

Synthesis and characterization of 1,3,5-trisubstituted pyrazoline derivatives by ultrasonic irradiation method and evaluation of its antibacterial activity

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ABSTRACT

A series of novel 1,3,5-trisubstituted pyrazoline derivatives (P₁-P₁₀) have been synthesized by the reaction of substituted chalcones (C₁-C₁₀) with 4-hydroxybenzhydrazide. The starting material, chalcones were prepared by Claisen Schmidt condensation of 4-methylacetophenone with substituted aldehydes in the presence of sodium hydroxide in ethanol. 4-hydroxybenzhydrazide was synthesized by condensing methyl 4-hydroxybenzoate with hydrazine hydrate. The cycloaddition of chalcones with 4-hydroxybenzhydrazide gives 1, 3, 5-trisubstituted pyrazoline derivatives. The structures of synthesized derivatives were confirmed by IR, ¹H NMR and ¹³C NMR spectrum. The synthesized compounds were screened for their antibacterial and antifungal activity.

Keywords: 4-methylacetophenone; ultrasonic irradiation; chalcone; 2-pyrazoline; antibacterial, antifungal

1. INTRODUCTION

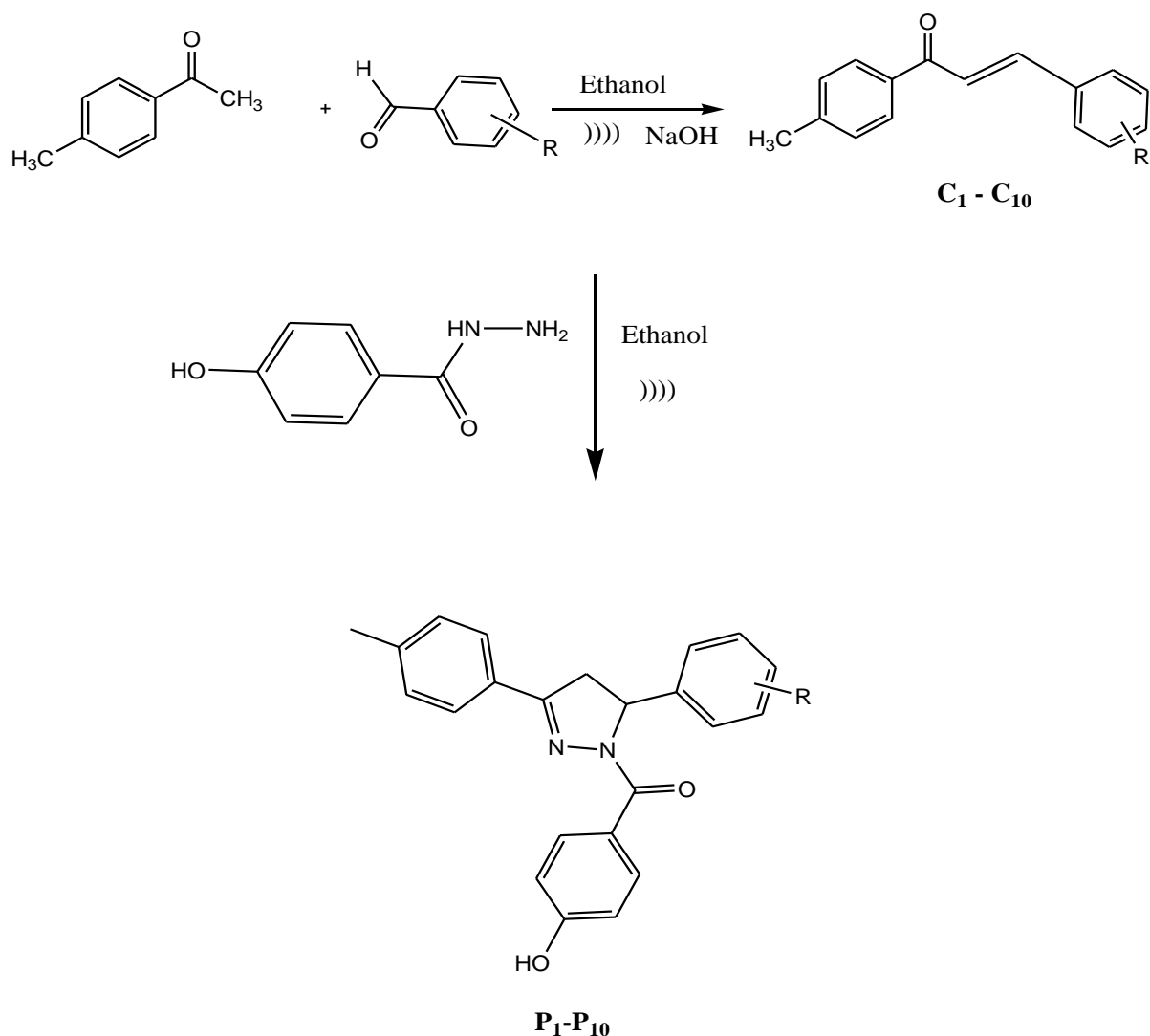
Nitrogen containing heterocycles are perhaps by far the most explored heterocyclic compounds because of their occurrence in a myriad of natural products and biologically active compounds. For this reason, synthetic chemists continue to be interested in the construction and functionalization of these heterocycles. The most common examples of naturally occurring N-heterocycles which otherwise too are of fundamental importance to life are haemoglobin and chlorophyll.

