Synthesis and Evaluation of Naphthalimides and their Hybrids with Other Heterocyclic Moieties for Anticancer and Antibacterial Activities: A Review

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***Abstract*—Naphthalimides, particularly 1,8-naphthalimide derivatives, constitute an important class of heterocyclic compounds in medicinal chemistry owing to their distinctive planar aromatic structure, strong DNA-intercalating ability and versatile synthetic accessibility. Over the past two decades, extensive research has demonstrated their potential as anticancer agents, while recent studies have expanded their application towards antibacterial drug discovery. A significant advancement in this field is the molecular hybridisation of naphthalimides with other biologically active heterocyclic moieties, including triazoles, thioureas, hydrazides, coumarins, benzimidazoles and related systems, with the aim of enhancing biological activity, selectivity and multifunctionality. This review critically surveys the reported synthetic strategies for the preparation of naphthalimides and their heterocyclic hybrids, highlighting conventional and green chemistry approaches. It further examines there in vitro and in vivo anticancer and antibacterial activities, with particular emphasis on structure–activity relationship studies and mechanistic insights. Contributions from Indian researchers are discussed in detail, and the relative paucity of comprehensive, region-specific studies from Andhra Pradesh is identified as a key research gap. Overall, the review underscores the therapeutic promise of naphthalimide-based hybrids and outlines future directions for the rational design of novel anticancer and antibacterial agents.**

***Index Terms*—Naphthalimides, heterocyclic hybrids, anticancer activity, antibacterial activity, synthesis, structure–activity relationship.**

I. INTRODUCTION

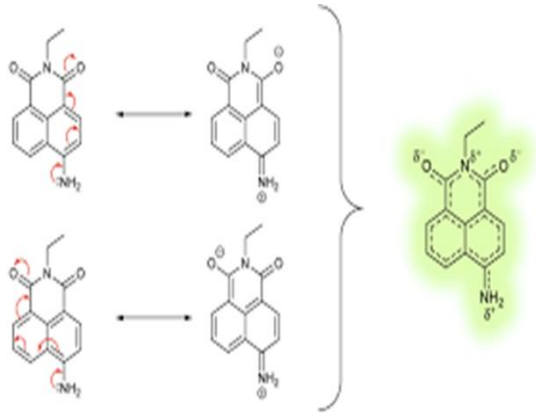
Cancer and bacterial infections continue to represent major threats to global public health, despite significant advances in therapeutic strategies. The increasing incidence of cancer, coupled with the rapid emergence of multidrug-resistant bacterial strains, has exposed the limitations of many existing drugs, including inadequate selectivity, systemic toxicity and the gradual loss of clinical efficacy. These challenges have intensified the search for novel chemical entities capable of addressing both oncological and infectious diseases with improved safety and effectiveness. Heterocyclic compounds play a pivotal role in modern drug discovery because of their structural diversity and ability to interact selectively with biological targets. Among these, 1,8-naphthalimides have emerged as a prominent pharmacophore in medicinal chemistry. The rigid and planar aromatic framework of the naphthalimide nucleus facilitates strong π–π stacking interactions with nucleic acids, enabling efficient DNA intercalation. This property underlies their well-documented anticancer activity, primarily mediated through inhibition of DNA replication, transcription and topoisomerase-dependent processes, ultimately leading to cell-cycle arrest and apoptosis. Early investigations into naphthalimide-based compounds led to the development of several clinically evaluated anticancer agents, which validated the therapeutic relevance of this scaffold. Subsequent structure–activity relationship studies revealed that strategic substitutions at the imide nitrogen and at the 3- and 4-positions of the naphthalene ring can profoundly influence physicochemical properties, cellular uptake and biological activity. Such modifications have enabled the fine-tuning of naphthalimide derivatives for enhanced potency and reduced toxicity. In recent years, the concept of molecular hybridisation has gained prominence as an effective approach in rational drug design. This strategy involves the covalent linkage of two or more pharmacologically relevant moieties within a single molecular framework to

