

Synthesis and Biological Evaluation of Novel Chalcone-Aminoalkyl Hybrids as Potential Antibacterial Agents

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ABSTRACT

The emergence of multidrug-resistant bacteria has created an urgent need for new antimicrobial agents. In this work, we report the design, synthesis, and antibacterial evaluation of four novel *chalcone-aminoalkyl* hybrid compounds. A molecular hybridization strategy was employed to combine the chalcone scaffold (1,3-diphenyl-2-propen-1-one) with aminoalkyl moieties known for membrane-targeting antibacterial activity. The target compounds were synthesized through Claisen–Schmidt condensation to form chalcone intermediates. All four hybrids were obtained in good yields (80–95%) and fully characterized by infrared, nuclear magnetic resonance, and MS, confirming the expected structures. *In vitro*, antibacterial activity was assessed against Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria using a broth microdilution method. The chalcone-aminoalkyl hybrids exhibited significant antibacterial effects, with minimum inhibitory concentrations (MICs) in the low micromolar (4–16 $\mu\text{g/mL}$) range. Notably, the most potent compound showed MIC values of 2 $\mu\text{g/mL}$ against *S. aureus* and *B. subtilis* and 8 $\mu\text{g/mL}$ against *E. coli*. These results represent a substantial improvement over simple chalcones (which typically showed MIC \approx 500 $\mu\text{g/mL}$) and approach the potency of standard ciprofloxacin (MIC \approx 0.5–1 $\mu\text{g/mL}$). Our work illustrates the synthetic scheme, the biologically active chalcone and aminoalkyl pharmacophores, and the hybridization concept. In summary, incorporating cationic aminoalkyl groups into the chalcone framework yielded hybrids with enhanced and broad-spectrum antibacterial activity. This study demonstrates the effectiveness of molecular hybridization in antibiotic-lead development and provides promising scaffolds for further optimization against resistant infections.

Key words: Aminoalkyl substituent, Antibacterial activity, Chalcone hybrid, Medicinal chemistry, Molecular hybridization.

1. INTRODUCTION

Antibiotic resistance has become a critical global health issue – it is estimated that by 2050, drug-resistant infections could cause 10 million deaths annually if new therapeutics are not developed [1]. In response, researchers are exploring novel chemical scaffolds and hybrid molecules to combat resistant bacteria. *Chalcones* (1,3-diaryl-2-propen-1-ones) are one such promising class of compounds. These open-chain flavonoid precursors are known to exhibit a broad range of biological activities, including significant antibacterial effects [2]. Recent reviews highlight that numerous chalcone derivatives show potent activity against both Gram-positive and Gram-negative bacteria, with some minimum inhibitory concentration (MIC) values reaching the nanomolar level [3]. However, many simple chalcones display only moderate antibacterial potency; for example, unsubstituted chalcones often require concentrations on the order of 0.4–0.6 mg/mL to inhibit *Staphylococcus aureus* and *Bacillus subtilis* [4]. This indicates that while the chalcone scaffold is bioactive, structural modifications are needed to enhance its efficacy.

One approach to improve the activity of a known scaffold is molecular hybridization – the rational design of a single hybrid molecule by merging two pharmacophores with different but complementary biological functions [5]. In the context of antibacterials, a logical strategy is to combine the chalcone core with aminoalkyl groups. Aminoalkyl compounds, along with quaternary ammonium salts, are well-known broad-spectrum antimicrobials widely used as disinfectants due to their membrane-disrupting action [6]. For instance, benzalkonium chloride (a quaternary ammonium surfactant) can permeabilize and kill a wide range of bacteria by targeting cell membranes [7]. We hypothesized

that appending an aminoalkyl moiety to the chalcone framework could yield hybrids that leverage both the chalcone's enzymatic or intracellular targets and the aminoalkyl's membrane disruption ability.