Pyrazoline derivatives have attracted attention of medicinal chemists for both with regard to heterocyclic chemistry and the pharmacological activities associated with them. Many pyrazole derivatives are reported to have a broad spectrum of biological activities, such as anti-inflammatory¹, antifungal², antiviral³, cytotoxic⁴, A₃ adenosine receptor antagonists⁵, antioxidant¹, antihypertensive⁶, tranquilizing, muscle relaxant, psychoanaleptic, hypnotic, ulcerogenic, antidepressant, antibacterial and analgesic effects⁷. Sonochemistry is attracting considerable research activity within the synthetic chemistry community, because it offers a new approach to the preparation of organic compounds. In the last two decades, sonochemical

methods have become widely used in organic synthesis⁸. Now a days, the ultrasonic irradiation technique has been employed, not only to decrease reaction times, but also to improve yields in a large variety of polyfunctionalized heterocycles. Compared with traditional methods, this method is more convenient and easily controlled. A large number of organic reactions can be carried out in a higher yield shorter reaction time and milder conditions under ultrasound⁹. Pyrazoles and their derivatives are widely used as pharmaceutical¹⁰⁻¹² and agrochemical agents¹³ and consequently a large number of synthetic routes to pyrazoles has been reported¹⁴⁻¹⁸

In view of these observations and in continuation of our research programme on the synthesis of five-membered heterocyclic compounds, we report herein the synthesis of some pyrazoline derivatives from substituted chalcone using ultrasonic irradiation, which have been found to possess an interesting profile of antimicrobial activity.

2. CHEMISTRY



Scheme 1. Synthesis of Chalcone and pyrazoline derivatives.

In the present work, (E)-3-(substitutedphenyl)-1-p-tolylprop-2-en-1-one (C₁-C₁₀) was prepared by reaction of 4-methylacetophenone with substituted benzaldehyde in dilute ethanolic sodium hydroxide solution under ultrasonic irradiation in the water bath of an ultrasonic cleaner at room temperature in accordance with the method described in the literature. The application of ultrasound in synthetic organic chemistry became more and more interesting. "Sonochemistry" is a new trend in organic chemistry, offering a versatile and pathway for a large variety of syntheses. Therefore, a large number of organic reactions can be carried out under ultrasonic irradiation in high yields, short time and mild conditions. Cavitation is the formation, growth and collapse of bubbles in an irradiated liquid. This effect induces very high local pressure and temperatures inside the bubbles and enhances mass transfer and turbulent flow in the liquid. Ultrasound has been utilized to accelerate a number of synthetically useful reactions, especially in heterocyclic chemistry

The synthetic route of compound C₁-C₁₀ and P₁-P₁₀ is outlined in **Scheme 1**. The physical data along with reaction time and yield of synthesized chalcone compounds were reported in **Table 1**.

3. RESULTS AND DISCUSSION

The IR spectra for synthesized chalcones (C₁ - C₁₀) observed the shifting of absorption band of carbonyl group for the two reactants 4-methylacetophenone and substituted benzaldehyde is higher to lower wave number, which is a strong evidence for the formation of conjugated enone of chalcone. Other strong bands appeared at 1589-1602 cm⁻¹, corresponding to C=C of the enone and aromatic rings, also the disappearance of aldehydic (CH) bands is a good evidence for the formation of chalcones.

The IR spectra of condensed product (P₁ - P₁₀) displayed disappearance of the characteristic absorption at 1651-1663 cm⁻¹ for -C=O of conjugated carbonyl and presence of characteristic absorption band at 1589-1595 cm⁻¹ due to C=N of pyrazoline in the IR spectrum⁸. Synthesized compounds (P₁ - P₁₀) showed weak C-H stretching bands near 3066-3076 cm⁻¹ and absorption around 2914-2956 cm⁻¹ for aliphatic nature of compounds /substituents.

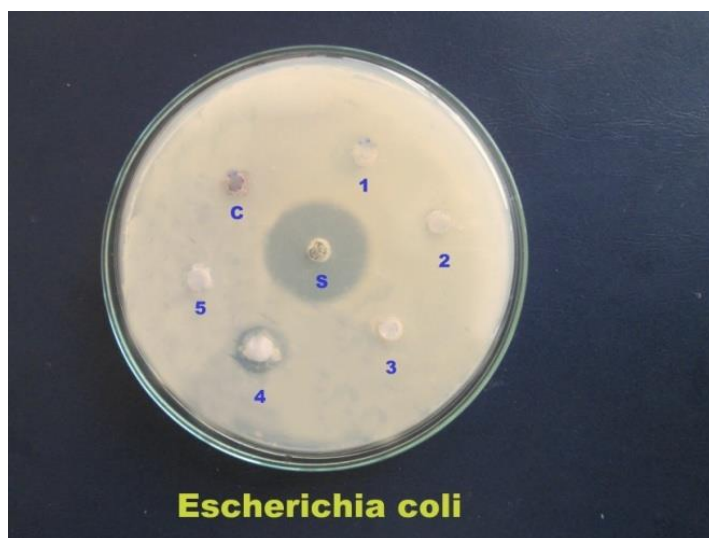
The ¹H NMR spectra of products showed characteristics ABX system due to geminal-vicinal multiple coupling between 4-CH₂ and 5-CH protons^{19,20}. The high field double doublet at δ 3.01-4.36 ppm and δ 3.10-4.74 ppm due to H_A and H_B respectively of C-4 protons and low field δ 4.19-5.77 ppm due to H_x at C-5 are characteristics signals due to vicinal coupling with the two magnetically nonequivalent protons of methylene group at position 4 of the pyrazolines ring. In all the compounds absorption as multiplet at δ 6.73-8.35 ppm was assigned to aromatic protons. In all the compounds absorption as singlet at δ 2.15-2.67 ppm was assigned to -CH₃ protons

¹³C-NMR spectra of all compounds were recorded in DMSO and CDCl₃, spectral signals which are in good agreement with the probable structures.

