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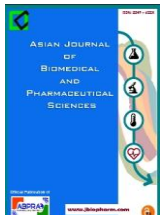

RESEARCH ARTICLE

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Synthesis and Inhibition of Microbial Growth by Benzophenone Analogues - A Simplistic Approach

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Abstract

The current study has been undertaken to synthesize different 4-hydroxy benzophenones and their acetic acid derivatives with pharmaceutical importance. The synthesized compounds 4a-j and 6a-j have been evaluated to study the effect of 4-hydroxy and carboxylic group in benzophenone on antibacterial activities against the microorganisms *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus*. Targeted molecules have been synthesized by multi step synthesis. The antibacterial activity of the compounds 4a-j and 6a-j were studied against *S. auerus, E.coli* and *B. subtilis* using serial dilution method. The structure of the synthesized compounds was analyzed by IR, NMR, mass and CHN analysis. The effect of substitution on 4-hydroxy benzophenones and their acetic acid derivatives were tested for antibacterial activity. The present study reports that 4-hydroxy benzophenones 4a-j showed significant bacterial growth inhibition with the minimal inhibition concentration (MIC) ranging from 3-16 µg/mL when compared to 4-benzoyl-phenoxy acetic acid analogues (12-46 µg/mL).

Keywords: synthesis, benzophenone, antibacterial activity

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INTRODUCTION

Survival of the fittest is the basis for life and for the human beings also. The biggest threats for human beings are the various diseases, scientists and doctors are still fighting to find solutions with various forms of medications. Chemical biology is one of the most active field in modern medicinal chemistry. Medicinal chemistry is emerging as a rapid growing field with its applications in medical and pharmacy field for the purpose of manufacturing new drugs at the bulk level. Recently, need for designing new drugs with improved properties have forced fast development of novel molecules. Thus, researchers have been focused on investigation of new drugs at the molecular level, with the aim to understand and manipulate the features that are substantially different from the present drugs.

The emergence of microbial resistance is an evolutionary process based on selection for organisms that have enhanced ability to survive doses of antibiotics that would have previously been lethal. Survival of bacteria often results from an inheritable resistance. [1, 2] Moreover, antibiotic resistance may impose a biological cost and consequently, spread of antibiotic resistant bacteria may be hampered by reduced fitness associated with the resistance. However, additional mutations may compensate for this fitness cost and aids the survival of these bacteria [3-6] hence, the search for new and potent antimicrobial agents is gaining interest. When the era of synthetic drugs began, it opened thousand doors for the development of various synthetic molecules with potential action. The compounds with the backbone of benzophenones have been reported to possess various biological activities such as antimicrobial,[7] anti-inflammatory,[8] antiangiogenic,[9] antioxidant,[10] anticancer[11] properties.

During the past few years all-embracing evidences have been accumulated to establish the efficiency of benzophenone analogues as antimicrobial agents. [12,13] *Rheedia brasiliensis* fruit containing benzophenone analogous and prenylated benzophenone from roots of *Cudrania cochinchinensis* showed antimicrobial activity against *Streptococcus mutans*. [14,15] Further, The efficiency of phenoxy acetic acid analogues as chemotherapeutic agents especially as analgesics, which is comparable to that of morphine is well documented.[16] Insight of the above observations and continuation of our research on in vitro antimicrobial activity, herein we report the synthesis of series of 4-hydroxy benzophenones and (4-benzoyl-phenoxy) acetic acid analogues and inhibition of *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus* virulence factors.

