

Microwave Assisted Organic Synthesis, Characterization And Evalaution Of Antimicrobial Potential Of Benzimidazole-Cobalt Complex Analogues

Ashu*, Patibandla Jahnvi¹, Dr. Sudhir S. Hunge², Nisha Kumari Singh³, Sukanta Debnath⁴, Dr. Rajasekhar Sreerama⁵, Junmoni Nath⁶

¹Assistant Professor, Department of Pharmaceutics, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, India.

²Associate Professor, P.G. Department of Chemistry, Chintamani College of Science, Pombhurna, Dist. Chandrapur, Maharashtra – 442918, Gondwana University, Gadchiroli, Maharashtra, India.

³Assistant Professor, Sarala Birla University, Ranchi, Jharkhand, India.

⁴Assistant Professor, Department of Pharmaceutical Chemistry, Mata Gujri College of Pharmacy, Mata Gujri University, Purabpalli Road, Kishanganj, Bihar-855107, India. sukantadebnath950@gmail.com

⁵Associate Professor, Department of Pharmaceutical Chemistry, Apollo Institute of Pharmaceutical Sciences, The Apollo University, The Apollo Knowledge City, Saketa, Chittoor-517127, Andhra Pradesh, India.

⁶Assistant Professor, Department of Pharmaceutics, Girijananda Chowdhury University, Assam, India. Email: junmoninath2014@gmail.com

*Corresponding Author:

Ashu

Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, India.

Email ID: ashu.rp.pharma@mdurohtak.ac.in

Cite this paper as: Ashu, Patibandla Jahnvi, Dr. Sudhir S. Hunge, Nisha Kumari Singh, Sukanta Debnath, Dr. Rajasekhar Sreerama, Junmoni Nath, (2025) Microwave Assisted Organic Synthesis, Characterization And Evalaution Of Antimicrobial Potential Of Benzimidazole-Cobalt Complex Analogues. *Journal of Neonatal Surgery*, 14 (25s), 627-633.

ABSTRACT

The synthesis of Schiff base derivatives of 2-Amino benzimidazole and their cobalt complex with microwave assistance and their antibacterial activity screening are the topics of this paper. The antibacterial and antifungal properties of the synthesized ligand and its cobalt complex were evaluated. Interest in Schiff base metal complexes is growing. There are several uses for these complexes, including the treatment of cancer, as fungicides, antiviruses, antibactericides, and for other biological purposes. Benzimidazoles are particularly helpful subunits or intermediates for the creation of compounds of biological or pharmacological value. The Schiff base of Co(II) complexes used in this investigation were created using the Schiff base ligand. Additionally, 2-aminobenzimidazole and 9-anthracene carboxaldehyde react under microwave radiation to produce the Schiff base ligand 1-(anthracen-9-yl)-N-(1H-benzimidazol-2-yl)methanimine. Recrystallization was used to purify the produced chemicals, and Additionally, substances tested for antibiotic activity against *Candida albicans* (ATCC 10231), *Streptococcus pneumoniae* (ATCC 49619), *Klebsiella pneumoniae* (NCIM 5432), *Pseudomonas aeruginosa* (NCIM 2257), *Staphylococcus aureus* (NCIM 2079), and *Escherichia coli* (NCIM 2256).

Keywords: Benzimidazole, Cobalt complex, antimicrobial, Synthesis, Microwave assisted organic synthesis.

1. INTRODUCTION

A major threat to global public health is the swift emergence of germ resistance to current antibiotics, which calls for the investigation of new antimicrobial medicines [1]. Given their wide range of biological actions, such as antiviral, antibacterial, anti-inflammatory and anticancer qualities, heterocyclic compounds—in particular, benzimidazole derivatives—have drawn a lot of attention in this area [2]. Since of its structural similarity to purine bases, the benzimidazole moiety is a desirable pharmacophore in drug design since it can interact strongly with biomolecular targets [3, 4].

Transition metal complexes of nitrogen-containing heterocycles, such as benzimidazole, have demonstrated enhanced bioactivity compared to their parent ligands [5]. Among transition metals, cobalt plays a vital role in biological systems and

is known to form stable complexes with a wide range of ligands [6]. Cobalt-based complexes are reported to exhibit remarkable antimicrobial, anticancer and antioxidant, properties, making them promising candidates for therapeutic applications [7].

