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Development of Acylated Pyrazole-Containing Heterocyclic Chalcones: Synthesis, Spectral Studies, and Antibacterial Assessment

[1]Poonam Kumaria, [2]Niranjan Kumar Mandala, and [3]Ranjan Kumar
[1,2]Department of Chemistry, S. K. M. University, Dumka, India
[3]Department of Chemistry, Godda College, Godda,0 India

Abstract - In this study, a novel series of 1-[3-(4-fluoro-3-methylphenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl]ethan-1-one derivatives (3a-i) were synthesized, and their chemical structures were studied by 1H NMR, IR, and mass spectroscopy. TLC was used to examine the products that were isolated to determine their level of purity. The results of this study show that these derivatives have interesting properties. The disc diffusion method was used to test the in vitro antimicrobial activity of the synthesized compounds against Escherichia coli (MCC 2412), Staphylococcus aureus (MCC 2408), Bacillus subtilis (MCC 2010), Pseudomonas aeruginosa (MCC 2080), Saccharomyces cerevisiae (MCC 1033), and Candida albicans (MCC 1439).

Keywords - Chalcone-pyrazole derivatives, Antifungal, Antibacterial, Acylated Pyrazole

INTRODUCTION

The escalating global challenge of antimicrobial resistance (AMR) underscores an urgent need for the development of novel antibacterial agents with distinct mechanisms of action [1,2]. The declining efficacy of conventional antibiotics against multidrug-resistant pathogens has intensified research efforts toward designing and synthesizing new chemical entities capable of overcoming existing resistance mechanisms [3,4]. Among various pharmacophores explored, chalcones, 1,3-diaryl-2-propen-1-ones, have garnered significant attention due to their structural simplicity, synthetic accessibility, and broad-spectrum biological activities, including notable antibacterial effects [5,6].

Chalcones serve as versatile intermediates in organic synthesis and represent a privileged scaffold in medicinal chemistry [7,8]. Their antibacterial activity is often attributed to the presence of an α, β-unsaturated ketone system, which can act as a Michael acceptor, interfering with cellular processes in microorganisms [9,10]. Structural modifications on the aryl rings have been extensively investigated to enhance potency and selectivity, with electron-withdrawing and electron-donating groups significantly influencing bioactivity [11,12]. In particular, the incorporation of nitrogen-containing heterocycles, such as pyrazole, has been shown to improve pharmacological profiles due to increased hydrogen bonding capacity, bioavailability, and target affinity [13,14].
Further derivatization through acylation can fine-tune electronic properties, lipophilicity, and metabolic stability, thereby potentially enhancing membrane penetration and interaction with bacterial enzymes [15,16]. Although numerous chalcone derivatives have been reported, the design and systematic evaluation of acylated pyrazole-integrated chalcones remain relatively unexplored. Such hybrid molecules synergize the bioactive pyrazole nucleus with the chalcone framework, potentially leading to compounds with improved antibacterial efficacy.

In this study, we report the rational design, synthesis, and comprehensive spectral characterization of a novel series of acylated pyrazole-containing heterocyclic chalcones. The antibacterial potential of these synthesized compounds was evaluated against a panel of Gram-positive and Gram-negative bacteria. The structure-activity relationships (SAR) were elucidated to provide insights into the role of acylation and heterocyclic integration on antimicrobial performance, contributing to the ongoing search for new antibacterial candidates.

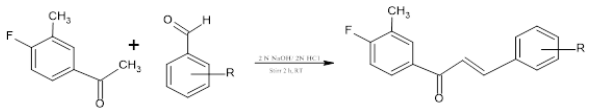
Experimental

Materials and methods

The Barnstead Electrothermal 9100 melting point was used to determine the melting points (uncorrected). The deuterated chloroform (CDCl3) served as the solvent for the 1H NMR spectra that were recorded on a Bruker Avance spectrometer at 400 MHz. The values for the chemical shift were presented in □ (ppm) scales. Infrared (IR) spectra were collected for analysis using a spectrometer manufactured by Bruker. The ESMS was captured using a Bruker IMPACT HD instrument. To monitor and detect the chemicals, thin-layer

chromatography (TLC) alumina sheets precoated with silica gel (0.2 mm thickness) were utilized. The spots on the sheets were seen under a UV light at 254 nm. There was no need for additional purification because all of the chemicals and reagents used were analytical.

