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RESEARCH ARTICLE

Growth Inhibitory Properties of Synthetic Chalcones

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Abstract: ***Background:*** In the present study, chalcones were synthesized from 2-hydroxy-1-acetonaphthone and substituted aromatic aldehydes were synthesized by Claisen Schmidt condensation reaction using potassium hydroxide as a base. The synthesized chalcones were purified by recrystallization from ethanol and evaluated for antibacterial activity by well diffusion method. The antibacterial activity was evaluated against *Bacillus licheniformis, Bacillus species, Escherichia coli and Staphylococcus aureus* using Ciprofloxacin as a standard.

Methods: The target molecules were prepared by reacting 2-hydroxy-1-acetonaphthone and various substituted aromatic aldehyde in the presence of suitable condensing agents. The structure of synthesized compounds was confirmed on the basis of elemental analysis, IR, ^{1}H NMR and ^{13}C NMR spectral data. These synthesized compounds were also screened for antibacterial activity.

Results: In the present study, free hydroxyl group in position 2 or 4 of aldehyde ring of synthesized chalcones appears to be a very important requirement in increasing the activity (**2-5** and **8-13**). When the hydroxyl group in position 4 is alkylated (**14, 15**), the chalcones become less active. When more complex substituent is present on the aldehyde ring (**6, 7**) there is a decrease in the activity.

Conclusion: Newly synthesized chalcones (**1-15**) show good and moderate antibacterial activity. We believe that the new hydroxy substituted (in aldehyde ring) chalcones (**2-5** and **8-13**) reported in this work may provide an interesting insight for further optimization.

Keywords: 2-hydroxy-1-acetonaphthone, chalcones, antibacterial activity, Minimum Inhibitory Concentration (MIC), hybrid molecules, aromatic aldehydes.

1. INTRODUCTION

The discovery of antibiotics has long been regarded as one of the most significant medical achievements of the twentieth century. Antibiotics have saved millions of lives [1] and enabled important medical procedures, including surgery and cancer chemotherapy. The emergence and spread of antibacterial resistance in all geographical areas, including in bacteria that cause hospital- and community-acquired infections, is, however, jeopardizing the effectiveness of these potentially life-saving treatments [2]. The threat includes the spread of multidrug-resistant bacteria, and infections with no therapeutic options have been reported [3].

The number of life threating infections caused by multidrug-resistant Gram-positive pathogens has reached an alarming level in hospitals and the community infections caused by these organisms create a serious challenge to the scientific community and the need for an effective therapy has lead to a search for novel antibacterial agents [4]. Antibacterial agents are among the most commonly used and misused of all drugs [5] they reduce or completely block the growth and multiplication of bacteria. This has made them unique for the control of deadly infectious disease caused by a variety of pathogens [6]. Although deaths from bacterial infection have dropped in the developed worlds and these are still the major cause of death in the developing world. The inevitable consequence of the widespread use of antibacterial agents has been the emergence of antibiotic-resistant pathogens, fueling an ever-increasing need for new drugs. In the design of new compounds, development of hybrid molecules through the combination of different pharmacophore in one structure may lead to compounds with increased antibacterial activity.

Chalcones, considered as the precursors of flavonoids and isoflavonoids [7], are abundant in edible plants. Chemically they consist of three carbons α, β-unsaturated carbonyl system. Condensation of aromatic aldehydes with aromatic ketones in the presence of catalyst yields chalcones [8]. Chalcones commence a diversity of chemical reactions together with the synthesis of pyrimidine, isoxazoles and pyrazolines. Chalcones act as mediators in the synthesis of beneficial therapeutic compounds special attention has been given to chalcones due to their simple structure and diverse pharmacological activities including anticancer [9-11], antioxidant [12-14], antiinflammatory [15, 16] antimicrobial

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[17-19], antifungal [20], antibacterial [21], antimalarial [22, 23], antitumor [24], antiviral [25], antitubercular [26], antimitotic [27], anti-leishmanial [28], anti-platelet [29] and antihypertensive activities [30]. Due to the above-stated reasons, the synthesis of chalcones and chalcone based functionalized derivatives had remained the primary objective.

A number of techniques and methods have been reported for the synthesis of chalcones. Among all stated methods, Aldol condensation and Claisen Schmidt condensation still hold a high position. The best method for the synthesis of chalcones is the conventional Claisen Schmidt condensation in the presence of aqueous alkaline bases [31].