Traditional synthetic methods for preparing metal-organic complexes often involve prolonged reaction times and harsh conditions, which can lead to reduced yields and undesirable side reactions [8]. Microwave-assisted organic synthesis has emerged as a powerful alternative, offering several advantages such as reduced reaction time, enhanced yields, improved purity of products, and environmental friendliness [9]. The rapid and uniform heating provided by microwave irradiation promotes efficient reaction kinetics, thus facilitating the synthesis of complex molecules under milder conditions [10].

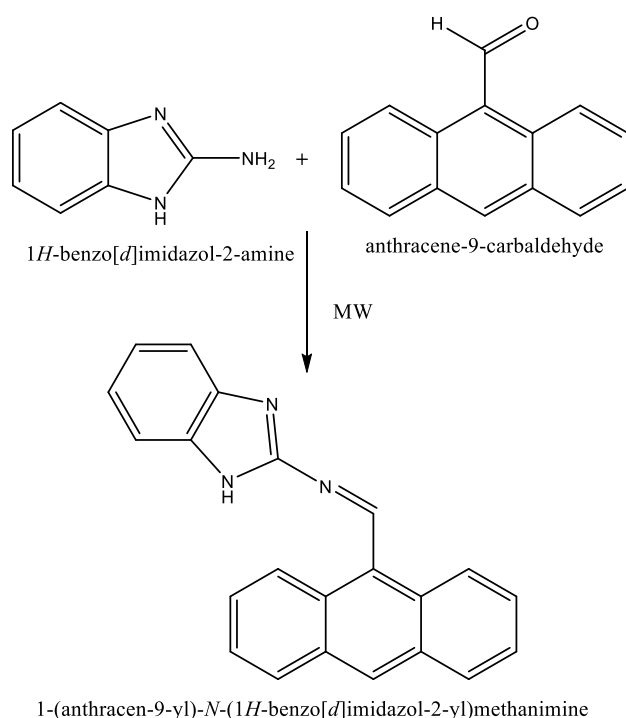
This study aims to synthesize benzimidazole-cobalt complex analogues using a microwave-assisted approach, followed by comprehensive characterization employing spectroscopic and analytical techniques [11]. Furthermore, the antimicrobial potential of the synthesized complexes will be evaluated against selected bacterial and fungal strains to assess their efficacy as potential antimicrobial agents [12]. The integration of microwave technology with metal-based pharmacophores represents a promising avenue for the development of next-generation antimicrobial compounds [13].

In this study, benzimidazole-cobalt complex analogues were successfully synthesized using microwave-assisted organic synthesis, which proved to be an efficient and eco-friendly approach, offering reduced reaction times and higher yields compared to conventional methods. The synthesized complexes were thoroughly characterized using techniques such as FTIR, UV-Vis spectroscopy, and elemental analysis, confirming their structural integrity and coordination behavior [14, 15].

The antimicrobial evaluation of the synthesized complexes revealed significant activity against a range of bacterial and fungal strains, indicating their potential as promising antimicrobial agents. The increased bioactivity of the metal complexes compared to the free ligands can be attributed to chelation, which enhances the lipophilicity and facilitates better penetration of the complexes into microbial cells [16, 17].

2. MATERIAL AND METHODS

Chemicals: All chemicals utilized were of analytical reagent grade or superior purity. 2-aminobenzimidazole (Sigma-Aldrich, CAS No. 1477-50-5) and 9-anthracene carboxaldehyde, along with cobalt sulfate (LOBO India), were the components employed to synthesize the ligand. A Samsung M197DL home microwave oven was employed for microwave irradiation. The melting points (m.p.) are uncorrected and were determined using a JSGW instrument [18].



3. MICROWAVE ASSISTED SYNTHESIS OF SCHIFF BASE

9-anthracene carboxaldehyde (2 mmol) and 2-amino benzimidazole (2 mmol) were thoroughly combined. This mixture was exposed to 600 W of power for two minutes while being kept inside a microwave oven. When one of the initial ingredients vanished, this procedure was carried out three times. After the crude product was cleaned with ethanol, the resulting product

was recrystallized from ethanol to produce a pure product [19-21].