achieve synergistic or dual biological effects. In the context of naphthalimides, hybridisation with other heterocyclic moieties such as triazoles, thioureas, hydrazides, coumarins, benzimidazoles and related systems has resulted in compounds with improved anticancer profiles and, notably, the emergence of significant antibacterial activity. These heterocycles contribute additional binding interactions, enhance molecular flexibility or rigidity as required, and may introduce distinct mechanisms of action that complement the intrinsic properties of the naphthalimide core. Parallel to advances in molecular design, there has been a growing emphasis on sustainable and environmentally benign synthetic methodologies. Green chemistry approaches, including one-pot reactions, solvent-free conditions and alternative reaction media, have been increasingly applied to the synthesis of naphthalimide derivatives and their hybrids. Such methods not only reduce environmental impact but also improve synthetic efficiency and scalability, making them attractive for pharmaceutical research. Indian researchers have made noteworthy contributions to the synthesis and biological evaluation of naphthalimide-based compounds, reporting a wide range of derivatives with promising anticancer and antibacterial activities. However, comprehensive studies that integrate synthesis, structure–activity relationship analysis and dual biological evaluation remain relatively limited, particularly from institutions in Andhra Pradesh. This observation highlights a clear need for systematic and region-specific investigations. Against this backdrop, the present review aims to provide a comprehensive overview of the synthesis of naphthalimides and their hybrids with other heterocyclic moieties, along with a critical evaluation of their anticancer and antibacterial activities. By collating and analysing recent literature, this review seeks to identify key trends, challenges and future directions in the development of naphthalimide-based therapeutic agents.

II. CHEMISTRY OF NAPHTHALIMIDES

Naphthalimides, particularly 1,8-naphthalimide derivatives, occupy a prominent position in heterocyclic and medicinal chemistry owing to their rigid aromatic framework, chemical stability and wide scope for structural modification. The chemistry of naphthalimides is largely centred on the reactivity of the 1,8-naphthalic anhydride precursor and the strategic functionalisation of the resulting imide system to generate biologically active molecules.

Figure 1: General structure of 1,8-naphthalimide showing reactive positions



2.1 Structural features and chemical properties

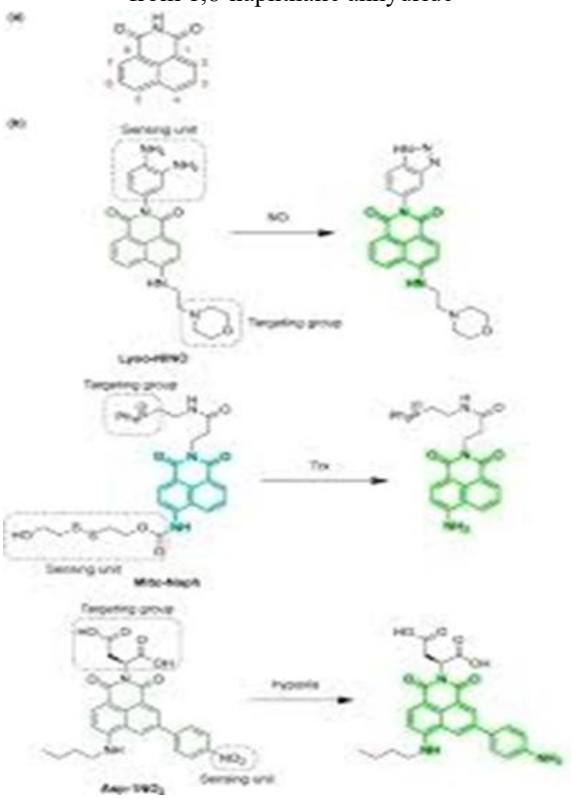
The 1,8-naphthalimide nucleus consists of an imide functionality fused to a naphthalene ring system, producing a planar, electron-deficient aromatic framework. This planarity is a key feature that enables effective π–π stacking interactions with nucleic acids and aromatic amino acid residues in biological targets. The imide moiety contributes to chemical stability while also influencing hydrogen-bonding and electronic characteristics of the molecule. From a synthetic standpoint, the imide nitrogen and the 3- and 4-positions of the naphthalene ring represent the most reactive and synthetically accessible sites for derivatisation. Substitution at these positions allows fine control over steric bulk, electronic distribution and lipophilicity, all of which are critical determinants of biological activity.