The C₄ and C₅ carbon of pyrazolines resonated at 42.37-56.97 and 56.53-69.19 ppm, respectively. The carbon of -CH₃ in all compounds resonates at 14.42-29.69 ppm, respectively. The carbon of (C=O) displayed signals at 160.49-169.45 ppm. All the compounds showed signal at 119.46-139.69 ppm were assigned to the aromatic carbon. All the compounds showed signals at 147.30-156.29 ppm assigned to (C=N).

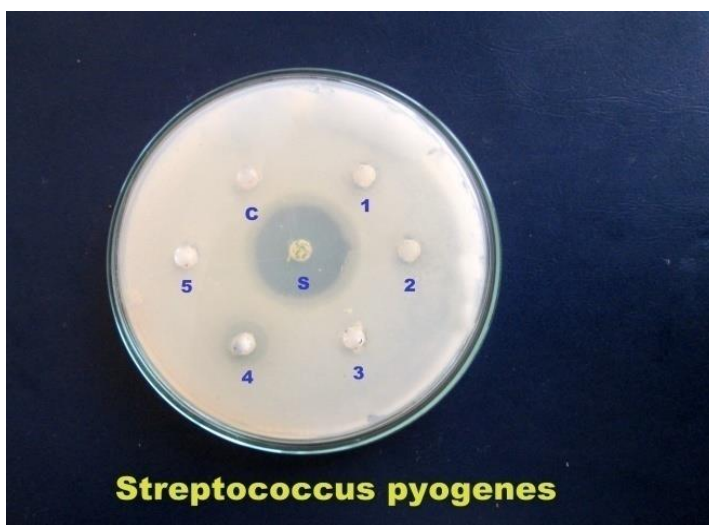
3. 1. Antibacterial studies

The synthesized pyrazoline derivatives were screened for the antibacterial activity against three Gram-positive bacteria viz., *Streptococcus pyogenes*, *Bacillus subtilis* and *Staphylococcus aureus* and two Gram-negative bacteria viz., *Escherichia coli* and *Pseudomonas aeruginosa* by using the disc diffusion method²¹. Ciprofloxacin was used as reference standard for comparing the results. The antibacterial activity of the pyrazoline derivatives are shown in **Fig. 1** for Plates **1-10**, and the zone of inhibition values are given **Table 2**. The Clustered column **Fig. 2** Showed that pyrazoline derivatives of (**P₁**) to (**P₁₀**) posses significant activity almost equipotent with the standard Ciprofloxacin against both Gram +ve and Gram -ve pathogenic organism. Thus the substituent's place a vital role in imparting enhanced antibacterial activity to the compounds.