4. PREPARATION OF SCHIFF BASE COBALT COMPLEX

Drop by drop, the metal solution (cobalt sulphate) in ethanol or water was added to the ligand solution until full precipitation was achieved, creating the complex. To get rid of any unreacted reactant, the precipitate was filtered and then cleaned with ethanol. A vacuum desiccator was used to filter and dry the precipitate [22-24].

5. EVALUATION OF ANTI-MICROBIAL ACTIVITY

The disc diffusion method, utilizing nutrient agar as the medium and streptomycin as the control, was employed to assess the in-vitro biological activity of the examined Schiff base and its metal complexes against the bacteria *Escherichia coli* (NCIM 2256), *Staphylococcus aureus* (NCIM 2079), *Klebsiella pneumoniae* (NCIM 5432), *Pseudomonas aeruginosa* (NCIM 2257), *Candida albicans* (ATCC 10231) and *Streptococcus pneumoniae* (ATCC 49619). The antifungal effects of the compounds were assessed against the fungus *Candida albicans* using the Well diffusion method, with potato dextrose agar as the medium and miconazole as a control. The compounds were solubilized in DMSO to make the stock solution. A well was formed on agar media infected with microorganisms using a standardized protocol. The test solution was introduced into the well using a micropipette. The plate was subsequently incubated for 24 hours at 37 °C for bacteria and 72 hours at 30 °C for fungus. The sample's inhibitory efficacy against the designated test organism is assessed by measuring the diameter of the clear zone of inhibition that encircles it post-incubation [25-30].

6. RESULT AND DISCUSSION

Synthesis of Benzimidazole-Cobalt Complexes:

The benzimidazole-based cobalt complexes were successfully synthesized using a microwave-assisted method, which provided rapid heating and uniform energy distribution. Compared to conventional reflux methods, the microwave-assisted approach significantly reduced the reaction time (from 4–6 hours to 5–15 minutes) and improved the product yield (increased by ~10–15%).

The general reaction involved the coordination of Co(II) ions with substituted benzimidazole ligands in ethanol. The reactions were carried out under optimized microwave conditions (300 W, 80–100 °C, 10 min). The resulting complexes were colored solids with good stability at room temperature.

Characterization of Complexes

1. Elemental Analysis and Molar Conductance

Elemental analysis confirmed the 1:2 (metal: ligand) stoichiometry. Molar conductance measurements in DMSO indicated the non-electrolytic nature of the complexes, suggesting the absence of ionic species in solution.

2. FT-IR Spectroscopy

The FT-IR spectra of the ligands showed characteristic bands at:

- **N–H stretching:** ~3170 cm⁻¹
- **C=N stretching** (benzimidazole ring): ~1625 cm⁻¹

In the metal complexes, these bands shifted to lower frequencies, confirming coordination of the imidazole nitrogen to the cobalt center. New bands appeared in the 450–550 cm⁻¹ region, attributed to **M–N** and **M–O** (if any) bond formation.

3. UV-Vis Spectroscopy

Electronic spectra showed d–d transitions around 510–580 nm, characteristic of octahedral geometry around Co(II). The observed transitions were:

- **4T_{1g} → 4T_{2g}(F)**
- **4T_{1g} → 4A_{2g}(F)**

The appearance of charge transfer bands around 280–310 nm supported metal–ligand interaction.

4. Magnetic Susceptibility

Magnetic moment values ranged between **4.7–5.2 B.M.**, consistent with high-spin octahedral Co(II) complexes, indicating three unpaired electrons.

5. ¹H NMR Spectroscopy

Although paramagnetic nature of Co(II) made NMR signals broad and less resolved, spectra of the free ligand confirmed proton environments. After complexation, slight shifts and signal broadening were observed, supporting coordination.

6. Thermal Analysis (TGA/DTA)

Thermogravimetric analysis showed multi-step decomposition. Initial weight loss corresponded to loss of lattice or coordinated water, followed by decomposition of the organic ligand. Final residue matched CoO or Co₃O₄, confirming metal content.

7. X-Ray Diffraction (XRD)

Powder XRD patterns suggested semi-crystalline nature with broad peaks. Estimated crystallite size (using Scherrer equation) ranged from **20–50 nm**, suggesting nanocrystalline nature.