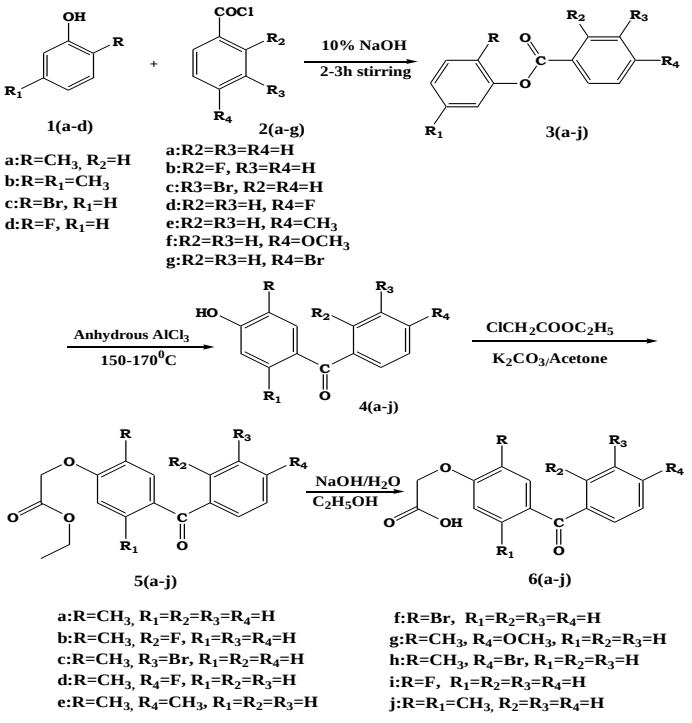
MATERIALS AND METHODS

Chemicals and Instruments

All solvents and reagents were purchased from Sigma Aldrich Chemicals Pvt Ltd. Melting points (MP) were determined on an electrically heated VMP-III melting point apparatus. The elemental analysis of the compounds was performed on a Perkin Elmer 2400 Elemental Analyser. The FT-IR spectra were recorded using KBr discs and Nujol on FT-IR Jasco 4100 infrared spectrophotometer. The ^{1}H NMR spectra were recorded using Bruker DRX 400 spectrometer at 400 MHz with TMS as the internal standard. Mass spectra were recorded on LC-MS (API-4000) Mass spectrometer.

Chemistry

The reaction sequence for title compounds **4a-j** and **6a-j** is outlined in Scheme 1. The starting material substituted phenyl benzoates **3a-j** were synthesized according to a reported procedure through the reaction of substituted phenols **1a-d** with substituted acid chlorides **2a-g** in the presence of 10% sodium hydroxide. The phenyl benzoates **3a-j** on subjecting to Fries rearrangement afforded hydroxy benzophenones **4a-j.** Ethyl (2-aroyl-4-methylphenoxy) acetates **5a-j** was achieved in excellent yield by reacting compounds **4a-j** with ethyl chloroacetate in presence of anhydrous potassium carbonate and dry acetone. Finally, alkaline hydrolysis of compounds **5a-j** furnished (4-aroyl-2-methylphenoxy) ethanoic acid analogues **6a-j**. [17]



SCHEME- 1

Scheme 1: **Synthesis of 4-hydroxy benzophenones 4a-j and (4-benzoyl-phenoxy) acetic acid analogues 6a-j**

General procedure for the preparation of phenyl benzoates 3a-j

Substituted benzoates **3a-j** were synthesized by benzoylation of substituted phenols **1a-d** with corresponding benzoyl chlorides **2a-g** (1:1) using 10% sodium hydroxide solution. Stirred reaction mass for 2 h at 0°C, reaction was monitored by thin layer chromatography (TLC) using 4:1 n-hexane:ethyl acetate solvent mixture. After completion of the reaction the oily product was extracted with ether layer. Ether layer was washed with 10% sodium hydroxide solution (3×50 mL) followed by water (3×30 mL) and then dried over anhydrous sodium sulphate and solvent was evaporated under pressure to afford compounds **3a-j.** Compound **3a** is taken as a representative example to explain the characterization data.

3a: Yield 90%. Pale yellow liquid; IR (Neat): 1715 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 2.45 (s, 3H, Ar-CH_3), 7.5-8.2 (m, 9H, Ar-H). Anal. Cal. for $C_{14}H_{12}O_2$ (212): C, 79.22; H, 5.70; Found: C, 79.18; H, 5.76%.

Substituted 4-hydroxybenzophenones **4a-j** commonly known as hydroxy benzophenones were synthesized by Fries rearrangement. Compounds **3a-j** on treated with anhydrous aluminum chloride as a catalyst at 150-170°C temperature under without solvent condition for about 2 h, then the reaction mixture was cooled to room temperature and quenched the reaction with 6 N HCl in the presence of ice water and stirred the reaction mixture for about 2-3 h and filtered. The solid was then recrystallized using methanol to obtain compounds **4a-j** in pure state.

4a: Yield; 72%, M.P:: 125-128°C; IR: (KBr disc) 1640 (CO), 3510-3600 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 6.71-7.50 (m, 8H, Ar-H), 12.20 (bs, 1H, -OH). LC-MS m/z 212 (M^+,83), 211 (100), 105 (56), 77 (52); Anal. calculated data for $C_{14}H_{12}O_2$: C,79.22; H, 5.70;. Found: C,79.18; H,5.69%.

