# Design, Synthesis and Biological Evaluation of Novel Quinolinone Derivatives

Sajid Kausar Shah[1], Khushbu S. Jaiswal[2], M.M. Kodape[3], N.D. Gawhale[4]
[1]*Research centre, Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati*
[2,3]*Department of Chemistry, Sant, Gadge Baba Amravati University, Amravati*
[4]*Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati*
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***Abstract*—Quinolinones are an important class of heterocyclic compounds with a wide range of pharmacological activities. In this study, a series of novel quinolinone derivatives were rationally designed and synthesized using an efficient and practical synthetic strategy. The reactions were carried out under optimized conditions, providing the target compounds in good to excellent yields. The structures of the synthesized derivatives were confirmed by comprehensive spectroscopic analyses, including $^1$H NMR and GC-MS. The synthesized compounds were further evaluated for their biological activities using standard in vitro assays. Several derivatives exhibited significant biological activity, suggesting that the nature and position of substituents on the quinolinone scaffold play a crucial role in modulating activity. These findings highlight the potential of these novel quinolinone derivatives as promising leads for further pharmacological and drug development studies.**

***Index Terms*—Quinolinone derivatives, Heterocyclic synthesis, biological evaluation, Structure-activity relationship (SAR), bioactive compounds**

## I. INTRODUCTION

Infections with gram-positive, gram-negative, and fungal germs that can be lethal have become much more common in recent years. These are thought to be among the most significant global health concerns of the twenty-first century. Rapidly growing drug-resistant infections significantly diminish the efficacy of currently available treatments. [1] According to a 2024 research, one million people die each year from antibiotic resistance globally, and by 2050, that figure is expected to rise to 10 million. [2] Human health is also at risk from fungal infections, particularly in individuals with compromised immune systems. [3–5] *Aspergillus* and *Candida* species are responsible for more than 90% of potentially lethal invasive fungal infections (IFI). [6] Candida albicans is the most frequent cause of IFI and the fourth most prevalent cause of nosocomial bloodstream infections in hospitals, with a mortality rate of roughly 40%. [7–9] The discovery of novel antibacterial and antifungal drugs is a significant obstacle in averting these serious health problems. The development of a novel class of antimicrobial medications with distinct molecular structures and activities is essential to the replacement or substitution of existing antibiotics. In recent decades, a lot of researchers have been working on creating new targets and designing drugs based on structure in order to bring new chemotherapeutics that can overcome acquired resistance. [10-12]. The chemistry of heterocyclic compounds is currently one of the most important scientific areas in the pharmaceutical industry. Quinoline was initially isolated from coal tar by F.F. Runge in 1834. Later in 1842, it was isolated as a result of degraded quinine and cinchonine. Quinoline (1-azanaphthalene) is among the most versatile heterocyclic nitrogen nuclei. Quinolines are a fascinating class of chemicals with a wide range of pharmacological actions, including anti-oxidant, anti-inflammatory [14], anticonvulsant [15], antitubercular [16], anticancer [17], antimalarial [18], and antibacterial [19], including antiatherosclerotic, vasodilator, bronchodilator Klusa et al., and hepatoprotective activities [20, 21]. This has piqued the interest of medical researchers. The antiviral (Elvitegravir), antifungal (clioquinol), antibacterial

(Norfloxacin, Ciprofloxacin), antimalarial (Chloroquine, Amodiaquine), and numerous other drugs that are undergoing clinical trials are notable commercial drugs that contain quinoline nuclei. [22] Quinoline has garnered a lot of attention as a crucial element in drug research and development. To ascertain the medicinal importance of quinolone hybrids as a potential therapeutic agent, it was believed to be advantageous to synthesize and construct particular biologically active molecules and test them for their antibacterial and anthelmintic qualities both in vitro and in vivo.

## II. MATERIAL AND METHODS

All chemicals used in the experiments were of analytical reagent (AR) grade. Analytical thin-layer chromatography (TLC) was carried out on Merck pre-coated silica gel 60 F254 aluminium sheets. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded in $CDCl_3$ on a 500 MHz spectrometer with tetramethylsilane (TMS) serving as the internal standard.

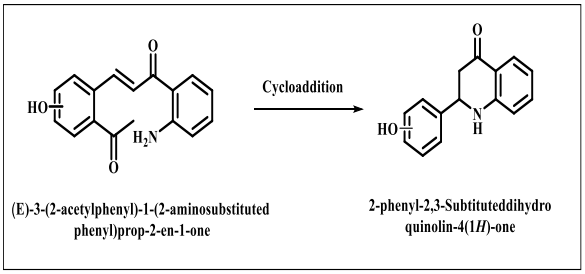
## III. CHARACTERIZATION TECHNIQUES

The structure of synthesized compounds was determined by chemical properties elemental analysis and spectral data. $^1$H-NMR spectra were recorded on Bruker Avance Neo 500 MHz spectrometer using $CDCl_3$ solvent and TMS as internal standards at SAIF, Punjab University, Chandigarh (India). Chemical shifts are expressed in ppm. Mass spectrums were recorded on Thermo Scientific TSQ 8000 Gas Chromatogram.