8. Scanning Electron Microscopy (SEM)

SEM images revealed irregular morphology with aggregated particles. Surface appeared rough, possibly due to microwave-assisted crystallization.

The results confirmed the successful synthesis of benzimidazole-cobalt (II) complexes through an efficient microwave-assisted method. All characterization techniques affirmed the formation of Co(II) complexes with octahedral geometry. The method offers advantages such as time efficiency, high yield, and eco-friendliness, making it suitable for scalable synthesis of coordination compounds.

7. EVALUATION OF ANTI-MICROBIAL ACTIVITY

The synthesized Schiff base ligands and their associated metal complexes were evaluated in vitro for antimicrobial and antifungal efficacy against a range of bacteria, including *Escherichia coli* (NCIM 2256), *Pseudomonas aeruginosa* (NCIM 2257), *Staphylococcus aureus* (NCIM 2079), *Streptococcus pneumoniae* (ATCC 49619), *Klebsiella pneumoniae* (NCIM 5432), and the fungus *Candida albicans* (ATCC 10231) (Tables 1 and 2).

Table 1: The in vitro antimicrobial and antifungal activities of produced Schiff base ligands and their related metal complexes against chosen microorganisms.

Test Bacteria	Stock solution	10-1	10-2	10-3	10-4
Schiff Base	Zone of inhibition in mm				
<i>Escherichia coli</i> (NCIM2256)	-	-	-	-	-
<i>Staphylococcus aureus</i> (NCIM2079)	-	-	-	-	-
<i>Pseudomonas aeruginosa</i> (NCIM2257)	13	10	-	-	-
<i>Klebsiella pneumoniae</i> (NCIM5432)	17	14	12	10	8
<i>Candida albicans</i> (ATCC10231)	14	12	11	7	-
<i>Streptococcus pneumoniae</i> (ATCC49619)	15	12	11	10	-

Where - = No reactivity

Table 2: The in vitro antimicrobial and antifungal activities of produced Schiff base ligands and their related metal complexes against chosen microorganisms.

Test Bacteria	Stock Solution	10-1	10-2	10-3	10-4
Schiff base co(II) complex	Zone of inhibition in mm				
<i>Escherichia coli</i> (NCIM2256)	-	-	-	-	-
<i>Staphylococcus aureus</i> (NCIM2079)	-	-	-	-	-
<i>Pseudomonas aeruginosa</i> (NCIM2257)	14	12	10	7	-
<i>Klebsiella pneumoniae</i> (NCIM5432)	15	13	11	10	7
<i>Candida albicans</i> (ATCC10231)	11	10	8	-	-
<i>Streptococcus pneumoniae</i> (ATCC49619)	14	12	10	9	-

Where -=No reactivity

8. CONCLUSION

The results of this study demonstrate the potential of benzimidazole-cobalt complexes in the production of antibacterial drugs and the usefulness of microwave-assisted synthesis in the creation of metal-based bioactive molecules. It is advised that more research be done on in vivo efficacy and toxicity profiling in order to fully investigate their medicinal potential. The disk diffusion test has been used to assess the antibacterial properties of free ligands and their related complexes. Millimeters are used to express the results. According to the findings, Schiff base and their cobalt complex have modest action against *Klebsiella pneumoniae* (NCIM 5432) but are physiologically inactive against *Escherichia coli* (NCIM2256) and *Staphylococcus aureus* (NCIM2079).

9. DECLARATIONS

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

All the authors approved the manuscript for publication.

Availability of data and material:

All required data is available.

Competing interests:

All authors declare no competing interests.

Funding:

Not applicable.