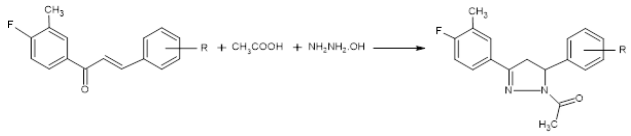
General procedure for synthesis of chalcones (2a–i):
In ethanol (25 mL), a mixture of 4-fluoro-3-methylacetophenone (1) (10 mmol) and cyano- and chloro-substituted benzaldehydes (a-i) (10 mmol) was mixed. The total amount of each component was 10 mmol. The combination received 15 milliliters of an aqueous solution of sodium hydroxide at a concentration of 2N. The reaction mixture was agitated for a total of thirty minutes at room temperature. 2N HCl was used to achieve the desired pH level for the reaction mass. After the solid result was filtered, washed with water, and dried to yield the solid, the corresponding chalcones (2a–i) were prepared through the process of recrystallization using ethanol. TLC was used to check whether or not the reaction was successful [14].



Scheme 1: General procedure for the synthesis of chalcones (2a–i)

General procedure for the synthesis of pyrazolines derivatives (3a–i):

A solution containing a combination of chalcones (2a–h) (10 mmol) was subjected to reflux with the required amount of hydrazine hydrate (20 mmol) in glacial acetic acid for an extended period. The reaction mixture underwent a cooling process and was subsequently transferred into crushed ice. The resulting residue was then separated using filtration, followed by a thorough washing and drying procedure, resulting in the formation of compounds (3a–h). The advancement of the reaction was monitored using thin-layer chromatography (TLC) [15].



Scheme 2: General procedure for the synthesis of acylated pyrazolines derivatives (3a–i)

2-[1-acetyl-3-(4-fluoro-3-methylphenyl)-4,5-dihydro-1H-pyrazol-5-yl]benzonitrile (3a):
White solid, yield: (214 mg, 66.67 %), m. p: 188 □C; IR (cm-1): 3063(CO–CH3), 2924 (-CH3), 2229 (CN), 1719 (C=O), 1630 (C=N), 1502/1400 (C=C aromatic ring), 1362 (C-F), 1012 (N-N); 1H NMR (400 MHz, CDCl3): □ 2.331 (s, 3H, Co-CH3), 2.414 (s, 3H, -CH3), 3.112-3.156 (dd, 1H, pyrazole-H, J = 11.44, 7.95 Hz), 3.774-3.848 (dd, 1H, pyrazole-H, J = 11.44, 4.26 Hz), 5.622-5.621 (dd, 1H, pyrazole-H, J = 8.06, 4.27 Hz), 7.073-7.117 (dd, 1H, Ar-H, J = 8.40, 0.54 Hz), 7.473-7.638 (m, 7H, Ar-H). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 321.35; Found: 321.554. Anal. calcd for C19H16FN3O: C, 71.01; H, 13.02; F, 5.91; N, 13.08; O, 4.98.

3-[1-acetyl-3-(4-fluoro-3-methylphenyl)-4,5-dihydro-1H-pyrazol-5-yl]benzonitrile (3b):
White solid, yield: (249 mg, 71.55 %), m. p: 183; IR (cm-1): 3065(CO–CH3), 2926 (-CH3), 2229 (CN), 1725 (C=O), 1605 (C=N), 1501/1411 (C=C aromatic ring), 1363 (C-F), 1037 (N-N); 1H NMR (400 MHz, CDCl3): □ 2.331 (s, 3H, Co-CH3), 2.414 (s, 3H, -CH3), 3.112-3.156 (dd, 1H, pyrazole-H, J = 11.44, 7.95 Hz), 3.774-3.848 (dd, 1H, pyrazole-H, J = 11.44, 4.26 Hz), 5.622-5.621 (dd, 1H, pyrazole-H, J = 8.06, 4.27 Hz), 7.073-7.117 (dd, 1H, Ar-H, J = 8.40, 0.54 Hz), 7.473-7.638 (m, 7H, Ar-H). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 321.35; Found: 321.554. Anal. calcd for C19H16FN3O: C, 71.01; H, 13.02; F, 5.91; N, 13.08; O, 4.98.