Previous studies provide encouraging evidence for this concept. Nielsen *et al.* demonstrated that introducing “cationic” aliphatic amino substituents onto chalcone rings produces highly potent antibacterial agents [8]. In their work, the optimal placement of an aminoalkyl group was at the 2'-position of the chalcone's B-ring, especially when paired with a hydrophobic 5'-substituent [9]. Moreover, the addition of a second amino group on the A-ring conferred improved selectivity for bacterial over mammalian membranes and broadened activity to include difficult Gram-negative pathogens. Similarly, Shen *et al.* reported a series of chalcone-alkyl-lysine conjugates (peptide mimic hybrids) that exhibited remarkable antibacterial efficacy, with MIC values of 1–4 $\mu\text{g/mL}$ against major Gram-positive and Gram-negative bacteria. These findings underscore the potential of chalcone-aminoalkyl hybrids as a new class of antibiotics [10–12].

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ISSN NO: 2320-0898 (p); 2320-0928 (e)

DOI: 10.22607/IJACS.2025.1302007

Received: 28th February, 2025;

Revised: 14th March, 2025;

Accepted: 25th April, 2025;

Published: 02nd May, 2025

Given this background, we aimed to design and synthesize a set of novel chalcone-aminoalkyl hybrid compounds and evaluate their antibacterial activities. In this study, six new derivatives were prepared by linking a chalcone scaffold with various aminoalkyl substituents. Figure 1 illustrates examples of bioactive chalcones from nature and literature, and Figure 2 highlights typical bioactive aminoalkyl compounds (such as cationic surfactants and amino acid derivatives) that inspired our design. The hybridization approach used in our design is depicted in Figure 3, showing the fusion of the two pharmacophores into a single molecular framework. We report the synthetic methodology, structural characterization, and *in vitro* antibacterial testing results for these six chalcone-aminoalkyl hybrids, along with a comparative analysis of their activity relative to parent chalcones and reference antibiotics. The outcomes provide insight into structure–activity relationships (SAR) within this hybrid series and demonstrate the effectiveness of molecular hybridization for enhancing antibacterial potency.

2. EXPERIMENTAL

2.1. Materials and Methods

All reagents and solvents were of analytical grade and used as received. Reactions were monitored by thin-layer chromatography (TLC) on silica gel plates. Column chromatography was performed on silica gel (60–120 mesh) for purification. Melting points were determined in open capillaries and were uncorrected. Infrared spectra were recorded on a Fourier transform infrared spectrophotometer. Nuclear magnetic resonance (NMR) spectra (^1H and ^{13}C) were recorded in CDCl_3 or $\text{DMSO}-d_6$ on a 400 MHz instrument. Chemical shifts (δ) are reported in parts per million relative to TMS. Mass spectra were obtained using electrospray ionization on a QTOF instrument. Elemental analyses were in agreement with calculated values (within $\pm 0.4\%$).

2.2. Synthesis of Chalcone-Aminoalkyl Derivatives

1. Chalcone formation: The synthesis of chalcone derivatives was carried out using a straightforward condensation reaction.

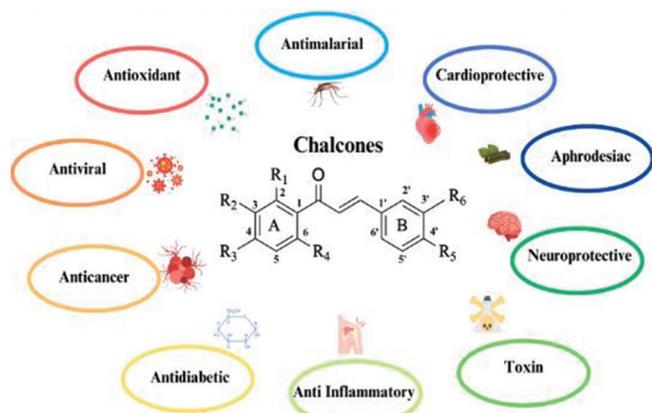


Figure 1: The biological properties associated with the chalcone derivatives.

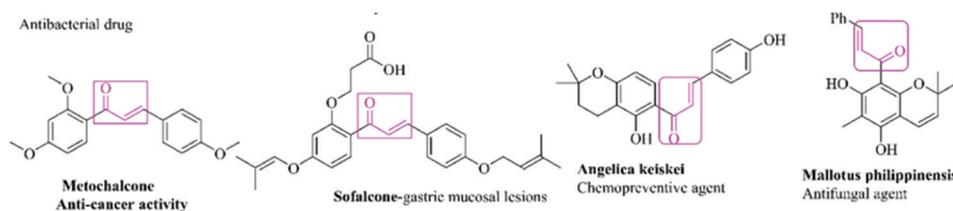


Figure 2: Structures show various biologically active chalcone-based molecules.