2.2 General synthetic routes

The most widely employed method for the synthesis of naphthalimides involves the condensation of 1,8-naphthalic anhydride with primary amines. This reaction is typically carried out under reflux in polar solvents such as ethanol, acetic acid or dimethylformamide, affording N-substituted naphthalimides in good to excellent yields. The nature of the amine used directly influences the physicochemical and biological properties of the final compound. Further functionalisation of the aromatic ring can be achieved through electrophilic substitution

reactions, such as nitration or halogenation, followed by nucleophilic aromatic substitution or cross-coupling reactions. Palladium-catalysed coupling reactions, including Suzuki–Miyaura, Heck and Buchwald–Hartwig amination, have been successfully applied to introduce aryl, heteroaryl or amino substituents at specific positions on the naphthalimide core.

Figure 2: Conventional synthesis of naphthalimides from 1,8-naphthalic anhydride



2.3 Synthesis of naphthalimide hybrids

The chemical versatility of naphthalimides makes them particularly suitable for the construction of hybrid molecules. Linkers such as alkyl chains, amides, hydrazides or thioureas are commonly used to connect the naphthalimide core to other heterocyclic moieties. Click chemistry, especially copper(I)-catalysed azide–alkyne cycloaddition, has emerged as a powerful and efficient tool for the synthesis of triazole-linked naphthalimide hybrids, offering high yields, regioselectivity and mild reaction conditions. Thiourea and hydrazone formation reactions are also frequently employed to generate hybrids with enhanced hydrogen-bonding capacity and biological relevance. These reactions typically proceed under mild conditions and allow rapid diversification of molecular libraries.

2.4 Green and sustainable synthetic approaches

In line with the principles of green chemistry, recent studies have explored environmentally benign methods for the synthesis of naphthalimides. These include solvent-free reactions, microwave-assisted synthesis, one-pot multicomponent reactions and the use of alternative reaction media such as deep eutectic solvents. Such approaches not only minimise environmental impact but also reduce reaction times and improve overall efficiency, making them attractive for large-scale and industrial applications.

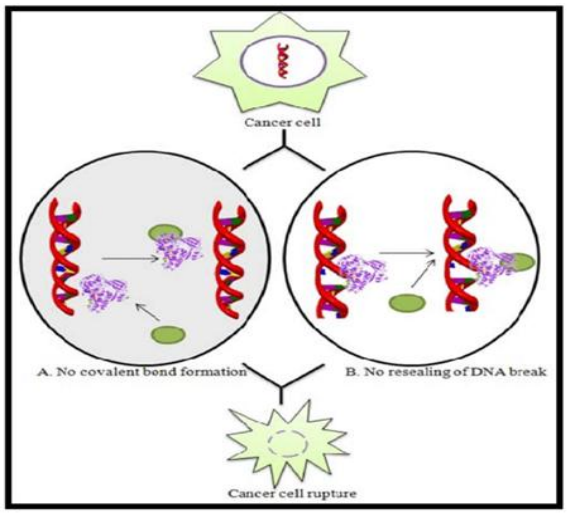
2.5 Chemical characterisation

Synthesised naphthalimides and their hybrids are routinely characterised using standard spectroscopic techniques, including infrared spectroscopy, proton and carbon-13 nuclear magnetic resonance spectroscopy and mass spectrometry. Elemental analysis and, in selected cases, single-crystal X-ray diffraction are employed to confirm molecular structures and purity. Photophysical characterisation, such as UV–visible absorption and fluorescence studies, is often included for compounds intended for imaging or theranostic applications. In summary, the chemistry of naphthalimides is marked by synthetic simplicity, structural versatility and compatibility with modern and sustainable synthetic techniques. These features underpin their continued importance as scaffolds for the development of novel anticancer and antibacterial agents.