4b: Yield; 78%, M.P: 150-153°C; IR: (Nujol) 1650 (CO), 3500-3615 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), 6.70-7.50 (m, 7H, Ar-H), 11.90 (bs, 1H, -OH). LC-MS m/z 230 (M^+,80), 229 (100), 123 (54), 95 (50); Anal. calculated data for $C_{14}H_{11}FO_2$: C,73.03; H, 4.82;. Found: C,73.00; H,4.85%.

4c: Yield; 80%, M.P: 153-156°C; IR: (Nujol) 1635 (CO), 3515-3600 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.33 (s, 3H, CH_3), 6.72-7.70 (m, 7H, Ar-H), 12.10 (bs, 1H, -OH). LC-MS m/z 289 (M^+,86), 288 (100), 182 (56), 154 (50); Anal. calculated data for $C_{14}H_{11}BrO_2$: C,57.76; H, 3.81;. Found: C,57.72; H,3.85%.

4d: Yield; 85%, M.P: 147-149°C; IR: (Nujol) 1645 (CO), 3510-3615 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 6.75-7.60 (m, 7H, Ar-H), 11.80 (bs, 1H, -OH). LC-MS m/z 230 (M^+,83), 229 (100), 123 (56), 95 (52); Anal. calculated data for $C_{14}H_{11}FO_2$: C,73.03; H, 4.82;. Found: C,73.01; H,4.85.%.

4e: Yield; 78%, M.P: 155-156°C; IR: (Nujol) 1660 (CO), 3520-3620 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 6.71-7.71 (m, 7H, Ar-H), 11.00 (bs, 1H, -OH). LC-MS m/z 226 (M^+,80), 225 (100), 119 (54), 91 (52); Anal. calculated data for $C_{15}H_{14}O_2$: C,79.62; H, 6.24;. Found: C,79.60; H,6.29%.

4f: Yield; 80%, M.P: 160-162°C; IR: (Nujol) 1640 (CO), 3510-3600 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 6.71-7.50 (m, 8H, Ar-H), 12.0 (bs, 1H, -OH). LC-MS m/z 276 (M^+,81), 275 (100), 105 (56), 77 (50); Anal. calculated data for $C_{13}H_9BrO_2$: C,56.34; H, 3.27;. Found: C,56.33; H,3.31%.

4g: Yield; 72%, M.P: 149-151°C; IR: (Nujol) 1630 (CO), 3515-3610 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 3.35 (s, 3H,OCH_3), 6.73-7.50 (m, 7H, Ar-H), 12.20 (bs, 1H, -OH). LC-MS m/z 242 (M^+,85), 241 (100), 135 (56), 107 (52); Anal. calculated data for $C_{15}H_{14}O_3$: C,74.36; H, 5.82;. Found: C,74.33; H,5.89.%.

4h: Yield; 80%, M.P: 150-152°C; IR: (Nujol) 1635 (CO), 3515-3600 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.33 (s, 3H, CH_3), 6.72-7.70 (m, 7H, Ar-H), 12.10 (bs, 1H, -OH). LC-MS m/z 289 (M^+,83), 288 (100), 182 (56), 154 (53); Anal. calculated data for $C_{14}H_{11}BrO_2$: C,57.76; H, 3.81;. Found: C,57.72; H,3.85%.

4i: Yield; 72%, M.P: 143-146°C; IR: (Nujol) 1620 (CO), 3500-3610 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 6.74-7.60 (m, 8H, Ar-H), 11.50 (bs, 1H, -OH). LC-MS m/z 216 (M^+,83), 215 (100), 105 (56), 77 (52); Anal. calculated data for $C_{13}H_9FO_2$: C,72.22; H, 4.20;. Found : C,72.23; H,4.25%.

4j: Yield; 78%, M.P: 153-154°C (Lit: 168-170°C); IR: (Nujol) 1640 (CO), 3510-3600 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 6.71-7.70 (m, 7H, Ar-H), 12.20 (bs, 1H, -OH). LC-MS m/z 226 (M^+,83), 225 (100), 105 (56), 77 (52); Anal. calculated data for $C_{15}H_{14}O_2$: C,79.62; H, 6.24;. Found: C,79.64; H,6.30%.