Escherichia coli

Plate 1



Streptococcus pyogenes

Plate 2

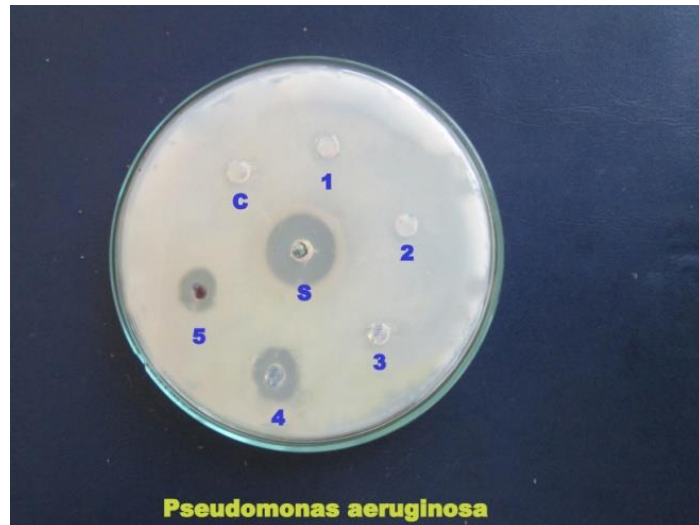


Plate 3

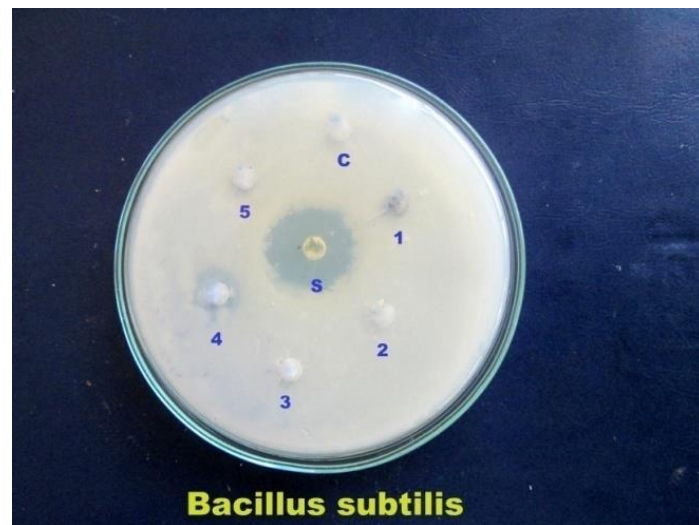


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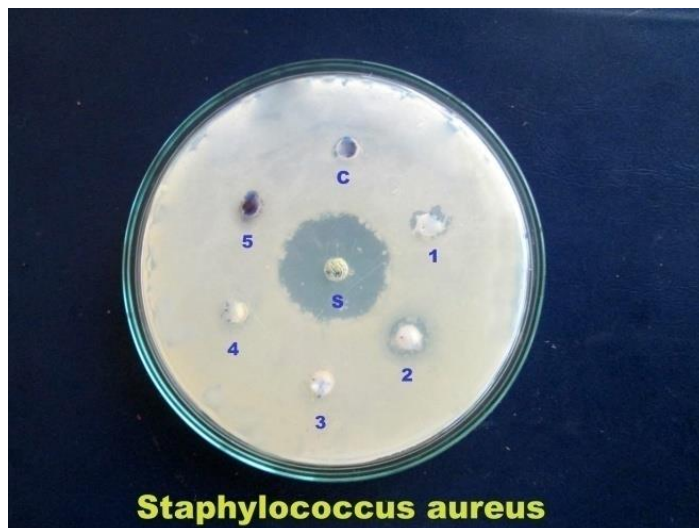
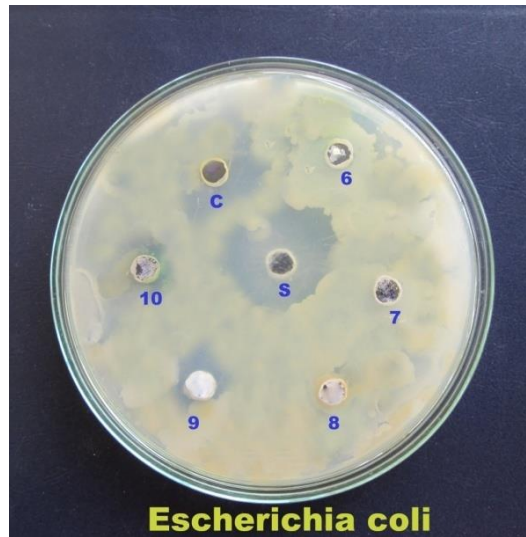
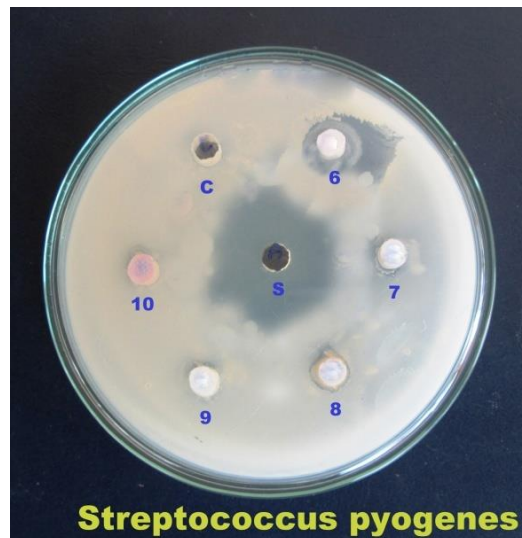


Plate 5



Escherichia coli
Plate 6



Streptococcus pyogenes
Plate 7



Pseudomonas aeruginosa
Plate 8

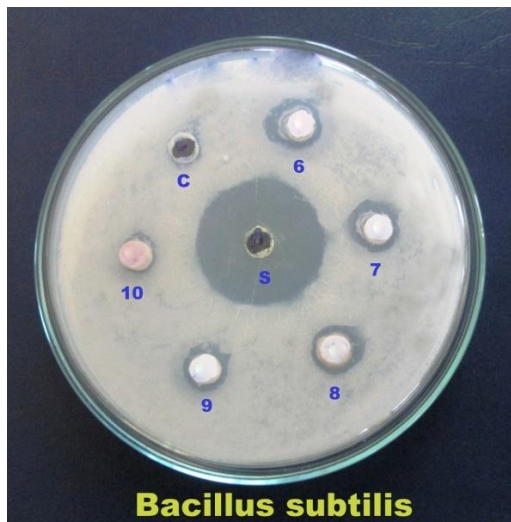


Plate 9



Plate 10

Figure 1. Antibacterial activities by zone of inhibition of pyrazoline derivatives (P₁-P₁₀).

The screening results indicate that compounds (P₆), (P₈), (P₉) and (P₁₀) were found to be active against *S. aureus*. Compounds (P₁), (P₂) and (P₅) were found to be moderately active against *S. aureus*, whereas compounds (P₃), (P₄) and (P₇) were found to be inactive against *S. aureus*. Compounds (P₄), (P₆), (P₇) and (P₉) were found to be active against *B. subtilis*. Compounds (P₈) and (P₁₀) were found to be moderately active against *B. subtilis*, whereas compound (P₁) and (P₂), (P₃) and (P₅) was found to be inactive against *B. subtilis*. Compound (P₉) and (P₁₀) was found to active against *E. coli*. Compounds (P₄), (P₅) and (P₈) were found to be moderately active against *E. coli*, all other compounds were found to be inactive against *E. coli*.

Table 1. The antibacterial activities of pyrazoline derivatives by disc diffusion method (P₁-P₁₀).

