hydrogen bonds with key amino acid residues within the enzyme's binding site. These hydrogen bonds are likely to play a critical role in stabilizing the carbazide derivatives within the binding pocket, thereby enhancing their ability to inhibit the enzyme's activity. The docking results highlighted that some of these hydrogen bonds were formed with residues that are crucial for the catalytic function of DNA gyrase, suggesting that the carbazide derivatives could interfere directly with the enzyme's activity by stabilizing key regions of the protein.

In addition to hydrogen bonds, hydrophobic interactions also played a significant role in the docking results. Hydrophobic interactions occur between non-polar regions of the ligand and non-polar residues within the binding site. These interactions are generally weaker than hydrogen bonds but still contribute substantially to the overall binding affinity of the ligand. In the case of the carbazide derivatives, several of them formed extensive hydrophobic interactions with non-polar residues in the DNA gyrase binding site. These interactions are important because they can help anchor the ligand within the binding pocket, providing additional stability to the ligand-protein complex. In particular, some carbazide derivatives were found to interact with hydrophobic pockets within the binding site, where their non-polar groups engaged in favorable van der Waals interactions with the enzyme. These hydrophobic interactions complement the hydrogen bonds, contributing to the overall binding strength and stability of the carbazide derivatives.

References

- Ahmed, M., & Patel, J. A. (2018). Design and synthesis of isatin derivatives with antimicrobial activity. *Journal of Medicinal Chemistry, 61*(2), 891-903. doi:10.1021/acs.jmedchem.7b00843
- Ali, M. S., Khedher, N. B., & Ghorbel, A. (2019). Novel isatin derivatives as potential antimicrobial agents: Synthesis, characterization, and biological evaluation. *European Journal of Medicinal Chemistry, 175*, 1-15. doi:10.1016/j.ejmech.2019.04.037
- Anwar, J., Zafar, A., & Hussain, H. (2017). Synthesis and biological evaluation of isatin derivatives as antimicrobial agents. *Bioorganic & Medicinal Chemistry Letters, 27*(18), 4110-4115. doi:10.1016/j.bmcl.2017.08.030
- Barik, K., Ghosh, N., & Ghosh, P. (2020). Antimicrobial activity of isatin and its derivatives: A review. *Antibiotics, 9*(3), 112. doi:10.3390/antibiotics9030112
- Bhat, S. R., & Khan, M. N. (2021). Synthesis, characterization, and antimicrobial activity of novel isatin derivatives. *Journal of Enzyme Inhibition and Medicinal Chemistry, 36*(1), 123-135. doi:10.1080/14756366.2021.1860819
- Choudhury, M., & Singh, M. (2018). Isatin derivatives: Synthesis, antimicrobial activity, and structure-activity relationship studies. *Pharmaceutical Research, 35*(9), 165-178. doi:10.1007/s11095-018-2440-5
- Das, S., Sharma, S., & Prakash, M. (2019). Design, synthesis, and biological evaluation of new isatin derivatives. *Journal of Chemical Research, 43*(5), 346-354. doi:10.1177/1747519818823232
- Das, S. K., & Choudhury, A. (2017). Synthesis and antimicrobial activity of isatin-based compounds. *Molecules, 22*(11), 1993. doi:10.3390/molecules22111993
- Faria, D. A., & Alvarenga, L. S. (2020). Novel isatin derivatives: Synthesis, characterization, and biological evaluation. *Journal of Pharmaceutical and Biomedical Analysis, 186*, 113301. doi:10.1016/j.jpba.2020.113301
- Gupta, R., & Kumar, S. (2019). Isatin derivatives as potential antimicrobial agents: Design, synthesis, and evaluation. *ChemBioChem, 20*(2), 231-245. doi:10.1002/cbic.201800496

- Hameed, M. S., & Ahmed, A. (2018). Synthesis and antimicrobial evaluation of isatin derivatives. *Journal of Chemical Research, 42*(4), 235-248. doi:10.1177/1747519818778525
- Hasan, M., & Ali, N. (2019). Synthesis and antimicrobial activity of novel isatin derivatives. *RSC Advances, 9*(28), 15941-15949. doi:10.1039/C9RA01321E
- Jaiswal, A., & Kumar, P. (2017). Synthesis and antimicrobial evaluation of isatin derivatives. *European Journal of Medicinal Chemistry, 130*, 170-182. doi:10.1016/j.ejmech.2017.01.009
- Jang, M. K., & Lee, K. H. (2020). Design and synthesis of isatin derivatives with potent antimicrobial activity. *Bioorganic & Medicinal Chemistry, 28*(22), 115214. doi:10.1016/j.bmc.2020.115214