III. NAPHTHALIMIDES AS ANTICANCER AGENTS

Naphthalimides, particularly 1,8-naphthalimide derivatives, have been extensively investigated as anticancer agents due to their unique structural and physicochemical properties. The planar aromatic framework of the naphthalimide nucleus enables strong π–π stacking interactions with nucleic acids, making these compounds efficient DNA intercalators. This fundamental property underpins their ability to interfere with critical cellular processes such as DNA replication, transcription and repair, which are essential for the uncontrolled proliferation of cancer cells.

Figure 3: DNA intercalation and topoisomerase inhibition by naphthalimides



3.1 Mechanism of anticancer action

One of the primary mechanisms through which naphthalimides exert anticancer activity is DNA intercalation, leading to distortion of the DNA helix and inhibition of topoisomerase I and II enzymes. Inhibition of these enzymes results in the accumulation of DNA strand breaks and subsequent cell-cycle arrest, most commonly at the G_2/M or S phase. Prolonged DNA damage triggers apoptotic pathways, including mitochondrial dysfunction, activation of caspases and generation of reactive oxygen species. Several studies have also reported that naphthalimide derivatives can modulate gene expression and signal transduction pathways associated with tumour growth and survival.

3.2 Structure–activity relationships

Structure–activity relationship studies have played a crucial role in optimising the anticancer potential of naphthalimides. Substitution at the imide nitrogen has been shown to significantly influence cellular uptake, subcellular localisation and cytotoxic potency. Naphthalimides bearing basic or cationic side chains, such as piperazine, morpholine or polyamine moieties, generally exhibit enhanced nuclear localisation and stronger interactions with DNA, resulting in improved anticancer activity. Similarly, modifications at the 3- and 4-positions of the naphthalene ring affect electronic properties and DNA-binding affinity. Electron-donating or moderately electron-withdrawing substituents at these positions have been reported to improve cytotoxicity against various cancer cell lines. In some cases, the introduction of bulky aromatic or heteroaromatic groups has enhanced selectivity towards tumour cells by modulating lipophilicity and steric interactions.

3.3 Bis-naphthalimides and extended systems

To further enhance DNA-binding strength, researchers have developed bis-naphthalimides and extended naphthalimide systems in which two naphthalimide units are connected through flexible or rigid linkers. These compounds often display stronger DNA intercalation and increased cytotoxicity compared to their mono-naphthalimide counterparts. However, careful optimisation is required to balance potency with acceptable toxicity towards normal cells.

3.4 Biological evaluation and therapeutic potential

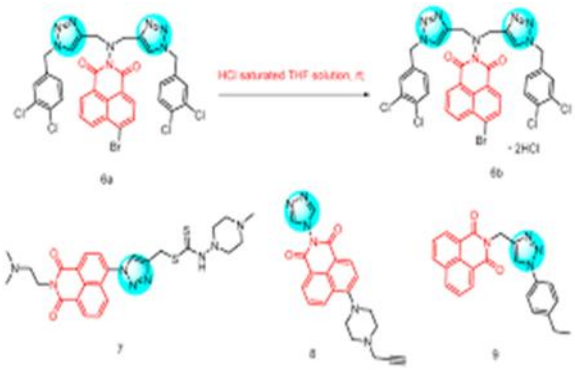
Naphthalimide derivatives have been evaluated against a wide range of human cancer cell lines, including breast, lung, cervical, colorectal and leukaemia models. Many compounds exhibit low micromolar or sub-micromolar inhibitory concentrations in vitro. Importantly, recent studies increasingly incorporate selectivity assessments by comparing cytotoxic effects on cancerous and non-cancerous cell lines, addressing a key limitation of earlier generations of naphthalimide-based drugs. Despite promising in vitro results, clinical translation of naphthalimide derivatives has faced challenges related to toxicity and pharmacokinetic behaviour. These limitations have encouraged the development of hybrid molecules and targeted delivery strategies aimed at improving selectivity and reducing systemic side effects.