S. No.	Bacteria	Streptomycin (standard)	Zone of inhibition(mm)									
			P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
			1	2	3	4	5	6	7	8	9	10
1	<i>Bacillus subtilis</i>	25	-	-	-	12	-	12	12	11	12	8
2	<i>Escherichia coli</i>	24	-	-	-	12	9	-	-	10	15	16
3	<i>Pseudomonas aeruginosa</i>	24	8	8	-	14	12	14	13	13	17	16
4	<i>Staphylococcus aureus</i>	25	7	11	-	-	10	21	-	18	19	20
5	<i>Streptococcus pyogenes</i>	26	7	7	6	14	7	23	12	10	8	-
6	<i>Control</i>	-	-	-	-	-	-	-	-	-	-	-

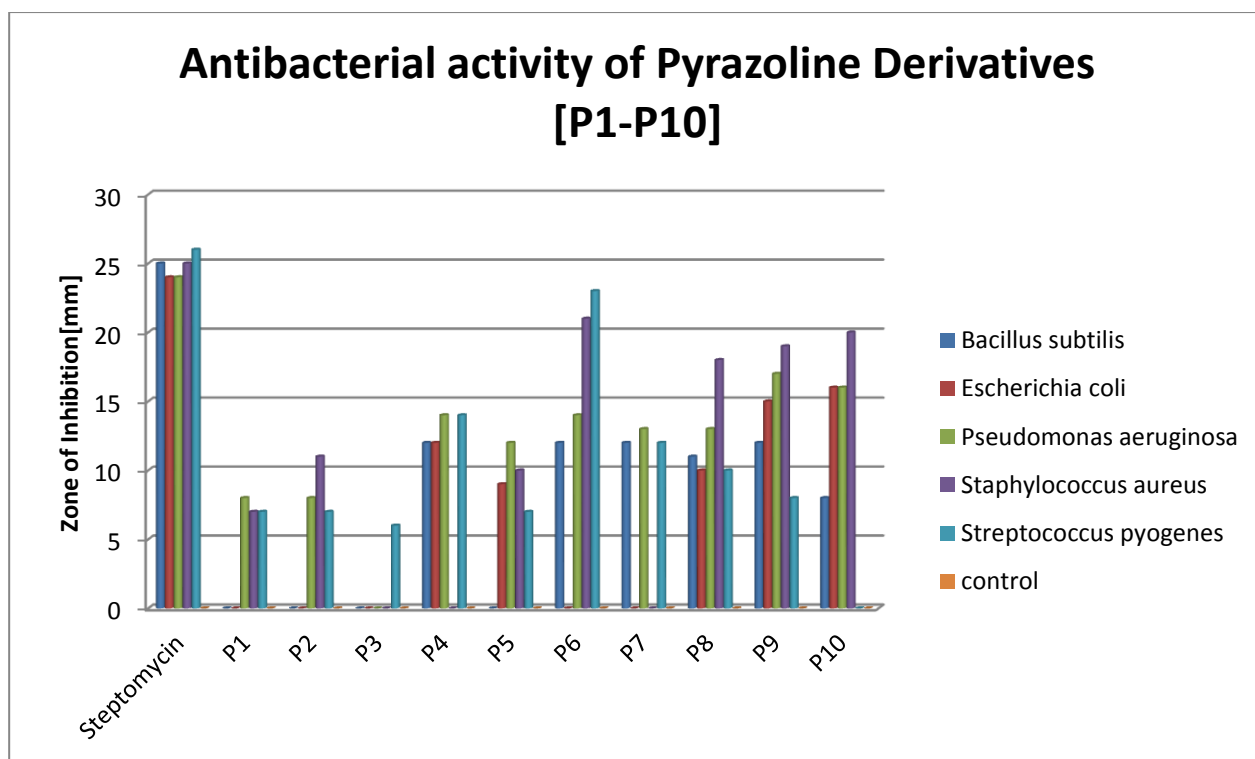
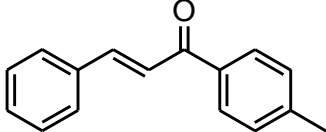
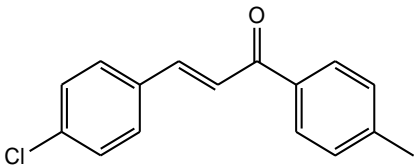
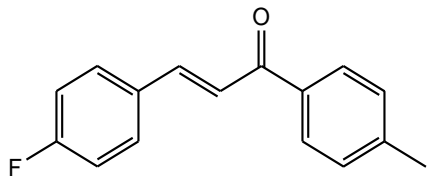
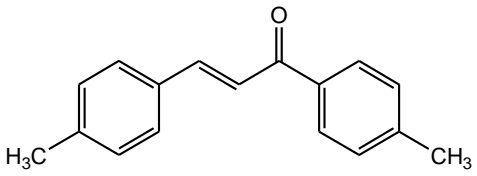
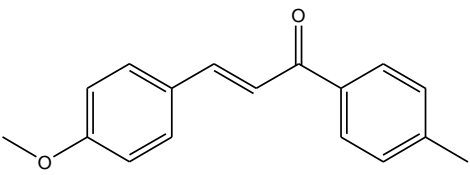
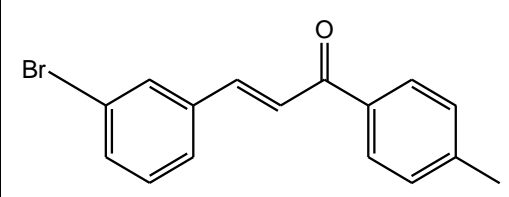
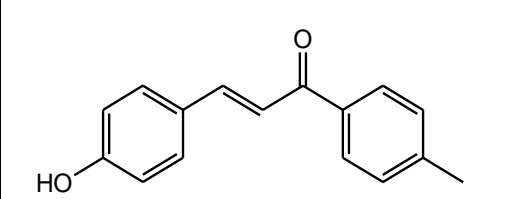
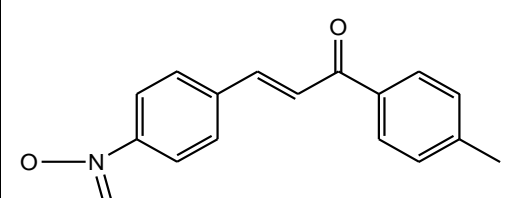
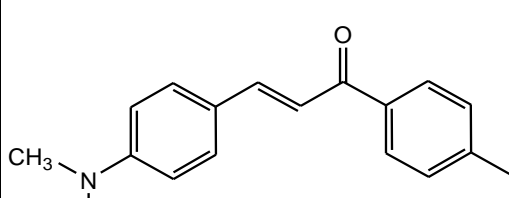
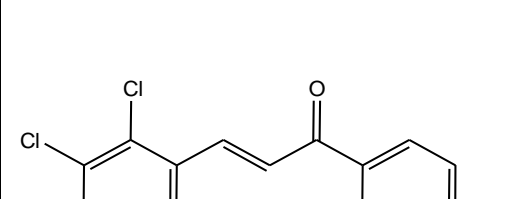