Experimental

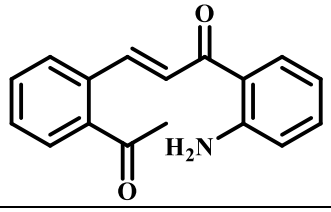
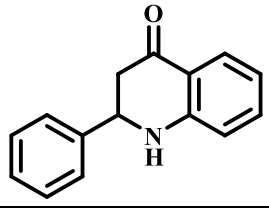
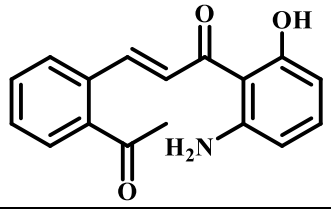
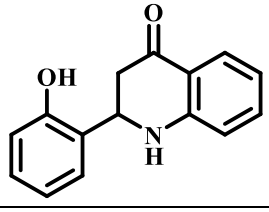
General Reaction for synthesis of 2-phenyl-2,3-Subtituteddihydroquinolin-4(1H)-one

Quinoline is synthesized experimentally from chalcones in a number of processes, including the use of bleaching earth clay as a heterogeneous catalytic media and PEG-400 as a solvent. The addition of substituted chloroquinoline-3-carbaldehyde starts the synthesis. After 10 hours of stirring at 25 $^o$C, the reaction mixture is acidified with 10% aqueous HCl, the organic material is removed using dichloromethane, and the mixture is then rinsed with water. The desired chalcone compound is subsequently obtained by drying the result with anhydrous $Na_2SO_4$ and then concentrating it. A silica gel column in a 9:1 ratio of $CHCl_3$:$CH_3OH$ is used in the purifying procedure. Depending on the catalyst and reaction conditions, the yield of the produced compounds can vary from 75% to 85%.




Scheme 1. Synthesis of 2-phenyl-2,3-Subtituteddihydroquinolin-4(1H)-one

Table 1. Scope of (E)-3-(2-acetylphenyl)-1-(2-aminosubstitutedphenyl) prop-2-en-1-one

| Sr.No | Substrate | Product | Time in Hrs. | Yield |
|---|---|---|---|---|
| 1 |  |  | 10 | 71 |
| 2 |  |  | 10 | 79 |

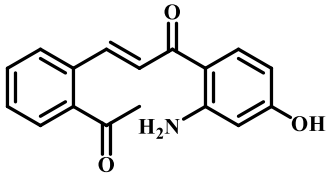
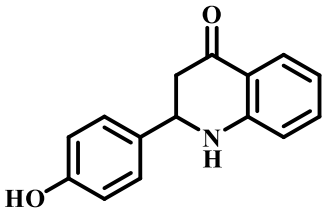
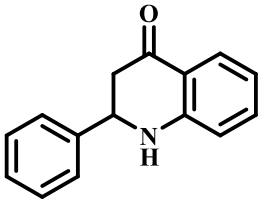
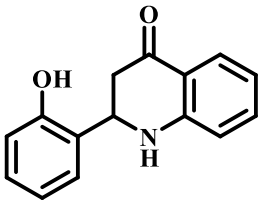
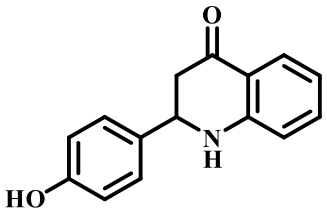
| | | | | |
|---|---|---|---|---|
| 3 |  |  | 10 | 84 |

Table 2. Structural Analysis

| Sr. No | Structure of Products | Structural analysis by $^1$HNMR and GCMS |
|---|---|---|
| 1 |  (a) | $^1$HNMR (500MHz, $CDCl_3$):δ 8.28 (s,1H), 6.70-7.71 (m, 9H), 4.40 (dd,1H), 2.90 (dd,2H)<br>GCMS: Cal m/z: 223.28 Found m/z: 223.24 |
| 2 |  (b) | $^1$HNMR (500MHz, $CDCl_3$):δ 9.66 (s,1H), 8.29 (s,1H), 6.71-7.72 (m, 9H), 4.42 (dd,1H), 2.92 (dd,2H)<br>GCMS: Cal m/z: 239.27 Found m/z: 239.25 |
| 3 |  (c) | $^1$HNMR (500MHz, $CDCl_3$):δ 9.06 (s,1H), 8.30 (s,1H), 6.74-7.76 (m, 9H), 4.45 (dd,1H), 2.94 (dd,2H)<br>GCMS: Cal m/z: 239.27 Found m/z: 239.22 |

Biological Investigation of 2-phenyl-2,3-Subtituteddihydroquinolin-4(1H)-one

Antioxidant activity

Method: DPPH Free Radical Scavenging Assay

$$\text{(\%)Free radical scavenging effect} = \frac{[\text{Absorbance of control (Ac)- Absorbance of sample(As)}]}{\text{Absorbance of control (Ac)}} \times 100$$

Antioxidant activity of 2-phenyl-2,3-Subtituteddihydroquinolin-4(1H)-one

Table 3. % Antioxidant Potential Using DPPH Assay Method (Conc. used 1 mg)

| Compound Code | Antioxidant Potential (%) (Mean±SD) | |
|---|---|---|
| | R | |
| a | -H | 39.264±1.39 |
| b | 2-OH | 41.559±1.44 |
| c | 4-OH | 43.2.09±2.20 |
| Standard | 90.79±2.19 | |

## IV. CONCLUSION

The synthetic series of 2-phenyl-2,3-Subtituteddihydroquinolin-4(1H)-one (compound 3a-c) is a potential moiety that can exhibit substantial biological activity in the current work. Additionally, the structure's benzo ring inflection purposefully

incorporates methoxy (para-OH) and hydroxyl (ortho-OH) groups over the ring. This demonstrates the robust and encouraging biological activity. In summary, our findings demonstrate robust action against microorganisms and play a substantial role in creating a structural moiety and interacting link. which will be helpful in future medication design strategies.

Conflict of Interest: Authors have declared that no competing interests exist.

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