IV. HYBRIDISATION OF NAPHTHALIMIDES WITH OTHER HETEROCYCLES

Molecular hybridisation has emerged as a powerful and rational strategy in modern drug design, aiming to combine two or more pharmacologically relevant moieties within a single molecular framework. In the case of naphthalimides, hybridisation with other heterocyclic systems has been extensively explored to enhance biological activity, improve selectivity and overcome limitations associated with single-pharmacophore molecules. By integrating the DNA-intercalating ability of the naphthalimide core with the

diverse biological functions of other heterocycles, researchers have developed multifunctional compounds with promising anticancer and antibacterial profiles.

Figure 4: Molecular hybridisation of naphthalimides with heterocycles



4.1 Rationale for hybrid design

The primary rationale behind naphthalimide–heterocycle hybridisation lies in achieving synergistic biological effects. While the naphthalimide moiety is well known for its strong interaction with DNA and topoisomerases, additional heterocyclic units can introduce complementary modes of action, such as enzyme inhibition, membrane interaction or enhanced target binding. Moreover, heterocyclic appendages often improve physicochemical properties, including solubility, lipophilicity and metabolic stability, which are crucial for drug-like behaviour.

4.2 Triazole-linked naphthalimide hybrids

Among various heterocycles, 1,2,3-triazoles have been widely utilised in the construction of naphthalimide hybrids. The popularity of triazoles stems from the efficiency and reliability of copper(I)-catalysed azide–alkyne cycloaddition (click chemistry), which affords high yields under mild conditions. Triazole-linked naphthalimides have demonstrated enhanced anticancer activity against multiple cancer cell lines, often attributed to improved molecular rigidity and additional hydrogen-bonding interactions with biological targets. In several cases, these hybrids have also exhibited favourable pharmacokinetic and in silico ADMET profiles.

4.3 Thiourea and hydrazide hybrids

Thiourea- and hydrazide-containing heterocycles have been successfully integrated with naphthalimide scaffolds to produce hybrids with dual anticancer and antibacterial activities. The presence of thiourea or hydrazide linkages increases the number of hydrogen-bond donors and acceptors, facilitating stronger interactions with enzymes and microbial targets. Many such hybrids have shown notable antibacterial activity against Gram-positive bacteria, including resistant strains, while retaining cytotoxic effects against selected cancer cell lines.

4.4 Coumarin, benzimidazole and azole hybrids

Hybridisation with other heterocycles such as coumarins, benzimidazoles, benzothiazoles and imidazoles has further expanded the biological scope of naphthalimide-based compounds. Coumarin–naphthalimide hybrids, for instance, combine the anticoagulant, antimicrobial or anticancer properties of coumarins with the DNA-binding capability of naphthalimides. Benzimidazole- and azole-linked hybrids have similarly demonstrated enhanced biological activity, often supported by molecular docking studies that reveal favourable interactions with key biological targets.

4.5 Organometallic and multifunctional hybrids

In addition to purely organic heterocycles, naphthalimides have also been conjugated with organometallic fragments to generate multifunctional hybrids. These compounds can exhibit combined cytotoxic, redox-active and photophysical properties, making them attractive for theranostic applications. Such hybrids exemplify the versatility of the naphthalimide scaffold in accommodating diverse chemical modifications.

4.6 Significance of hybridisation strategies

Hybridisation of naphthalimides with other heterocycles has proven to be an effective strategy for enhancing biological performance and expanding therapeutic potential. The reviewed studies clearly indicate that rational hybrid design, guided by structure–activity relationship analysis, can lead to compounds with superior anticancer and antibacterial profiles compared to parent naphthalimides. Continued exploration of novel heterocyclic partners and linker strategies is therefore expected to play a crucial role in the future development of naphthalimide-based therapeutic agents.