Fig. 2. Antibacterial activities by zone of inhibition of pyrazoline derivatives (P₁-P₁₀).

Table 2. Physical properties of chalcone derivatives (C₁-C₁₀).

S. No	Structure	Molecular Weight	Melting Point	Yield	IR Spectral Data
1.		222.28	71 °C	78%	Aliphatic CH: 2920, Aromatic CH: 3030, C=O: 1661, C=C: 1602.
2.		256.73	122 °C	81%	Aliphatic CH: 2918, Aromatic CH: 3030, C=O: 1661, C=C: 1602.
3.		240.27	92 °C	75%	Aliphatic CH: 2914, Aromatic CH: 3030, C=O: 1653, C=C: 1597.
4.		236.31	112 °C	86%	Aliphatic CH: 2920, Aromatic CH: 3030, C=O: 1654, C=C: 1600.
5.		251.31	102 °C	82%	Aliphatic CH: 2920, Aromatic CH: 3030, C=O: 1654, C=C: 1600.

6.		301.18	126 °C	77%	Aliphatic CH: 2922, Aromatic CH: 3049, C=O: 1663, C=C: 1598
7.		267.28	162 °C	79%	Aliphatic CH: 2920, Aromatic CH: 3055, C=O: 1651, C=C: 1598.
8.		238.28	144 °C	69%	Aliphatic CH: 2922, Aromatic CH: 3051, C=O: 1661, C=C: 1589
9.		265.35	126 °C	72%	Aliphatic CH: 2920, Aromatic CH: 3059, C=O: 1660, C=C: 1595.
10.		290.12	138 °C	66%	Aliphatic CH: 2916, Aromatic CH: 3049, C=O: 1659, C=C: 1595.

Compound (**P**₆) was found to be active against *S. pyogenes*. Compounds (**P**₄), (**P**₇) and (**P**₈) were found to be moderately active against *S. pyogenes*. where as (**P**₁), (**P**₂), (**P**₃), (**P**₅) and (**P**₉) were found to be less active against *S. pyogenes*.

Compounds (**P**₉) and (**P**₁₀) were found to be active against *P. aeruginosa*. Compounds (**P**₄), (**P**₅), (**P**₆), (**P**₇) and (**P**₈) were found to moderately active be active against *P. aeruginosa*. whereas compounds (**P**₁) and (**P**₂) were found to be less active be active against *P. aeruginosa*.

3. 2. Experimental protocols

Melting points were determined by open capillary method and are uncorrected. The IR spectra (in KBr pellets) were recorded on a Shimadzu FT-IR 157 spectrophotometer. ¹H NMR spectra were recorded either on a Bruker 400 MHz NMR spectrometer using TMS as an internal standard. The purity of the compounds was checked by thin layer chromatography (TLC) on silica gel plate using petroleum ether and ethyl acetate.

3. 2. 1. General Procedure for the preparation of (E)-1,3-dip-tolylprop-2-en-1-one (C₁-C₁₀)

4-methylacetophenone (2.5 mmol), Substituted benzaldehydes (2.5 mmol) 95 % Ethanol (20 ml) and 2 N NaOH (3 ml) were taken into a 100 ml conical flask. The mixture was irradiated by an ultrasonic generator in a water-bath at 30-35 °C for 3 min. The product was filtered with suction on a Buchner funnel, washed with cold water until the washings were neutral to litmus and then with ice cold ethanol. The crude product was recrystallized from ethanol.

3. 2. 2. Procedure for the preparation of 4,5-dihydro-3,5-dip-tolylpyrazole-1-carboxamide (P₁)

(E)-3-phenyl-1-p-tolylprop-2-en-1-one (C₁), (2.5 mmole), 4-Hydroxybenzhydrazide, (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford pale yellow coloured crystals. Yield: 70%; m.p. 226 °C; M.F; C₂₃H₂₀N₂O₂; IR (KBr) ν_{max} cm⁻¹: 3070 (Ar-H), 2920 (C-H), 1591 (HC=N), 1666 (C=O); ¹H-NMR (DMSO-*d*₆) (δ/ppm): 7.28-8.18 (m, 13H, Ar-H), 4.26 (dd, 1H, H_x), 3.38 (dd, 1H, H_A), 3.54 (dd, 1H, H_B), 2.15 (s, 3H, CH₃); ¹³C- NMR (DMSO-*d*₆) (δ/ppm): 167.93 (C=O), 155.75 (C=N), 122.56-138.95 (Ar-C), 61.95 (CH), 43.65 (CH₂), 21.20 (CH₃).