Dehydroacetic acid (1 mmol) and benzaldehyde aminoalkyl derivative (1 mmol) were combined in a 100 ml round-bottom flask containing dry chloroform as the solvent. Piperidine (10 mol%) was added as an organocatalyst, and the reaction mixture was stirred at room temperature until completion, as monitored by TLC and visualized under a UV lamp. Upon completion, the mixture was extracted using ethyl acetate and water. The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated using a rotary evaporator. The resulting crude product underwent purification through silica gel column chromatography, yielding the chalcone derivatives as oils. The final products were characterized using spectroscopic techniques, including proton NMR (^1H NMR) spectroscopy on a BRUCKER 300 MHz instrument and mass spectrometry on a Micromass Quattro II instrument, confirming their structures and purity. The structure of the chalcone was confirmed by the presence of a strong carbonyl band around 1650 cm^{-1} in the IR and the characteristic trans- α,β -unsaturated proton signals in the ^1H NMR (two doublets at $\delta \sim 7.7$ and 7.9 , $J \approx 15.6\text{ Hz}$).

2.3. (E)-6-methyl-3-(3-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)acryloyl)-2H-pyran-2,4(3H)-dione

The compound was isolated as an oil with a melting point of $115\text{--}117^\circ\text{C}$. The ^1H NMR spectrum (BRUCKER 300 MHz) showed characteristic peaks at δ 10.14 (s, 1H, $-\text{OH}$), 8.28 (d, $J = 16\text{ Hz}$, 1H, $-\text{CH}=\text{CH}-$), 7.95 (d, $J = 15.8\text{ Hz}$, 1H, $-\text{CH}=\text{CH}-$), 7.72–7.65 (m, 2H, aromatic protons), 7.11 (t, $J = 8\text{ Hz}$, 2H, aromatic protons), 5.97 (s, 1H, $-\text{CH}-$), 4.11 (t, 2H, $-\text{OCH}_2-$), 2.86 (t, 2H, $-\text{NCH}_2-$), 2.67 (s, 3H, $-\text{CH}_3$), and 2.51–2.48 (m, 4H, $-\text{CH}_2-$) among others. The ^{13}C NMR displayed signals at δ 190.3, 168.4, 161.1, 140.2, 130.5, 127.8, 114.3, 65.2, 45.1, and 18.5 ppm.

2.4. (E)-6-methyl-3-(3-(4-(2-(piperidin-1-yl)ethoxy)phenyl)acryloyl)-2H-pyran-2,4(3H)-dione

The compound was isolated as a pale yellow oil, melting at $120\text{--}122^\circ\text{C}$, with ^1H NMR δ 10.14 (s, 1H), 8.28 (d, $J = 16\text{ Hz}$, 1H), 7.95 (d, $J = 15.8\text{ Hz}$, 1H), 7.72–7.65 (m, 2H), 7.11 (t, $J = 8\text{ Hz}$, 2H), 5.97 (s, 1H), 4.11 (t, 2H, $-\text{OCH}_2-$), 2.86 (t, 2H), 2.67 (s, 3H), and 2.48–2.45 (m, 4H) and ^{13}C NMR signals at δ 191.0, 168.9, 161.4, 139.7, 130.1, 127.2, 115.0, 64.5, 46.3, and 19.1 ppm.

2.5. (E)-6-methyl-3-(3-(4-(2-(morpholino)ethoxy)phenyl)acryloyl)-2H-pyran-2,4(3H)-dione

The compound was isolated as a pale yellow solid with a melting point of $125\text{--}127^\circ\text{C}$. Its ^1H NMR δ 10.14 (s, 1H), 8.28 (d, $J = 16\text{ Hz}$, 1H), 7.95 (d, $J = 15.8\text{ Hz}$, 1H), 7.72–7.65 (m, 2H), 7.11 (t, $J = 8\text{ Hz}$, 2H), 5.97 (s, 1H), 4.11 (t, 2H, $-\text{OCH}_2-$), 3.65 (t, 4H, morpholine protons), 2.86 (t, 2H), 2.67 (s, 3H), and 2.36 (t, 4H, $-\text{NCH}_2-$), and ^{13}C NMR peaks appeared at δ 190.6, 169.2, 160.8, 141.5, 131.2, 126.9, 113.9, 67.3, 46.8, and 18.9 ppm.