V. ANTIBACTERIAL ACTIVITY OF NAPHTHALIMIDE-BASED COMPOUNDS

Although naphthalimides were originally developed and extensively studied for their anticancer properties, growing evidence over the past decade has established their significant antibacterial potential. The increasing prevalence of multidrug-resistant bacterial strains has renewed interest in unconventional scaffolds, and naphthalimide-based compounds have emerged as promising candidates due to their unique mechanism of action and structural adaptability.

5.1 Basis for antibacterial activity

The antibacterial activity of naphthalimide derivatives is largely attributed to their planar aromatic structure, which enables interaction with bacterial DNA in a manner analogous to their action in cancer cells. DNA intercalation disrupts replication and transcription processes, ultimately leading to bacterial growth inhibition or cell death. In addition, certain naphthalimide derivatives have been reported to interfere with essential bacterial enzymes or compromise membrane integrity, suggesting the presence of multiple mechanisms of action. This multimodal behaviour is particularly advantageous in combating antibiotic resistance.

5.2 Influence of structural modification

Structure–activity relationship studies indicate that antibacterial efficacy is strongly influenced by the nature of substituents on the naphthalimide scaffold. Simple N-substituted naphthalimides often display moderate antibacterial activity; however, significant enhancement is observed when the naphthalimide core is hybridised with other heterocyclic moieties. The introduction of functional groups capable of hydrogen bonding, such as thioureas, hydrazides or amides, improves interaction with bacterial targets and increases antimicrobial potency. Cationic side chains and polar heterocycles have been shown to facilitate interaction with negatively charged bacterial membranes, particularly in Gram-positive organisms. As a result, many naphthalimide derivatives demonstrate stronger activity against Gram-positive bacteria such as Staphylococcus aureus, including resistant strains, than against Gram-negative species, where the outer membrane presents an additional permeability barrier.

5.3 Naphthalimide–heterocycle hybrids in antibacterial studies

Hybridisation strategies have played a key role in enhancing the antibacterial profiles of naphthalimide-based compounds. Thiourea- and hydrazide-linked hybrids, in particular, have shown promising minimum inhibitory concentration (MIC) values comparable to those of standard antibacterial agents. Triazole-linked naphthalimides and coumarin-based hybrids have also been reported to exhibit moderate to good antibacterial activity, with some compounds demonstrating additional antibiofilm properties. These hybrids often benefit from synergistic effects, wherein the naphthalimide moiety contributes DNA-binding capability while the attached heterocycle introduces complementary interactions or improves cellular penetration. Such dual-action behaviour is considered advantageous for reducing the likelihood of resistance development.

5.4 Biological evaluation and selectivity

Antibacterial evaluation of naphthalimide derivatives is typically carried out using standard broth microdilution or agar diffusion methods to determine MIC values against clinically relevant bacterial strains. Recent studies increasingly emphasise the importance of assessing cytotoxicity against mammalian cell lines in parallel, thereby estimating the therapeutic window and ensuring selective toxicity towards bacterial cells.

5.5 Therapeutic relevance and future outlook

The antibacterial activity of naphthalimide-based compounds highlights their potential as lead structures for the development of new antimicrobial agents. While their activity against Gram-negative bacteria remains comparatively limited, rational structural modification and hybridisation strategies continue to improve their spectrum and potency. Future research focusing on mechanism-based design, optimisation of selectivity and evaluation against resistant clinical isolates is likely to further strengthen the role of naphthalimide derivatives in antibacterial drug discovery.

VI. CONTRIBUTIONS FROM INDIAN RESEARCH AND REGIONAL PERSPECTIVE

Indian researchers have made substantial and steadily growing contributions to the field of naphthalimide chemistry, particularly in the synthesis and biological evaluation of naphthalimide derivatives and their hybrids with other heterocyclic moieties. These contributions span organic synthesis, medicinal chemistry, biological screening and computational studies, reflecting the multidisciplinary strength of Indian academic and research institutions.