3. 2. 3. Procedure for the preparation of (5-(4-chlorophenyl)-4,5-dihydro-3-p-tolylpyrazol- 1-yl)(4-hydroxyphenyl)methanone (P₂)

(E)-3-(4-chlorophenyl)-1-p-tolylprop-2-en-1-one,(2.5mmole), 4-Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford pale yellow coloured crystals. Yield: 78%; m.p. 195 °C; M.F; C₂₃H₁₉ClN₂O₂; IR (KBr) ν_{max} cm⁻¹:

3078 (Ar-H), 2922(C-H), 1570(HC=N), 1676 (C=O); $^1\text{H-NMR}$ (DMSO-*d*₆) (δ /ppm): 7.02-7.39 (m, 12H, Ar-H), 4.74 (dd, 1H, H_x), 4.02 (dd, 1H, H_A), 4.28 (dd, 1H, H_B), 2.45 (s, CH₃); $^{13}\text{C-NMR}$ (DMSO-*d*₆) (δ /ppm): 168.41 (C=O), 153.71 (C=N), 119.46-139.46 (Ar-C), 56.53 (CH), 43.98 (CH₂), 23.08 (CH₃).

3. 2. 4. Procedure for the preparation of (5-(4-fluorophenyl)-4,5-dihydro-3-p-tolylpyrazol-1-yl)(4 hydroxyphenyl)methanone (P₃)

(E)-3-(4-fluorophenyl)-1-p-tolylprop-2-en-1-one, (2.5 mmole), 4-Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford pale yellow coloured crystals. Yield: 67%; m.p. 181 °C; M.F; C₂₃H₁₉FN₂O₂; IR (KBr) ν_{max} cm⁻¹: 3074 (Ar-H), 2956 (C-H), 1589 (HC=N); 1649 (C=O); $^1\text{H-NMR}$ (DMSO-*d*₆) (δ /ppm): 6.75-8.07 (m, 12H, Ar-H), 4.86 (dd, 1H, H_x), 4.22 (dd, 1H, H_A), 4.74 (dd, 1H, H_B), 2.26 (s, 3H CH₃); $^{13}\text{C-NMR}$ (DMSO-*d*₆) (δ /ppm): 147.32 (C=N), 123.54-139.65 (Ar-C), 65.05 (CH), 45.30 (CH₂), 23.40 (CH₃).

3. 2. 5. Procedure for the preparation of (4,5-dihydro-3,5-dip-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone (P₄)

(E)-1,3-dip-tolylprop-2-en-1-one (2.5 mmole), 4-Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford white coloured crystals. Yield: 71%; m.p. 211 °C; M.F; C₂₄H₂₂N₂O₂; IR (KBr) ν_{max} cm⁻¹: 3074 (Ar-H), 2935 (C-H), 1593 (HC=N); 1656 (C=O); $^1\text{H-NMR}$ (DMSO-*d*₆) (δ /ppm): 7.26-8.01 (m, 12H, Ar-H), 5.77 (dd, 1H, H_x), 3.13 (dd, 1H, H_A), 3.51 (dd, 1H, H_B), 2.44 (s, 6H CH₃); $^{13}\text{C-NMR}$ (DMSO-*d*₆) (δ /ppm): 165.47 (C=O), 160.46 (C=N), 120.98-130.94 (Ar-C), 61.25 (CH), 42.37 (CH₂), 29.69 (CH₃).

3. 2. 6. Procedure for the preparation (4,5-dihydro-5-(4-methoxyphenyl)-3-p-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone (P₅)

(E)-3-(4-methoxyphenyl)-1-p-tolylprop-2-en-1-one, (2.5 mmole), 4 Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford pale yellow coloured crystals. Yield: 86%; m.p. 143 °C; M.F; C₂₄H₂₂N₂O₃; IR (KBr) ν_{max} cm⁻¹: 3,056 (Ar-H), 2,921 (C-H), 1,597 (HC=N), 1,323 (O=S=O); $^1\text{H-NMR}$ (DMSO-*d*₆) (δ /ppm): 6.73-7.61 (m, 12H, Ar-H), 4.65 (dd, 1H, H_x), 3.83 (dd, 1H, H_A), 4.30 (dd, 1H, H_B), 2.45 (s, 3H CH₃); $^{13}\text{C-NMR}$ (DMSO-*d*₆) (δ /ppm): 167.40 (C=O), 156.29 (C=N), 121.61-139.37 (Ar-C), 65.95 (CH), 56.97 (CH₂), 14.42 (CH₃).

3. 2. 7. Procedure for the preparation of (5-(3-bromophenyl)-4,5-dihydro-3-p-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone(P₆)

(E)-3-(3-bromophenyl)-1-p-tolylprop-2-en-1-one, (2.5 mmole), 4-Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford pale yellow coloured crystals. Yield: 69%; m.p. 257 °C; M.F; C₂₃H₁₉BrN₃O₂; IR (KBr) ν_{\max} cm⁻¹: 3076 (Ar-H), 2953 (C-H), 1593 (HC=N), 1643 (C=O); ¹H-NMR (DMSO-*d*₆) (δ /ppm): 7.28-8.18 (m, 12H, Ar-H), 4.26 (dd, 1H, H_x), 3.37 (dd, 1H, H_A), 3.54 (dd, 1H, H_B), 23.40 (s, 3H, CH₃); ¹³C- NMR (DMSO-*d*₆) (δ /ppm): 169.45 (C=O), 154.75 (C=N), 124.06-139.89 (Ar-C), 61.08 (CH), 45.15 (CH₂), 23.40 (CH₃).