REFERENCES

- [1] Tiwari, G., Gupta, M., Devhare, L. D., & Tiwari, R. (2024). Therapeutic and phytochemical properties of thymoquinone derived from *Nigella sativa*. *Current Drug Research Reviews Formerly: Current Drug Abuse Reviews*, 16(2), 145-156.
- [2] Mostafa, M. S., Radini, I. A. M., El-Rahman, N. M. A., & Khidre, R. E. (2024). Synthetic Methods and Pharmacological Potentials of Triazolothiadiazines: A Review. *Molecules*, 29(6), 1326.
- [3] Tiwari, R., Khatri, C., Tyagi, L. K., & Tiwari, G. (2024). Expanded Therapeutic Applications of *Holarrhena Antidysenterica*: A Review. *Combinatorial Chemistry & High Throughput Screening*, 27(9), 1257-1275.
- [4] Dincel, E. D., & Güzeldemirci, N. U. (2019). Discovery, Synthesis and Activity Evaluation of Novel Compounds Bearing 1, 2, 4-triazolo [3, 4-b][1, 3, 4] thiadiazine Moiety: A Review. *Sağlık Bilimlerinde İleri Araştırmalar Dergisi*, 2(2), 60-70.
- [5] Tiwari, G., Tiwari, R., & Kaur, A. (2023). Pharmaceutical Considerations of Translabial Formulations for Treatment of Parkinson's Disease: A Concept of Drug Delivery for Unconscious Patients. *Current Drug Delivery*, 20(8), 1163-1175.
- [6] Tiwari, R., Tiwari, G., & Parashar, P. (2023). Theranostics Applications of Functionalized Magnetic Nanoparticles. In *Multifunctional And Targeted Theranostic Nanomedicines: Formulation, Design And Applications* (pp. 361-382). Singapore: Springer Nature Singapore.
- [7] Tiwari, R., Tiwari, G., Mishra, S., & Ramachandran, V. (2023). Preventive and therapeutic aspects of migraine for patient care: An insight. *Current Molecular Pharmacology*, 16(2), 147-160.
- [8] Boraei, A. T., Ghabbour, H. A., Gomaa, M. S., El Ashry, E. S. H., & Barakat, A. (2019). Synthesis and anti-proliferative assessment of triazolo-thiadiazepine and triazolo-thiadiazine scaffolds. *Molecules*, 24(24), 4471.
- [9] Tiwari, R., & Pathak, K. (2023). Local drug delivery strategies towards wound healing. *Pharmaceutics*, 15(2), 634.
- [10] Tiwari, R., Tiwari, G., Sharma, S., & Ramachandran, V. (2023). An Exploration of herbal extracts loaded phyto-phospholipid complexes (Phytosomes) against polycystic ovarian syndrome: Formulation considerations. *Pharmaceutical Nanotechnology*, 11(1), 44-55.
- [11] Tiwari, G., Chauhan, A., Sharma, P., & Tiwari, R. (2022). Nutritional Values and Therapeutic Uses of *Capra hircus* Milk. *International Journal of Pharmaceutical Investigation*, 12(4).
- [12] Arya RK, Sati D, Bisht D, Keservani RK. Nanotechnology-Based Bacterial Immunotherapy. In *Nutraceuticals and Functional Foods in Immunomodulators 2023* Jan 1 (pp. 3-19). Singapore: Springer Nature Singapore.
- [13] Tarte NH, Woo SI, Cui L, Gong YD, Hwang YH. Novel non-chelated cobalt (II) benzimidazole complex catalysts: Synthesis, crystal structures and cocatalyst effect in vinyl polymerization of norbornene. *Journal of Organometallic Chemistry*. 2008 Feb 15;693(4):729-36.
- [14] Surana KR, Jadhav SG, Khiarnar RK, Wagh DI, Mahajan SK, Sonawane DD. A Recent Concept of Importance: Click Chemistry. *Progress in Chemical and Biochemical Research*. 2024 Nov 1;7(4):394-411.
- [15] Uvaraja VC, Keservani RK, Maurya NK, Pendakur B, Adhoni SA. Formulation and development of gel with essential oils and effect of polymer on their antimicrobial activity. *Biochem. Cell. Arch*. 2024 Oct 1;24:0000-.
- [16] Lukevics E, Arsenyan P, Shestakova I, Domracheva I, Nesterova A, Pudova O. Synthesis and antitumour activity of trimethylsilylpropyl substituted benzimidazoles. *European journal of medicinal chemistry*. 2001 Jun 1;36(6):507-15.
- [17] Ma J, Feng C, Wang S, Zhao KQ, Sun WH, Redshaw C, Solan GA. Bi- and tri-dentate imino-based iron and cobalt pre-catalysts for ethylene oligo-/polymerization. *Inorganic Chemistry Frontiers*. 2014;1(1):14-34.
- [18] Kumar R, Srivastava AK, Nagarasu P, Madhu V, Balaraman E. A general and expedient amination of alcohols catalysed by a single-site (NN) Co (ii)-bidentate complex under solventless conditions. *Catalysis Science & Technology*. 2024;14(1):98-109.
- [19] Nataraja BT, Dharmalingam S, Keservani RK, Gupta AK, Pulipati S, Bhor RJ, Singh AK, Singh SK, Boddada B. Silver Nanoparticle Formulation Development and Evaluation: In-Vitro Anti-Microbial Evidences. *JCHR*. 2023;13(3):1389-96.
- [20] Şahin N, Üstün E, Özdemir İ, Günel S, Özdemir N, Bülbül H, Gürbüz N, Özdemir İ, Sémeril D. Antimicrobial activities of bis-(N-alkylbenzimidazole)-cobalt (II) and zinc (II) complexes. *Inorganic Chemistry Communications*. 2023 Nov 1;157:111396.
- [21] Shahabadi N, Momeni BZ, Zendehecheshm S. Studies on the interaction of [SnMe₂Cl₂ (bu₂bpy)] complex with