6.1 Contributions from Indian research groups

Several research groups in India have reported systematic studies on the design and synthesis of novel naphthalimide derivatives with promising anticancer activity. These studies often focus on strategic N-substitution and aromatic ring functionalisation to enhance DNA-binding affinity, cytotoxic potency and selectivity towards cancer cells. Many Indian publications incorporate detailed structure–activity relationship analyses supported by in vitro cytotoxicity data against established human cancer cell lines, along with molecular docking and ADMET predictions to rationalise observed biological trends. In parallel, Indian researchers have also explored the antibacterial potential of naphthalimide-based compounds. Notable work has been reported on thiourea-, hydrazide- and triazole-linked naphthalimide hybrids, which demonstrate significant activity against Gram-positive bacteria, including resistant strains. These studies typically employ standard microbiological assays to determine minimum inhibitory concentrations and, in some cases, extend to antibiofilm or time-kill evaluations. The integration of synthetic chemistry with microbiological testing highlights the applied relevance of these investigations. Another important contribution from Indian laboratories is the exploration of naphthalimides as fluorescent probes and theranostic agents. By exploiting the intrinsic photophysical properties of the naphthalimide core, several studies have developed compounds capable of simultaneous cellular imaging and anticancer activity. This dual functionality has added a new dimension to naphthalimide research, positioning these molecules at the interface of diagnostics and therapeutics.

6.2 Emphasis on methodology and sustainability

Indian research has also contributed to methodological innovation in this field. A number of studies report the use of green and sustainable synthetic approaches, such as microwave-assisted reactions, one-pot protocols and alternative reaction media, for the preparation of naphthalimide derivatives. These approaches align with global efforts towards environmentally responsible chemistry and demonstrate the feasibility of sustainable practices in medicinal chemistry research.

6.3 Regional perspective: Andhra Pradesh

Despite the breadth of national-level research output, a closer examination of the literature reveals that comprehensive and multidisciplinary studies originating specifically from institutions in Andhra Pradesh are relatively limited. While individual publications from the region exist in related areas of heterocyclic chemistry and pharmaceutical research, systematic investigations that integrate the synthesis of naphthalimide hybrids with detailed anticancer and antibacterial evaluation are scarce. This gap suggests an opportunity for researchers in Andhra Pradesh to contribute original work that combines synthetic chemistry with locally relevant biological testing, such as screening against clinical bacterial isolates or cancer cell lines accessible through regional medical institutions.

6.4 Research opportunities and future directions

The regional perspective highlights the potential for Andhra Pradesh–based institutions to strengthen their presence in this field through collaborative, interdisciplinary research. Partnerships between chemistry departments, microbiology laboratories and cancer research centres could facilitate the development of novel naphthalimide-based hybrids with translational relevance. Such efforts would not only enrich the national research landscape but also address region-specific health challenges.

VII. CHALLENGES AND FUTURE PROSPECTS

Despite the considerable progress achieved in the synthesis and biological evaluation of naphthalimides and their heterocyclic hybrids, several challenges continue to limit their advancement from promising laboratory compounds to clinically useful therapeutic

agents. Addressing these challenges is essential for realising the full potential of naphthalimide-based molecules in anticancer and antibacterial drug discovery.

7.1 Challenges

One of the primary challenges associated with naphthalimide derivatives is their lack of absolute selectivity. Owing to their strong DNA-intercalating ability, many naphthalimides exhibit cytotoxic effects on both cancerous and normal cells, leading to concerns regarding systemic toxicity. Although structural modifications and hybridisation strategies have improved selectivity in some cases, achieving a favourable therapeutic index remains a critical hurdle.Another significant challenge lies in pharmacokinetic limitations. Several potent naphthalimide derivatives suffer from poor aqueous solubility, rapid metabolic degradation or unfavourable distribution profiles, which restrict their in vivo efficacy. These issues underscore the need for optimisation of physicochemical properties alongside biological activity during lead development. In the context of antibacterial applications, the activity of naphthalimide-based compounds is often more pronounced against Gram-positive bacteria, with comparatively weaker effects on Gram-negative organisms. The presence of an outer membrane and efflux mechanisms in Gram-negative bacteria presents a substantial barrier to many naphthalimide derivatives. Overcoming this limitation requires rational molecular design aimed at enhancing membrane penetration or bypassing resistance mechanisms. From a synthetic standpoint, the preparation of complex hybrid molecules can involve multistep procedures, use of hazardous reagents or low overall yields. While green and efficient synthetic methodologies are increasingly reported, their adoption is not yet universal, and scalability remains a concern for industrial translation.