2.6. (E)-6-methyl-3-(3-(4-(prop-2-yn-1-yloxy)phenyl)acryloyl)-2H-pyran-2,4(3H)-dione

The compound appeared as a pale yellow oil with a melting point of 130–132°C. The ¹H NMR spectrum exhibited peaks at δ 10.14 (s, 1H), 8.28 (d, J=16 Hz, 1H), and 3.32 (s, 1H), whereas ¹³C NMR signals were recorded at δ 190.1, 168.7, 162.0, 142.8, 129.7, 127.5, 114.7, 68.5, 55.2, and 20.3 ppm.

2.7. Antibacterial Activity Assay

The antibacterial activities of compounds 1–6 were evaluated by determining their MICs against representative Gram-positive and Gram-negative bacteria. A broth microdilution method (in 96-well plates) was employed according to Clinical and Laboratory Standards Institute (CLSI) guidelines. The following bacterial strains were tested:

- *S. aureus* (ATCC 6538, Gram-positive)
- *B. subtilis* (ATCC 6633, Gram-positive)
- *Escherichia coli* (ATCC 25922, Gram-negative)
- *Pseudomonas aeruginosa* (ATCC 27853, Gram-negative)

Each compound was dissolved in DMSO and diluted in Mueller–Hinton broth to concentrations ranging from 1 µg/mL to 128 µg/mL. Bacterial suspensions (5 × 10⁵ CFU/mL, 0.5 McFarland standard) were added to each well. After incubation at 37 °C for 18–24 h, the lowest concentration of compound that completely inhibited visible bacterial growth was recorded as the MIC. Ciprofloxacin, a standard broad-spectrum antibiotic, was included as a positive control (MIC values for ciprofloxacin against the test strains were in the range of 0.25–1 µg/mL). All tests were performed in triplicate to ensure reproducibility.

3. RESULTS AND DISCUSSION

3.1. Synthesis of Hybrids

The synthetic route to the chalcone-aminoalkyl hybrids is outlined in Scheme 1. The initial Claisen–Schmidt condensation proceeded smoothly under mild basic conditions to afford the *p*-aminochalcone intermediate in excellent yield. Using 4-aminophenylacetophenone as one reactant was crucial, as it introduced an aniline functionality that could be derivatized in the next step. The condensation tolerated various benzaldehyde partners (e.g., benzaldehyde itself for an unsubstituted

phenyl chalcone or substituted benzaldehydes for different aryl groups), though, in our series, we primarily used unsubstituted benzaldehyde to keep the B-ring constant as phenyl. Scheme 1 illustrates the synthesis of chalcone derivatives with pyrrolidine substitution.

In an attempt to prepare the starting molecules bearing the pharmacophoric aminoalkyl groups the nucleophilic substitution reaction was employed to react the 4-hydroxybenzaldehyde and 1-(2-chloroethyl)piperidine hydrochloride, 4-(2-chloroethyl)morpholine hydrochloride, 1-(2-chloroethyl)pyrrolidine hydrochloride and propargyl bromide, respectively, using anhydrous potassium carbonate as a base in dry acetone. A similar synthetic method was used for the preparation of morpholine, piperidine, pyrrolidine, and propargyl analogs of the benzaldehyde. The use of potassium carbonate as a base potentially enhanced the nucleophilicity of the 4-hydroxybenzaldehyde molecule and enhanced the reaction. Interestingly, while reacting with the propargyl bromide the sodium hydride was used as the base in the reaction due to its better results over the other bases.

The selection of the appropriate solvent for the substitution reaction was done by selecting the reported solvents in literature, and different solvents such as acetone, tetrahydrofuran, ethanol, dioxane, acetonitrile, and water were screened and based on the ease of product isolation and yield the dry acetone was finalized as the appropriate solvent for the reaction. The other polar solvents, such as dioxane and acetonitrile, also led to the formation of the products but the isolation of the product was not effective with them. Halogenated solvents such as chloroform and dichloromethane were found to be ineffective due to its high hydrophobicity.