4-[1-acetyl-3-(4-fluoro-3-methylphenyl)-4,5-dihydro-1H-pyrazol-5-yl]benzonitrile (3c):
White solid, yield: (256 mg, 73.56 %), m. p: 193; IR (cm-1): 3038(CO–CH3), 2920 (-CH3), 2227 (CN), 1652 (C=O), 1605 (C=N), 1502/1409 (C=C aromatic ring), 1331 (C-F), 1016 (N-N); 1H NMR (400 MHz, CDCl3): □ 2.356 (s, 3H, CO-CH3), 2.458 (s, 3H, -CH3), 3.102-3.158 (dd, 1H, pyrazole-H, J = 8.05, 7.77 Hz), 3.775-3.849 (dd, 1H, pyrazole-H, J = 7.76, 4.25 Hz), 5.616-5.658 (dd, 1H, pyrazole-H, J = 8.06, 4.27 Hz), 7.069-7.114 (dd, 1H, Ar-H, J = 8.42, 0.54 Hz), 7.299-7.381 (ddd, 2H, Ar-H, J = 8.61, 1.65, 0.40 Hz), 7.550-7.615 (dd, 1H, Ar-H, J = 8.47, 0.55 Hz), 7.646-7.666 (ddd, 3H, Ar-H, J = 5.59, 1.95, 0.45 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 321.35; Found: 322.987. Anal. calcd for C19H16FN3O: C, 71.01; H, 5.02; F, 5.91; N, 13.08; O, 4.98.

1-[5-(2, 3-dichlorophenyl)-3-(4-fluoro-3-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (3d):
White solid, yield: (256 mg, 70.01 %), m. p: 199; IR (cm-1): 3067(CO–CH3), 2925 (-CH3), 1739 (C=O), 1605 (C=N), 1502/1402 (C=C aromatic ring), 1323 (C-F), 1010 (N-N), 818 (C-Cl); 1H NMR (400 MHz, CDCl3): □ 2.343 (s, 3H, CO-CH3), 2.520 (s, 3H, -CH3), 3.056 (dd, 1H, pyrazole-H, J = 13.66, 8.01 Hz), 3.841-3.915 (dd, 1H, pyrazole-H, J = 13.69, 4.25 Hz), 5.930-5.970 (dd, 1H, pyrazole-H, J = 8.06, 4.26 Hz),

6.989-7.008 (dd, 1H, Ar-H, J = 8.42, 0.55 Hz), 7.171-7.211 (dd, 1H, Ar-H, J = 1.87, 0.51 Hz), 7.300 (dd, 1H, Ar-H, J = 8.00, 1.10 Hz), 7.403-7.422 (dd, 1H, Ar-H, J = 8.33, 1.86 Hz), 7.548-7.616 (dd, 1H, Ar-H, J = 7.77, 1.11 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 365.23; Found: 363.147. Anal. calcd for C18H15Cl2FN3O: C, 59.19; H, 4.14; Cl, 19.41; F, 5.20; N, 7.67; O, 4.38.

1-[5-(2, 4-dichlorophenyl)-3-(4-fluoro-3-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (3e):
White solid, yield: (272 mg, 74.52 %), m. p: 188; IR (cm-1): 3067(CO–CH3), 2925 (-CH3), 1739 (C=O), 1605 (C=N), 1502/1402 (C=C aromatic ring), 1323 (C-F), 1010 (N-N), 818 (C-Cl); 1H NMR (400 MHz, CDCl3): □ 2.300 (s, 3H, CO-CH3), 2.449 (s, 3H, -CH3), 3.050 (dd, 1H, pyrazole-H, J = 13.66, 8.00 Hz), 3.810 (q, 1H, pyrazole-H, J = 13.71, 4.26 Hz), 5.858-5.899 (t, 1H, pyrazole-H, J = 8.03, 4.44 Hz), 7.015-7.051 (dd, 1H, Ar-H, J = 8.38, 0.49 Hz), 7.073-7.095 (dd, 1H, Ar-H, J = 8.29, 1.59 Hz), 7.212-7.232 (dd, 1H, Ar-H, J = 1.87, 0.52 Hz), 7.450 (dd, 1H, Ar-H, J = 1.63, 0.51 Hz), 7.545-7.559 (dd, 1H, Ar-H, J = 8.33, 1.88 Hz), 7.601-7.618 (dd, 1H, Ar-H, J = 8.28, 0.53 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 365.23; Found: 364.277. Anal. calcd for C18H15Cl2FN3O: C, 59.19; H, 4.14; Cl, 19.41; F, 5.20; N, 7.67; O, 4.38.