3. 2. 8. Procedure for the preparation of (4,5-dihydro-5-(4-nitrophenyl)-3-p-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone(P₇)

(E)-3-(4-nitrophenyl)-1-p-tolylprop-2-en-1-one, (2.5 mmole), 4-Hydroxybenzhydrazide, (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford light brown coloured crystals. Yield: 65%; m.p. 114 °C; M.F; C₂₃H₁₉N₃O₄; IR (KBr) ν_{\max} cm⁻¹: 3066 (Ar-H), 2914(C-H), 1600 (HC=N), 1629 (C=O); ¹H-NMR (DMSO-*d*₆) (δ /ppm): 6.84-7.75 (m, 12H, Ar-H), 5.13 (dd, 1H, H_x), 4.36 (dd, 1H, H_A), 4.74 (dd, 1H, H_B), 2.34 (s, 3H CH₃); ¹³C- NMR (DMSO-*d*₆) (δ /ppm): 167.50 (C=O), 155.75 (C=N), 124.51-139.59 (Ar-C), 59.85 (CH), 46.77 (CH₂), 24.10 (CH₃).

3. 2. 9. Procedure for the preparation of (4,5-dihydro-5-(4-hydroxyphenyl)-3-p-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone (P₈)

(E)-3-(4-hydroxyphenyl)-1-p-tolylprop-2-en-1-one, (2.5 mmole), 4-Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford yellow coloured crystals. Yield: 73%; m.p. 251 °C; M.F; C₂₃H₂₀N₂O₃; IR (KBr) ν_{\max} cm⁻¹: 3066 (Ar-H), 2916 (C-H), 1602 (HC=N) 1629 (C=O); ¹H-NMR (DMSO-*d*₆) (δ /ppm): 6.89-7.58 (m, 12H, Ar-H), 4.34 (dd, 1H, H_x), 3.81 (dd, 1H, H_A), 4.08 (dd, 1H, H_B), 2.27(s, 3H CH₃); ¹³C- NMR (DMSO-*d*₆) (δ /ppm): 160.49 (C=O), 155.64 (C=N), 120.88-139.33 (Ar-C), 65.94 (CH), 56.96 (CH₂), 14.42 (CH₃).

3. 2. 10. Procedure for the preparation of (5-(4-(dimethylamino)phenyl)-4,5-dihydro-3-p-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone(P₉)

(E)-3-(4-(dimethylamino)phenyl)-1-p-tolylprop-2-en-1-one (2.5 mmole), 4-Hydroxybenzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the

maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford light yellow coloured crystals. Yield: 67%; m.p. 234 °C; M.F; C₂₅H₂₅N₃O₂; IR (KBr) ν_{\max} cm⁻¹: 3074 (Ar-H), 2935 (C-H), 1595 (HC=N); 1668 (C=O); ¹H-NMR (DMSO-*d*₆) (δ /ppm): 7.65-8.35 (m, 12H, Ar-H), 4.58 (dd, 1H, H_x), 3.01 (dd, 1H, H_A), 3.10 (dd, 1H, H_B), 2.67 (s, 9H CH₃); ¹³C- NMR (DMSO-*d*₆) (δ /ppm): 163.38 (C=O), 155.40 (C=N), 120.32-139.61 (Ar-C), 69.19 (CH), 43.73 (CH₂), 29.69 (CH₃).

3. 2. 11. Procedure for the preparation of (5-(2,3-dichlorophenyl)-4,5-dihydro-3-p-tolylpyrazol-1-yl)(4-hydroxyphenyl)methanone(P₁₀)

(E)-3-(2,3-dichlorophenyl)-1-p-tolylprop-2-en-1-one, (2.5 mmole), 4-Hydroxy benzhydrazide (2.5 mmole) and gl. acetic acid (20 mL) were taken into a 100 mL conical flask. This reaction flask was suspended at the center of the ultrasonic cleaning-bath to get the maximum ultrasound energy and sonicated until crystals appeared or starting chalcone disappeared. The reaction-mixture was poured into crushed ice and left overnight. The precipitate was separated by filtration, washed well with water, dried and recrystallized from ethanol to afford light yellow coloured crystals. Yield: 61%; m.p. 104 °C; M.F; C₂₃H₁₈N₂O₂Cl₂; IR (KBr) ν_{\max} cm⁻¹: 3070 (Ar-H), 2922 (C-H), 1595 (HC=N), 1687 (C=O); ¹H-NMR (DMSO-*d*₆) (δ /ppm): 7.28-8.18 (m, 11H, Ar-H), 4.19 (dd, 1H, H_x), 3.36 (dd, 1H, H_A), 3.53 (dd, 1H, H_B), 2.61 (s, 3H CH₃); ¹³C- NMR (DMSO-*d*₆) (δ /ppm): 169.27 (C=O), 147.30 (C=N), 123.55-139.66 (Ar-C), 65.95 (CH), 46.07 (CH₂), 22.16 (CH₃).

3. CONCLUSION

In conclusion, the target compounds (P₁-P₁₀) were synthesized from 4-hydroxybenzoic acid which was converted to its ester by treating with methanol and few drops of sulphuric acid. The ester obtained was further converted to its hydrazide by reaction with hydrazine hydrate. The 4-hydroxybenzhydrazide obtained was heated with substituted chalcone to obtain 1,3,5-trisubstituted pyrazoline. Ultrasonic irradiation method was proved to be a better method as it produced much higher yield than the conventional method and synthesis provides an excellent approach for the safe, rapid, economical, environment friendly, non-hazardous, and easier work-up procedure. All the synthesized compounds were characterized by IR, NMR, spectra studies. Their purity was established by TLC. All the synthesized compounds of different classes were evaluated for antibacterial, antifungal and antioxidant studies. Some of the compounds exhibited moderate to significant activity compare with the standard drug.

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