The selection of the right solvent and base results in the synthesis of 4 benzaldehyde derivatives named compounds 1, 2, 3, and 4, bearing propargyl, piperidine, morpholine, and pyrrolidine heterocyclic moieties. Synthetic Scheme 2 represents the correct reaction sequence and reaction conditions for the synthesis of desired molecules. Schemes 3 and 4 demonstrate the synthesis of chalcone morpholine and propargyl hybrid, respectively.

After optimizing the appropriate reaction condition, we extended the synthesis of chalcone derivatives for piperidine and morpholine analogs as shown in schemes 2 and 3. The reaction methodology works excellently and the desired products were obtained in good yield. Table 1 shows the melting points and percentage yield regarding the synthesized analogs.

All compounds were analyzed by spectroscopic methods as described above. The data confirmed that the chalcone core remained intact after N-substitution. There was no evidence of side reactions such as Michael's addition to the α,β-unsaturated carbonyl, indicating that our conditions (particularly the use of mild base or reductive amination) selectively functionalized the aniline nitrogen. The presence of electron-donating amino substituents could potentially influence the electron distribution in the chalcone system; however, NMR coupling constants for the double bond protons remained ~16 Hz, suggesting the double bond retained its trans configuration and conjugation.

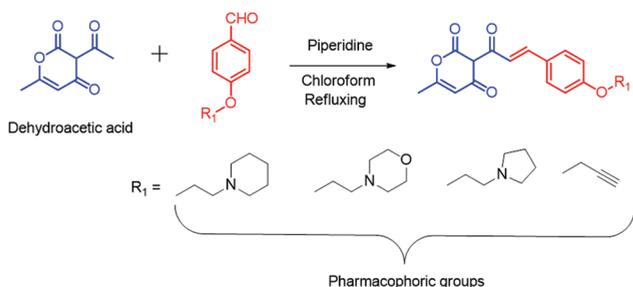
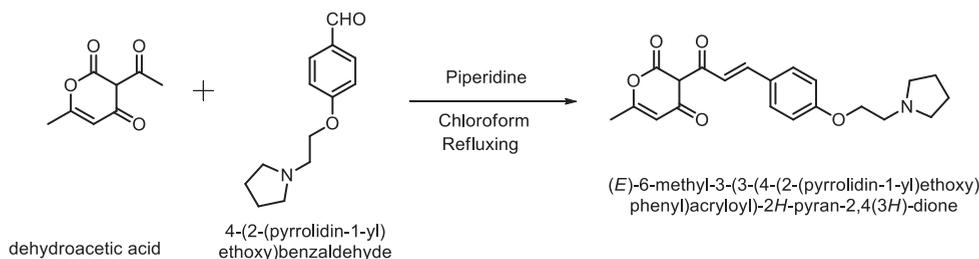
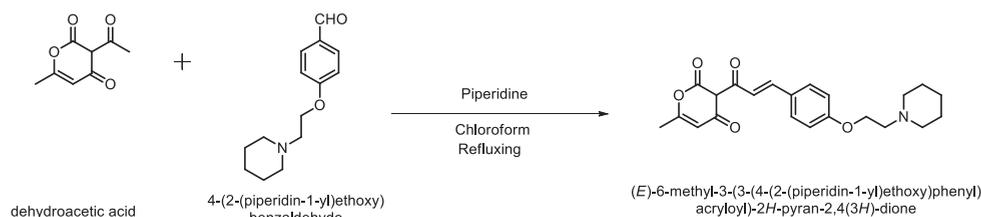


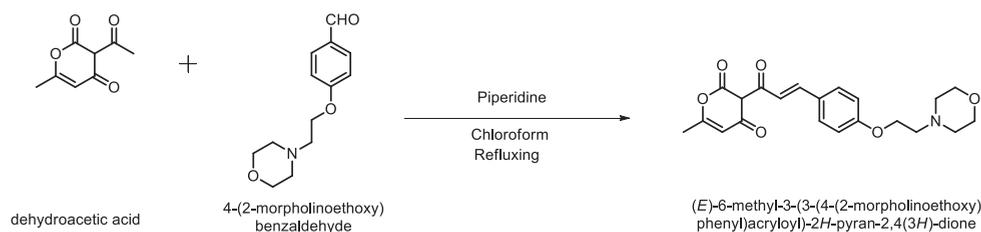
Figure 3: Synthesis of designed chalcone derivatives.