General procedure for the preparation of (4-Benzoyl-2-methyl-phenoxy)-acetic acid ethyl ester 5a-j

Compound **5a** was obtained by refluxing a mixture of compound **4a (**2.00 g, 0.013 mol) and ethyl chloroacetate (3.18 g, 0.026 mol) in presence of dry acetone (50 mL) and anhydrous potassium carbonate (2.69 g, 0.019 mol) for 8 h. The reaction mixture was cooled and solvent was removed by distillation. The residual mass was triturated with cold water to remove potassium carbonate and extracted with ether (3×50 mL). The ether layer was washed with 10% sodium hydroxide solution (3×50 mL) followed by water (3×30 mL) and then dried over anhydrous sodium sulphate and evaporated to dryness to obtain crude solid, which, on recrystallization with ethanol afforded compound **5a.** Compounds **5b-j** was synthesized analogously starting with **4b-j**, respectively. Compound **5a** is taken

as a representative example to explain the characterization data.

5a: Yield: 90%; M.P: 49-52°C; IR (Nujol): 1664 (C=O), 1760 cm^{-1} (ester, C=O); ^1H NMR ($CDCl_3$): δ 1.2 (t, 3H, CH_3 of ester), 2.3 (s, 3H, CH_3), 4.1 (q, 2H, CH_2 of ester), 4.5 (s, 2H, OCH_2), 7.1-7.7 (m, 8H, Ar-H). LC-MS m/z 298 (M^+,59), 225 (09), 211 (09), 221(100), 193 (05), 105 (56), 77 (29); Anal. Calcd. For $C_{18}H_{18}O_4$: C, 72.47; H, 6.04. Found: C, 72.46; H, 6.12%.

General procedure for the preparation of (4-Benzoyl-2-methyl-phenoxy)-acetic acids 6a-j

Compound **5a** (2.0 g, 6.0 mmol) was dissolved in ethanol (15 mL) and treated with a solution of sodium hydroxide (0.5 g, 15 mmol) in water (5 mL). The mixture was refluxed for 5 h, cooled, and acidified with 1 N hydrochloric acid. The precipitate was filtered and washed with water and crystallization from methanol afforded **6a** as a white solid in 85% yield. Compounds **6b-j** was synthesized analogously starting with **5b-j** respectively.

6a: Yield 75%; M.P: 130-132°C; IR (Nujol): 1675 (C=O), 1730 (acid C=O), 3400-3500 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.3 (s, 3H, CH_3), 4.46 (s, 2H, OCH_2), 7.2-7.7 (m, 8H, Ar-H), 9.5 (s, 1H, COOH). LC-MS m/z 270 (M^+,81), 269 (75), 225 (100), 221 (09), 105 (08), 77 (14); Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.13; H, 5.26%.

6b: Yield 80%; M.P: 112-115°C; IR (Nujol): 1655 (C=O), 1733 (acid C=O), 3450-3540 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.3 (s, 3H, CH_3), 4.44 (s, 2H, OCH_2), 6.9-7.55 (m, 7H, Ar-H), 9.2 (s, 1H, COOH). LC-MS m/z 288 (M^+,81), 287 (75), 244 (100), 229 (09), 193 (21), 165 (21), 123 (14); Anal. Calcd for $C_{16}H_{13}FO_4$: C, 66.66; H, 4.55. Found: C, 66.63; H, 4.59%.

6c: Yield 75%; M.P: 120-122^0 C; IR (Nujol): 1675 (C=O), 1730 (acid C=O), 3455-3550 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.4 (s, 3H, CH_3), 4.46 (s, 2H, OCH_2), 7.3-7.9 (m, 7H, Ar-H), 9.6 (s, 1H, COOH). LC-MS m/z 348 (M^+,81), 347 (75), 303 (100), 288 (09), 193 (21), 165 (08), 154 (14);Anal. Calcd for $C_{16}H_{13}BrO_4$: C, 55.04; H, 3.75. Found: C, 55.04; H, 3.79%.

6d: Yield 85%; M.P: 114-116°C; IR (Nujol): 1650 (C=O), 1730 (acid C=O), 3450-3540 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.3 (s, 3H, CH_3), 4.44 (s, 2H, OCH_2), 6.9-7.55 (m, 7H, Ar-H), 9.3 (s, 1H, COOH). LC-MS m/z 288 (M^+,81), 287 (75), 244 (100), 229 (09), 193 (21), 165 (21), 123 (14); Anal. Calcd for $C_{16}H_{13}FO_4$: C, 66.66; H, 4.55. Found: C, 66.63; H, 4.59%.