1-[5-(2, 5-dichlorophenyl)-3-(4-fluoro-3-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (3f):
White solid, yield: (263 mg, 73.42 %), m. p: 183; IR (cm-1): 3088(CO–CH3), 2925 (-CH3), 1740 (C=O), 1586 (C=N), 1502/1438 (C=C aromatic ring), 1362 (C-F), 1008 (N-N), 817 (C-Cl); 1H NMR (400 MHz, CDCl3): □ 2.345 (s, 3H, CO-CH3), 2.523 (s, 3H, -CH3), 2935 (dd, 1H, pyrazole-H, J = 13.66, 8.03 Hz), 3.820-3.894 (q, 1H, pyrazole-H, J = 13.60, 4.22 Hz), 5.866-5.907 (dd, 1H, pyrazole-H, J = 8.00, 4.21 Hz), 7.039-7.199 (dd, 2H, Ar-H, J = 8.44, 0.53 Hz), 7.220-7.262 (dd, 1H, Ar-H, J = 1.87, 0.55 Hz), 7.295-7.373 (dd, 1H, Ar-H, J = 8.10, 0.53 Hz), 7.547-7.624 (dd, 2H, Ar-H, J = 8.39, 1.88 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 365.23; Found: 367.335. Anal. calcd for C18H15Cl2FN3O: C, 59.19; H, 4.14; Cl, 19.41; F, 5.20; N, 7.67; O, 4.38.

1-[5-(2, 6-dichlorophenyl)-3-(4-fluoro-3-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (3g):
White solid, yield: (298 mg, 81.64 %), m. p: 194; IR (cm-1): 3052(CO–CH3), 2929 (-CH3), 1741 (C=O), 1581 (C=N), 1501/1432 (C=C aromatic ring), 1320 (C-F), 1017 (N-N), 821 (C-Cl); 1H NMR (400 MHz, CDCl3): □ 2.360 (s, 3H, CO-CH3), 2.392 (s, 3H, -CH3), 3.275-3.40 (q 1H, pyrazole-H, J = 8.44, 8.00 Hz), 3.665-3.742 (q, 1H, pyrazole-H, J = 8.26, 4.26 Hz), 6.225-6.278 (q, 1H, pyrazole-H, J = 8.00, 4.26 Hz), 7.069-7.091 (q, 1H, Ar-H, J = 8.42, 0.55 Hz), 7.113-7.192 (dd, 1H, Ar-H, J = 1.86, 0.53 Hz), 7.277-7.295 (dd, 1H, Ar-H, J = 8.06, 1.20 Hz), 7.542-7.556 (dd, 1H, Ar-H, J = 8.00, 0.49 Hz), 7.563-7.570 (dd, 1H, Ar-H, J = 8.11, 0.89 Hz), 7.575-7.661 (dd, 1H, Ar-H, J = 1.20, 0.51 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 365.23; Found: 365.003. Anal. calcd for C18H15Cl2FN3O: C, 59.19; H, 4.14; Cl, 19.41; F, 5.20; N, 7.67; O, 4.38.

1-[5-(3, 4-dichlorophenyl)-3-(4-fluoro-3-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (3h):
White solid, yield: (255 mg, 69.86 %), m. p: 182; IR (cm-1): 3066(CO–CH3), 2925 (-CH3), 1587 (C=O), 1587 (C=N), 1502/1402 (C=C aromatic ring), 1321 (C-F), 1013 (N-N), 819 (C-Cl); 1H NMR (400 MHz, CDCl3): □ 2.359 (s, 3H, CO-CH3), 2.469 (s, 3H, -CH3), 3.091-3.148 (dd 1H, pyrazole-H, J = 8.33, 7.99 Hz), 3.730-3.804 (dd, 1H, pyrazole-H, J = 8.48, 4.27 Hz), 5.518-5.480 (dd, 1H, pyrazole-H, J = 8.06, 4.20 Hz), 7.072-7.125 (dd, 3H, Ar-H, J = 8.00, 3.33 Hz), 7.283-7.372 (dd, 1H, Ar-H, J = 1.96, 0.54 Hz), 7.615 (dd, 1H, Ar-H, J = 8.39, 1.88 Hz), 7.634 (dd, 1H, Ar-H, J = 1.22, 0.49 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 365.23; Found: 368.116. Anal. calcd for C18H15Cl2FN3O: C, 59.19; H, 4.14; Cl, 19.41; F, 5.20; N, 7.67; O, 4.38.