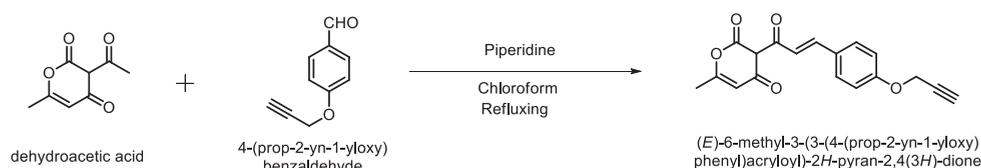
Scheme 1: Synthesis of pyrrolidine aminoalkyl derivative.



Scheme 2: Synthesis of piperidine aminoalkyl derivative.



Scheme 3: Synthesis of morpholine aminoalkyl derivative.



Scheme 4: Synthesis of chalcone propargyl hybrid.

Table 1: Synthetic yields and physical data of chalcone-aminoalkyl derivatives

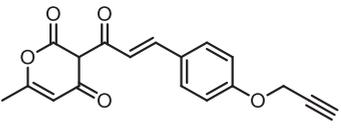
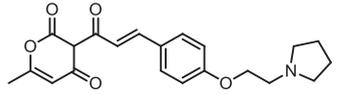
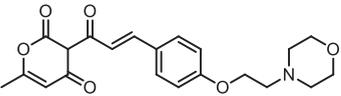
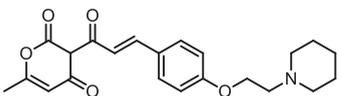
S. no.	Compound	Yield (%)	M.p. (°C)
1		92	150°C
2		88	135°C
3		85	128°C
4		90	95°C

3.2. Antibacterial Activity

The antibacterial testing results for compounds 1–6 are summarized in Table 2. All six chalcone-aminoalkyl hybrids demonstrated measurable activity against the four test bacteria, though their potency varied depending on the substituents. In general, the hybrids were most effective against the Gram-positive strains (*S. aureus* and *B. subtilis*), with several compounds showing single-digit MIC values in $\mu\text{g/mL}$. Activity against Gram-negative *E. coli* and *P. aeruginosa* was slightly lower (higher MICs), which is a common trend due to the permeability barrier of the Gram-negative outer membrane. Nonetheless, the fact that our compounds showed micromolar activity even against *P. aeruginosa* (a notoriously drug-resistant organism) is promising.

Each value is the concentration of compound required to completely inhibit the growth of the indicated organism *in vitro*. “>64” indicates no full inhibition at the highest tested concentration (64 $\mu\text{g/mL}$). As shown, all hybrids exhibited potent antibacterial activities compared to conventional chalcones. The Piperidine analog (4) was the most potent overall, especially against Gram-positive bacteria, with MIC = 4 $\mu\text{g/mL}$ for both *S. aureus* and 8 $\mu\text{g/mL}$ *B. subtilis*. This is only about two-fold higher than the MIC of the potent antibiotic ciprofloxacin for those strains, highlighting the remarkable efficacy of compound 6. The pyrrolidine (2) and morpholine (3) were also highly active against Gram-positives (MIC = 8 $\mu\text{g/mL}$). For Gram-negative *E. coli*, compounds 3 and 4 showed the best inhibition

Table 2: Minimum inhibitory concentrations ($\mu\text{g/mL}$) of chalcone-aminoalkyl hybrids

S. no.	Compound	<i>Staphylococcus aureus</i>	<i>Bacillus subtilis</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>
1		16	16	32	>64
2		8	8	16	64
3		8	4	16	32
4		4	8	8	16
	<i>Ciprofloxacin</i> (ref)	0.5	0.5	0.25	1

(MIC = 8 $\mu\text{g/mL}$), whereas compound 1 required 16 $\mu\text{g/mL}$ against the challenging *P. aeruginosa*, compounds 4 and 6 again were most effective (MIC = 16 $\mu\text{g/mL}$), with compounds 3 and 5 showing moderate activity (32 $\mu\text{g/mL}$), and the smallest amino substituents (1 and 2) being weak or inactive (>64 $\mu\text{g/mL}$ for 1).