6e: Yield 70%; M.P: 130-133°C; IR (Nujol): 1670 (C=O), 1735 (acid C=O), 3420-3510 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.5 (s, 3H, CH_3), 2.8 (s, 3H, CH_3), 4.46 (s, 2H, OCH_2), 7.1-7.6 (m, 7H, Ar-H), 9.8 (s, 1H, COOH). LC-MS m/z 284 (M^+,81), 283 (75), 239 (100), 226 (09), 193 (21), 120 (21), 91(14); Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.80; H, 5.70%.

6f: Yield 75%; M.P:128-130°C; IR (Nujol): 1655 (C=O), 1740 (acid C=O), 3410-3520 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 4.46 (s, 2H, OCH_2), 7.3-7.9 (m, 8H, Ar-H), 9.9 (s, 1H, COOH). LC-MS m/z 333 (M^+,81), 332 (75), 288 (100), 274 (45), 256 (21), 228 (21), 105 (08), 77 (14); Anal. Calcd for $C_{15}H_{11}BrO_4$: C, 53.76; H, 3.31. Found: C, 53.74; H, 3.36%.

6g: Yield 85%; M.P: 140-142^0 C; IR (Nujol): 1675 (C=O), 1720 (acid C=O), 3410-3530 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.44 (s, 3H, CH_3), 3.54 (s, 3H, CH_3), 4.48 (s, 2H, OCH_2), 7.0-7.6 (m, 7H, Ar-H), 9.4 (s, 1H, COOH). LC-MS m/z 300 (M^+,85), 299 (75), 256 (100), 241 (70), 193 (45), 165 (21), 135 (08), 107 (14); Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.94; H, 5.40%.

6h: Yield 78%; M.P: 155-157°C; IR (Nujol): 1655 (C=O), 1730 (acid C=O), 3450-3550 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.5 (s, 3H, CH_3), 4.45 (s, 2H, OCH_2), 7.3-7.9 (m, 7H, Ar-H), 9.6 (s, 1H, COOH). LC-MS m/z 348 (M^+,85), 347 (75), 303 (100), 288 (70), 193 (45), 165 (21), 154 (14); Anal. Calcd for $C_{16}H_{13}BrO_4$: C, 55.04; H, 3.75. Found: C, 55.04; H, 3.78%.

6i: Yield 80%; M.P:139-141°C; IR (Nujol): 1670 (C=O), 1740 (acid C=O), 3430-3520 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 4.40 (s, 2H, OCH_2), 7.0-7.6 (m, 8H, Ar-H), 9.5 (s, 1H, COOH). LC-MS m/z 274 (M^+,85), 273 (75), 229 (100), 215 (70), 197 (45), 169 (21), 105 (08), 77 (14); Anal. Calcd for $C_{15}H_{11}FO_4$: C, 53.76; H, 3.31. Found: C, 53.76; H, 3.36%.

6j: Yield 82%; M.P:140-142°C; IR (KBr): 1655 (C=O), 1725 (acid C=O), 3410-3520 cm^{-1} (acid OH); ^1H NMR ($CDCl_3$): δ 2.3 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 4.46 (s, 2H, OCH_2), 7.4-7.8 (m, 7H, Ar-H), 9.7 (s, 1H, COOH). LC-MS m/z 284 (M^+,85), 283 (75), 239 (100), 225 (70), 207 (45), 179 (21), 105 (08), 77 (14); Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.81; H, 5.67. Found: C, 71.85; H, 5.69%.

Biology

Culture of microorganisms

In this experiment *Escherichia coli* (MTCC 1652), *Bacillus subtilis (*MTCC 441) and *Staphylococcus aureus* (MTCC 3160) bacterial strains were used. These strains were procured from the National Chemical Laboratory (NCL), Pune, India. These strains were cultured for 24 h at 37 ^{0}C in Mueller-Hinton Broth. The final inoculum size was 10^6 CFU/ml (according to 0.5 McFarland standard; turbidimetric method was applied) for the antibacterial assay.