1-[5-(2, 3, 5-trichlorophenyl)-3-(4-fluoro-3-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (3i):
White solid, yield: (302 mg, 75.39 %), m. p: 196; IR (cm-1): 3055(CO–CH3), 2927 (-CH3), 1695 (C=O), 1585 (C=N), 1515/1444 (C=C aromatic ring), 1329 (C-F), 1019 (N-N), 817 (C-Cl); 1H NMR (400 MHz, CDCl3): □ 2.361 (s, 3H, CO-CH3), 2.395 (s, 3H, -CH3), 3.276-3.456 (dd 1H, pyrazole-H, J = 8.45, 8.01 Hz), 3.666-3.745 (dd, 1H, pyrazole-H, J = 8.20, 4.25 Hz), 6.222-6.277 (dd, 1H, pyrazole-H, J = 8.00, 4.26 Hz), 7.069-7.091 (dd, 1H, Ar-H, J = 8.40, 0.53 Hz), 7.115-7.190 (dd, 1H, Ar-H, J = 1.86, 0.53 Hz), 7.277-7.295 (dd, 1H, Ar-H, J = 8.06, 1.20 Hz), 7.542-7.556 (dd, 1H, Ar-H, J = 8.00, 0.49 Hz), 7.563-7.570 (dd, 1H, Ar-H, J = 8.11, 0.89 Hz). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 399.67; Found: 402.604. Anal. calcd for C18H14Cl3FN3O: C, 54.09; H, 3.53; Cl, 26.61; F, 4.75; N, 7.01; O, 4.75.

Antimicrobial screening:
Antimicrobial activity of the synthesized compounds was evaluated in vitro using four bacterial strains (Escherichia coli (MCC 2412), Bacillus subtilis (MCC 2010), Staphylococcus aureus (MCC 2408), Pseudomonas aeruginosa (MCC 2080)), two fungal strains (Saccharomyces cerevisiae, MCC 1033, and Candida albicans, MCC 1439). ZOI (zone of inhibition) and MIC (minimum inhibitory concentration) values were used to describe the antibacterial efficacy of the test substances. DMF served as a negative control, while streptomycin and

fluconazole served as the study's reference drugs. The following approach was used to conduct the tests in triplicate. Autoclaved Petri dishes were filled with sterilized bacterial (nutrient agar) and fungal (sabouraud dextrose agar) growth medium. In addition, 100 µl inocula of each test organism were swabbed onto the agar plates in a sterile environment. Adsorption was followed by creating wells of 6 mm diameter using a sterile metallic borer and filling them with solutions of the working substances (128 µg/20 µL). After 48 hours of incubation at 28 □C, the ZOI was determined. After incubation at 28 □C for 48 hours, the MIC values for each chemical were determined using the broth double-dilution method with a 100 µl inoculum of each fungal culture [16, 17].

Results and discussion:

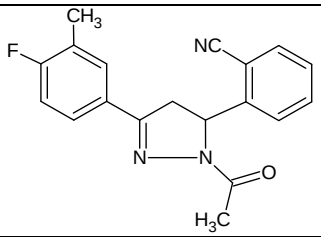
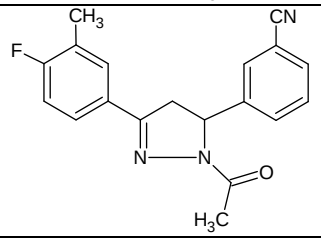
The condensation of 4-fluoro-3-methylacetophenone (1) with cyano- and chloro-substituted benzaldehydes (a-i) carried place in the presence of 2N sodium hydroxide and ethanol throughout the synthesis of chalcones (2a–1) according to Scheme 1. Pyrazoline derivatives (3a–h) were synthesized through a cyclization reaction that involved chalcones (3a–h) and hydrazine hydrate (Scheme 2). This reaction obtained place in the presence of glacial acetic acid.