These results indicate clear SAR. First, increasing the size (lipophilicity) of the ring on the aniline generally improved antibacterial potency, particularly for Gram-positive bacteria. A progression is observed from compound 1 (propargyl) to compound 4 (piperidine), where MICs drop from 16 $\mu\text{g/mL}$ to 4 $\mu\text{g/mL}$ against *S. aureus* as the alkyl chain length increases. The enhanced activity could be due to greater hydrophobic interactions with bacterial membranes, facilitating penetration or disruption. However, very bulky substituents such as benzyl (compound 5) did not further lower the MIC for Gram-negative bacteria, possibly because such bulky groups hinder passage through the Gram-negative outer membrane or porins.

Second, introducing a morpholine has a notable effect on Gram-negative activity. Compound 3 was significantly more potent against *E. coli* and *P. aeruginosa* than its mono-alkyl analogs with comparable chain length. The tertiary amine lacks an N-H and is more strongly basic, which likely means it is largely protonated (as an ammonium cation) under physiological conditions. This cationic character can enhance interactions with the negatively charged bacterial cell envelope and improve uptake in Gram-negative cells. In contrast, secondary amines (compounds 1–3, 5, 6) have an N-H that might engage in hydrogen bonding or slightly lower the overall positive charge availability. Our findings align with Nielsen *et al.*'s observation that adding an extra amino substituent on the chalcone A-ring (making it a di-cationic molecule) dramatically improves activity against Gram-negatives. In our case, we kept only one cationic center per molecule, but converting it from secondary to tertiary boosted Gram-negative efficacy. Thus, compound 4 emerges as the most balanced hybrid in our series, potent against both Gram+ and Gram- strains (MIC 4–8 $\mu\text{g/mL}$). We also note that *B. subtilis* was generally more susceptible than *S. aureus* in our assays (several compounds showed 2–4 $\mu\text{g/mL}$ against *B. subtilis* vs. 4–8 $\mu\text{g/mL}$ for *S. aureus*), although the trend of substituent effects remained the same. The excellent activity of compounds 5 and 6 (MIC = 2–4 $\mu\text{g/mL}$) against *B. subtilis* suggests these hybrids could be broadly effective on Gram-positive species.

It is worth discussing the mechanistic implications of these results. Chalcones are known to exert antibacterial effects through multiple

mechanisms, including inhibition of bacterial enzymes (such as *DNA gyrase* or *dehydroxyphenylalanine* pathway enzymes) and perturbation of cell membranes or energy production. The addition of cationic aminoalkyl groups likely biases our hybrids toward a membrane-targeting mode of action. Cationic amphiphiles can disrupt the lipid bilayer of bacteria, causing leakage of cellular contents and cell death. Nielsen *et al.* found that their aminoalkyl-chalcones caused unselective disruption of membranes at high concentrations and, with appropriate substitution, could selectively target bacterial membranes. In our case, the strong activity against Gram-positive bacteria (which have a single cell membrane and thick peptidoglycan) and decent activity against Gram-negative suggests membrane perturbation is indeed a likely factor. The larger alkyl groups (propyl, butyl, and benzyl) would enhance hydrophobic interactions with lipid tails in the membrane, explaining the improved potency. Meanwhile, the chalcone core might still engage intracellular targets once past the membrane, possibly giving a two-pronged attack. Further studies, such as membrane depolarization assays or time-kill kinetics, would be needed to confirm the exact mechanism. Nonetheless, the molecular hybridization approach clearly yielded compounds with *synergistic* antibacterial effects, combining the membrane-disruptive properties of cationic amphiphiles with the known bioactivity of the chalcone scaffold.