Determination of minimum inhibitory concentration (MIC)

MIC values were determined by serial dilution of inhibitors.[16] This was performed in 96 well microplates by filling all the wells with 100 µL of media containing serially diluted inhibitors of 4-hydroxy benzophenones and benzoyl phenoxy acetic acid analogues. Sterile control containing media alone, while the growth control contains both media and microbial strains

without inhibitors were also included. After adding 25 µL of microbial strains suspension (10^5 cells/mL) to all the wells except sterile control wells, the plate was incubated in micro aerobic condition at 37 ˚C overnight. Following morning the bacterial growth was assayed by measuring the absorbance at 600 nm. Amoxicillin was used as a standard.

RESULTS AND DISCUSSION

The results of antibacterial activity of synthesized compounds **4a-j** and **6a-j** against the tested bacteria are presented in Table 1.

compounds	MIC µg/mL			compounds	MIC µg/mL		
	E. coli	*S. aureus*	*B. subtilis*		*E. coli*	*S. aureus*	*B. subtilis*
4a	15.31	18.45	16.32	**6a**	18.15	16.98	17.35
4b	12.32	13.16	11.24	**6b**	17.56	18.65	20.26
4c	10.81	9.44	8.22	**6c**	**14.52 ***	16.10	15.92
4d	9.2	9.55	10.28	**6d**	42.98	40.45	45.65
4e	7.86	8.25	9.14	**6e**	45.63	48.32	42.24
4f	5.69	6.12	8.35	**6f**	22.76	25.42	28.86
4g	3.06	5.16	3.06	**6g**	16.45	18.58	17.56
4h	**2.36***	2.65	2.15	**6h**	31.25	30.45	30.35
4i	7.81	8.85	8.95	**6i**	33.78	38.34	36.32
4j	3.9	4.55	4.14	**6j**	31.92	32.56	30.48
Amoxicillin	26.1	27	26.5	**Amoxicillin**	26.1	27.2	26.5

Table 1: MIC of Compounds 4a-j and 6a-j against *E. coli, S. aureus and B. subtilis*

The MIC of all the synthesized compounds had shown good to moderate antibacterial activity against *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus* bacterial strains. However, the compounds **4h** and **6c** showed good antibacterial activities against all tested strains. Mainly in *E.coli* compound **4h** shown very good inhibition at **2.36** µg/mL and compound **6c** revealed enormous inhibition at **14.52** µg/mL.

Structure activity relationship revealed that the antimicrobial activity of compounds **4a-j** and **6a-j** was evaluated and compared with controls as shown in Table 1. Among the hydroxyl benzophenones **4a-h**, compound **4h** with methyl group at ortho position to hydroxyl group and bromo group at para position in another ring showed significant inhibitory activity. Compounds **4g** with methyl group at ortho position to hydroxyl group and methoxy group at para position in another ring and **4j** with two methyl groups at ortho and meta position to hydroxyl group showed less activity compared to compound **4h**. Similarly, other derivatives **4a-f** and **4i** showed a moderate activity. Among the benzoyl-phenoxy acetic acids **6a-j**, compound **4h** with methyl group at ortho position to acetic acid chain and bromo group at meta position in another ring showed good inhibitory activity. In contrast, the other compounds **6a-b** and **6d-j** showed a moderate activity. It is worth noting that the presence of bromo group is more significant than alkyl, methoxy and fluoro group to enhance the activity. From the results obtained, it reveals that compounds **4a-h** showed significant antibacterial activity compared to the compounds **6a-j.** The reason might be due to the increased in the length of the carbon chain in compounds **6a-h** which decreases the activity. The bulkiness of the carbon chain renders the molecule unable to penetrate through the cell wall of the bacteria. The inhibitory effect of microbial growth by **4h** and **6c** was further confirmed by electron microscopic observations.

CONCLUSION

A series of 4-hydroxy benzophenones **4a-j** and (4-benzoyl-phenoxy) acetic acid analogues **6a-j** were synthesized and their antimicrobial activities have been evaluated by using *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus* bacterial strains. Compounds **4h** and **6c** with methyl and bromo groups demonstrated significant *E.coli* growth inhibition when compared to alkyl, methoxy and fluoro groups. Compounds **4h** and **6c** were found to be effective in inhibiting *E.coli* growth by inhibiting the virulence factors present in them. Further, both the compounds **4h** and **6c** may find enhanced applications in *E.coli* growth inhibition.

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