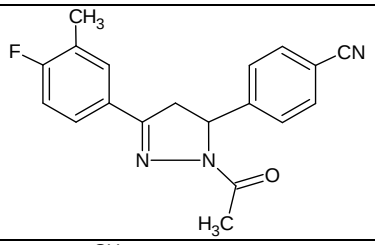
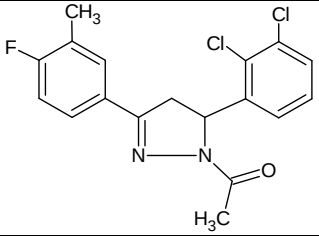
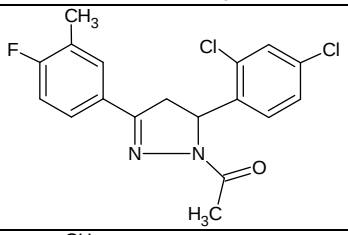
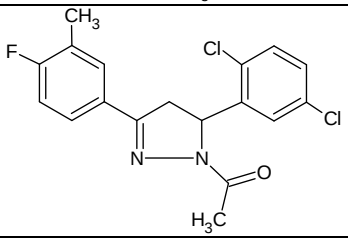
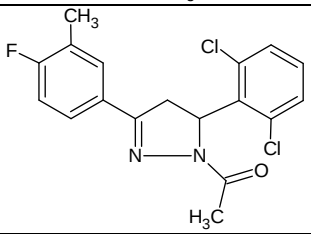
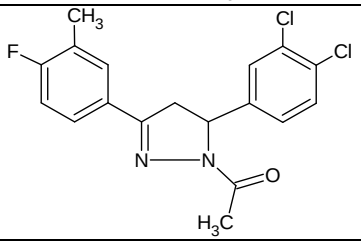
FT-IR, 1H NMR, and mass spectrometry were used to characterize the novel heterocyclic chalcone compounds containing acylated pyrazoles (3a–h). The presence of –C=N and carbonyl C=O groups was determined from the IR spectrum of compounds (3a–h), which displayed distinctive bands at around 1566–1630 cm-1 and 1652–1741 cm-1, respectively [18, 19]. The IR of the compounds (3a–h) displayed distinctive bands with wavelengths ranging from 2924–2929 cm-1. These bands were developed by the C–H sp3 stretching in the –COCH3 group [20]. A band at 1320-1363 cm-1 in the IR spectra of acylated pyrazoles (3a-i) is indicative of C-F stretching of the aromatic ring. Bands at 1008-1037 cm-1 were observed in the acylated pyrazoles (3a–i), indicating the presence of a (N-N) group. Absorption bands at 1501-1502 and 1400–1411 cm-1 were likewise present in compounds 3a–i, indicating the presence of the C=C aromatic ring. Identifiable bands at 2227-2229 cm-1, attributed to the stretching vibration of the -CN group, were also observed in the IR spectrum of the compounds (3a-c) [21]. At a range of 817–821 cm-1, the infrared spectrum of the pyrazoles (3d–i) displayed a band that was characteristic of the stretching of the C-Cl group [22].

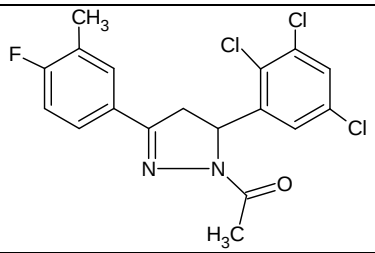
The 1H NMR spectra of the compounds (3a-i) confirmed their structures. Compounds 3a–i had a singlet of acyl group COCH3 protons at d 2.300–2.360 ppm in their 1H NMR patterns. The singlet readings that added up for three protons in the high field region (□2.414–2.523 ppm) were found to be -CH3 protons [23]. Compounds 3a-i exhibited a pair of doublet-of-doublet resonances at □2.935-3.158 ppm (J = 7.95-8.05 Hz, J = 7.77-18.15 Hz) and □3.774-3.915 ppm (J = 4.25-11.60 Hz, J = 7.76-18.15 Hz) for the CH2 protons of the pyrazoline ring [23]. The Hx-7 also showed up as a doublet-of-doublet at □5.622-6.278 (J = 0.54–4.44 Hz, J = 8.06–8.40 Hz). In the range from 7.015-7.666ppm [22-25], multiplets of five or six protons in the aromatic area were seen.

The mass spectrum confirmed the presence of M+ in the region, with a m/z measurement of 320.9945-398.2661, providing more evidence for the structure's accuracy.