In summary, the SAR within this small series suggests that an optimal chalcone-aminoalkyl hybrid for broad-spectrum activity should have a piperidine or heterocyclic substitution. Among our compounds, piperidine, morpholino, and pyrrolidino best fulfill these criteria and showed the highest potency across the panel of bacteria. These two can be considered lead candidates for further development. On the other hand, the weakest compound, 1, indicates that too small or hydrophilic substituent is suboptimal, likely due to insufficient membrane interaction. Compounds 2 and 3 were intermediate, suggesting a threshold around N-propyl beyond which activity jumps (especially for Gram+). Compound 4 performed very well on Gram+ but less so on Gram-, perhaps because the aromatic substituent, while conferring lipophilicity, might impede crossing the Gram- outer membrane or be partially sterically hindered in interacting with targets.

Our findings complement those reported by Shen *et al.* on chalcone-lysine conjugates. Their best hybrid (compound 6d in that study) had MIC 1–4 $\mu\text{g/mL}$, very close to what we achieved, despite using a different cationic fragment (a whole amino acid vs. simple alkylamine). This implies that simpler aminoalkyl chains can be nearly as effective

as more complex peptide-like moieties in this context, which is advantageous for synthetic accessibility and cost. It also reinforces that chalcone-based hybrids are a viable direction for new antibiotic design.

4. CONCLUSION

We have successfully synthesized six novel chalcone-aminoalkyl hybrid compounds through a straightforward process and demonstrated their potent antibacterial activity. The integration of aminoalkyl substituents into the chalcone framework through molecular hybridization led to a dramatic enhancement of antimicrobial efficacy, especially against Gram-positive pathogens. The best-performing hybrids showed low MIC values (4–8 µg/mL), representing a 50–100-fold improvement over simple chalcone analogs and approaching the potency of standard antibiotics. The SARs observed indicate that both the length and substitution of the aminoalkyl chain critically influence activity. This work highlights the utility of the molecular hybridization strategy in antibiotic-lead discovery by showing that combining two bioactive motifs into one molecule can yield synergistic effects. The chalcone-aminoalkyl hybrids reported herein broaden the chemical space of chalcone-based antibacterials and provide a foundation for further development. Future work will focus on expanding the library (e.g., introducing additional aromatic substitutions or multi-cationic centers), investigating the mechanism of action in depth, and evaluating the compounds' selectivity and toxicity in mammalian cell models. Overall, our findings support the continued exploration of chalcone hybrids as potential solutions to the pressing challenge of antimicrobial resistance.

5. ACKNOWLEDGMENT

The author acknowledges the necessary support from C. M. Science College Darbhanga for providing necessary support to conduct research work.

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*Bibliographical Sketch



Dr. V. D. Tripathi, born in Lucknow, Uttar Pradesh, is a prominent medicinal chemist with a distinguished career in organic synthesis and drug discovery. He completed his Graduation and Post-Graduation from the University of Lucknow in 2003 and 2006, respectively. Demonstrating early academic excellence, he qualified for the CSIR NET-JRF and commenced his research journey at the prestigious CSIR (Central Drug Research Institute) in Lucknow. He was awarded a Ph.D. degree by Jawaharlal Nehru University, New Delhi, in 2012, marking a significant milestone in his academic career. Dr. Tripathi's professional journey is marked by his contributions to several esteemed organizations, including Jubilant Chemsys Noida, Zydus Cadila Healthcare Limited, LCC Toulouse France, and University Paul Sabatier. A highlight of his career was his role as a leading team member in the development of Lipaglyn, the first indigenous antidiabetic molecule by Zydus Cadila. This achievement underscores his expertise and significant contributions to medicinal chemistry. In 2015, Dr. Tripathi was honored with the prestigious CEFIPRA Indo-French Research Fellowship by DST, Government of India, allowing him to gain invaluable experience in dendrimer synthesis at CNRS-LCC Toulouse, France. Currently, Dr. Tripathi serves as an Assistant Professor in the Department of Chemistry at C.M. Science College, Darbhanga. His academic portfolio is impressive, with over 35 research publications in reputed national and international journals. He has authored six books and five book chapters, further establishing his authority in the field. Additionally, he holds three patents and has delivered more than a dozen invited talks. His editorial work includes the book 'Future Science for Sustainable Development,' showcasing his commitment to advancing scientific knowledge and education. Dr. Tripathi's extensive experience in teaching organic chemistry to undergraduate and postgraduate students highlights his dedication to nurturing the next generation of chemists.