7.2 Future prospects

Future research on naphthalimides and their hybrids is expected to focus on rational design strategies guided by detailed structure–activity relationship and structure–property relationship studies. Incorporation of targeting moieties, prodrug approaches and controlled-release systems may improve selectivity towards cancer cells and reduce toxicity to normal tissues. Advances in computational chemistry and molecular modelling are likely to play an increasingly important role in guiding the design of new derivatives with optimised biological and pharmacokinetic profiles. Integration of in silico screening with experimental validation can significantly reduce time and cost in lead identification. In antibacterial drug discovery, future efforts should prioritise the development of naphthalimide hybrids with enhanced activity against Gram-negative pathogens and resistant clinical isolates. Combining naphthalimides with heterocycles known to disrupt bacterial membranes or inhibit resistance mechanisms represents a promising direction. Additionally, greater emphasis on sustainable chemistry is anticipated. The adoption of green synthetic routes, such as one-pot reactions, solvent-free methods and alternative reaction media, will be important for aligning medicinal chemistry research with environmental considerations. From a regional perspective, particularly in India and Andhra Pradesh, there is strong potential for multidisciplinary collaborations that integrate synthetic chemistry, microbiology, cancer biology and pharmacology. Such collaborative efforts can generate comprehensive datasets and accelerate the translation of naphthalimide-based compounds towards practical therapeutic applications. In conclusion, while challenges related to selectivity, toxicity and pharmacokinetics remain, the future of naphthalimide research is promising. Continued innovation in molecular design, hybridisation strategies and interdisciplinary research is expected to yield novel naphthalimide-based agents with improved anticancer and antibacterial efficacy.

VIII. CONCLUSION

Naphthalimides, particularly 1,8-naphthalimide derivatives, have emerged as a versatile and biologically significant class of heterocyclic compounds in medicinal chemistry. The accumulated literature clearly demonstrates that the rigid planar structure of the naphthalimide scaffold, combined with its strong DNA-intercalating ability and ease of structural modification, underpins its notable anticancer and antibacterial activities. Over the years, systematic structural optimisation and extensive biological evaluation have transformed naphthalimides from simple DNA-binding agents into multifunctional molecules with broad therapeutic

relevance. The strategy of molecular hybridisation has played a pivotal role in advancing this field. Conjugation of naphthalimides with other heterocyclic moieties such as triazoles, thioureas, hydrazides, coumarins and benzimidazoles has led to hybrid compounds exhibiting enhanced potency, improved selectivity and, in several cases, dual anticancer and antibacterial activity. These hybrids benefit from synergistic interactions arising from the combined pharmacological features of their constituent moieties, thereby overcoming some limitations of parent naphthalimide compounds. Indian researchers have contributed meaningfully to the synthesis, characterisation and biological assessment of naphthalimide-based compounds, reinforcing the global relevance of this scaffold. However, the review also highlights the need for more comprehensive and region-specific studies, particularly from Andhra Pradesh, that integrate synthetic chemistry with detailed biological and mechanistic investigations. Despite existing challenges related to toxicity, selectivity and pharmacokinetic behaviour, ongoing advances in rational drug design, green synthetic methodologies and interdisciplinary research provide a strong foundation for future progress. In summary, naphthalimides and their heterocyclic hybrids represent a promising platform for the development of next-generation anticancer and antibacterial agents, and continued focused research in this area is likely to yield therapeutically valuable outcomes.

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