Table 1: Structures, melting points, and molecular weight of compounds 3a-i

Comp Code	MW	Formula	MP	Structure
3a	321.39	$C_{19}H_{16}FN_3O$	188	
3b	321.39	$C_{19}H_{16}FN_3O$	183	

3c	321.39	$C_{19}H_{16}FN_3O$	178	
3d	365.23	$C_{18}H_{15}Cl_2FN_3O$	199	
3e	365.23	$C_{18}H_{15}Cl_2FN_3O$	188	
3f	365.23	$C_{18}H_{15}Cl_2FN_3O$	183	
3g	365.23	$C_{18}H_{15}Cl_2FN_3O$	178	
3h	365.23	$C_{18}H_{15}Cl_2FN_3O$	182	

3i	399.67	$C_{18}H_{14}Cl_3FN_3O$	196	

Antibacterial activities:

As indicated in Table 2, the antibacterial effect of the investigated compounds was evaluated by measuring the zone diameters, and the results were compared with those of well-known drugs (standard). It was found that compounds 3d and 3g showed greater inhibitory efficacy than compounds 3a, 3b, 3c, 3e, 3f, 3h, and 3i.

Table 2: Antibacterial studies of 2a-2i compounds

Compound	Antibacterial Activity (zone of inhibition)			
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
3a	14	7	12	13
3b	11	9	11	12
3c	10	8	12	8
3d	9	7	10	16
3e	14	7	0	9
3f	8	7	0	0
3g	12	9	12	23
3h	11	8	7	0
3i	8	10	0	8
Streptomycin	8	10	12	11

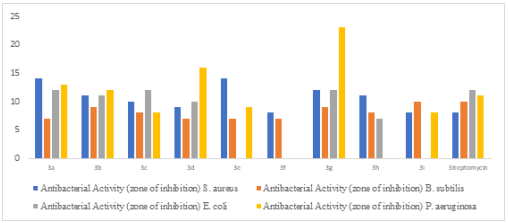


Figure 1: Antibacterial studies of 2a-i compounds

Antifungal activity:

For Candida albicans (MCC 1439), compounds 3c, 3d, and 3e showed the greatest inhibition, while compounds 3a, 3b, 3f, 3h, and 3i showed only moderate inhibition. Compounds 3c, 3d, and 3i demonstrated substantial inhibition against Saccharomyces cerevisiae (MCC 1033). To a lesser extent, compounds 3a, 3b, 3f, and 3g inhibited Saccharomyces cerevisiae (MCC 1033) growth [32-33]. Both fungal strains tested showed substantial action against chemicals 3c and 3d. Table 3 summarizes the results in detail.

Table 3: Antifungal activities of compounds 2a-i

Compound	Antibacterial Activity (zone of inhibition)	
	C Albican	*S. C.*
3a	8	8
3b	9	6

3c	12	12
3d	10	11
3e	0	11
3f	8	6
3g	7	20
3h	0	6
3i	0	7
Fluconazole	11	10

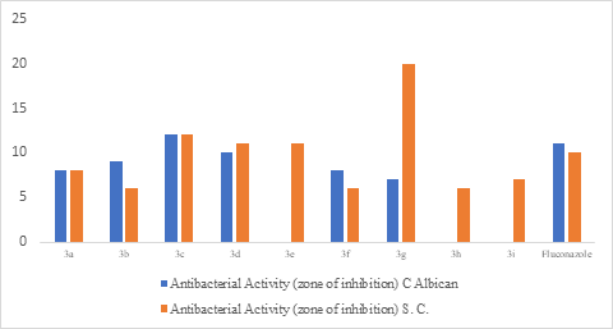


Figure 2: Antifungal activity of compounds 2a-i

II. CONCLUSION

The main objective of this research is to expand the existing knowledge base with the novel, useful chalcone compounds containing the pyrazoline structure. To assess their in vitro biological activity, we have developed and synthesized 9 novel pyrazoline-derived compounds. The structures of these compounds were analyzed using FT-IR, and 1H NMR spectrum spectroscopy. The next step was to test the efficacy of the pyrazolines (3a-i) against a variety of bacteria, including Gram-positive (Bacillus subtilis MCC 2010 and Staphylococcus aureus MCC 2408) and Gram-negative (E. coli MCC 2412 and Pseudomonas aeruginosa MCC 2080) strains. The chemicals proved to be efficient against a wide variety of bacteria, and their antibacterial activity was even higher than that of streptomycin. The binding free energy value of compounds 3h and 3i provides a starting point for the development of new antifungal and antibacterial inhibitors.

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