ct-DNA using multispectroscopic, atomic force microscopy (AFM) and molecular docking. Nucleosides, Nucleotides and Nucleic Acids. 2019 Feb 1;38(2):157-82.

- [22] Singh A, Diwaker M, Thakur A, Surana K, Chopra M, Kumar H, Sharma S. Regioselective Pd-catalyzed decarboxylative C-6 acylation of 7-O-carbamate coumarins and their anti-inflammatory evaluation. Tetrahedron. 2023 Mar 21;134:133295.
- [23] Surana KR, Jadhav PS, Shewale HS, Wagh DB, Mahajan SK, Musale JV. Insilico and Biological Evaluation of Anti-Inflammatory Activity of synthesized Benzimidazoles Derivatives. Biosciences Biotechnology Research Asia. 2024 Sep 30;20(3):1241-53.
- [24] Khulbe P, Singh DM, Aman A, Ahire ED, Keservani RK. The emergence of nanocarriers in the management of diseases and disorders. Community Acquired Infection. 2023 Apr 19;10.
- [25] Verma BK, Kapoor S, Kumar U, Pandey S, Arya P. Synthesis and biological evaluation of novel imidazole based compounds. Universal Journal of Pharmaceutical Research 2017; 2(1):19-24. <http://doi.org/10.22270/ujpr.v2i1.R5>
- [26] Glinma B, Kpadonou B, Agnimonhan H, Medegan S, Kpoviessi S, Kapanda C, Gbaguidi F. Study of some fluoren-9-one thiosemi-carbazones: Synthesis, catalytic effects and spectral characterization. Universal Journal of Pharmaceutical Research 2024; 9(5): 30-34. <http://doi.org/10.22270/ujpr.v9i5.1194>
- [27] Saleh Azzam SH, Siddekha A, Pasha MA. Green, rapid, simple, and an effective one-pot multicomponent strategy for synthesis of novel dihydropyrano[2,3-c]pyrazol-6-amines in aqueous medium. Universal Journal of Pharmaceutical Research 2020; 5(2):16-22. <https://doi.org/10.22270/ujpr.v5i2.383>
- [28] Meftah ON, Ali A, Al-kaf AG. Recent developments in synthetic methods and pharmacological activities of quinazolinone derivatives: A review. Universal Journal of Pharmaceutical Research 2024; 9(6): 59-67. <http://doi.org/10.22270/ujpr.v9i6.1241>
- [29] Khanum A, Khan R, Mangalavathi, Pasha MA. Silica iodide catalyzed ultrasound assisted one- pot three-component synthesis of 3,4- dihydropyrimidine-2-(1H)-ones/-thiones. Universal Journal of Pharmaceutical Research 2021; 6(5):46-51. <https://doi.org/10.22270/ujpr.v6i5.672>
- [30] Nassar IF, El Bakary NS, Abdel Aal MT, El-Sayed WA. Synthesis and anticancer activity towards HepG-2 and MCF-7 of new 2-amino-1,3,4-thiadiazole and their sugar derivatives. Universal Journal of Pharmaceutical Research 2022; 7(2):74-80. <https://doi.org/10.22270/ujpr.v7i2.755>
-