The particular relevance to the present work is the fact that the antibacterial properties of chalcones are highly influenced by the structure of the two aryl groups and their substitution pattern especially hydroxyl substituent is proven to be one of the key groups that enhances the antibacterial activity of chalcones. The presence of a reactive α, β-unsaturated keto functional group in chalcones is also found to be responsible for antibacterial activity [32, 33].

2. EXPERIMENTAL

2.1. Materials and Methods

All the chemicals used in the synthesis of chalcones were of laboratory grade. Melting points were determined in an open capillary tube and are uncorrected. The purity of compounds and completion of the reaction was monitored by thin layer chromatography using hexane/ethyl acetate (7:3) as the mobile phase on precoated sheets of silica gel-G (Merck, Germeny) using iodine vapour for detection. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. ^{1}HNMR spectra were recorded on Avance spectrometer (Bruker, Germany) 400 MHz in $CDCl_3$ using TMS as an internal standard and chemical shifts are reported in δ units and the coupling constants (J) are reported in Hertz. Elemental analysis was performed on Perkin-Elmer 240 CHN elemental analyzer.

2.1.1. General Procedure for the Synthesis of Chalcones (1-15)

2-hydroxy-1-acetonaphthone (0.001mol) and aromatic aldehydes (0.001mol) were dissolved in a minimum amount of 90% ethyl alcohol in warm condition to this solution add KOH solution (0.01mol) dropwise with constant shaking. The reaction mixture was kept in bulb oven overnight. The reaction mixture was neutralized by adding dilute HCl dropwise with the help of P^H paper [34]. The product was isolated by adding ice-cold water which was then filtered by a suction pump, dried and recrystallized from ethanol to get corresponding chalcones Scheme **1** (**1-15**).

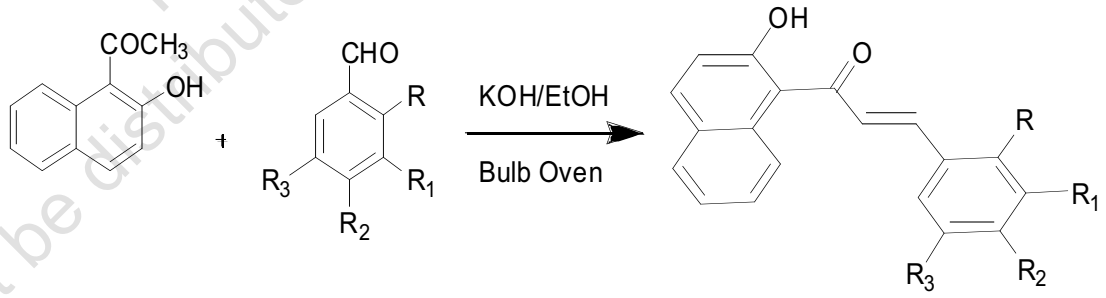
All the synthesized compounds **(1-15)** have been characterized by their melting points, Elemental analysis, IR, ^{1}H NMR and ^{13}CNMR spectra.

2.1.2. (E)-4-(3-(2-Hydroxynaphthalen-1-yl)-3-Oxoprop-1-en-1-yl) Benzonitrile (1)

Dark brown solid; 80%; 374-376^{o}C; IR (cm^{-1}): 3350 (OH), 3070 (=CH), 2150 (CN), 1640 (C=O), 1560 (C=C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-7.08 (m,10H Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35(broad s,1H, OH); ^{13}C NMR ($CDCl_3$,75 MHz): δ = 189.7, 162.2, 145.1, 139.5, 136.1, 135.0, 132.1, 131.6, 131.0, 130.2, 128.8, 126.9, 124.9, 121.5, 121.3, 118.6, 117.9, 111.8; MS. m/z 299 Anal. Calcd. For Formula: $C_{20}H_{13}O_2N$: C, 80.26; H, 4.34; N, 4.68; O, 10.69; Found: C, 80.24; H, 4.32; N, 4.66; O, 10.66.

2.1.3. (E)-3-(4-Hydroxy-3-Methoxyphenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1-One (2)

Dark brown solid; 80%; 441-443^{o}C; IR (cm^{-1}): 3360 (OH), 3070 (=CH), 2950 (CH), 1650 (C=O), 1560 (C=C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-7.08 (m,9H Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.25(broad s,1H, OH), 4.75 (broad s,1H, OH), 3.73 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$,75 MHz): δ = 189.7, 162.2, 149.1, 147.9, 145.1, 136.1, 135.0, 131.6, 131.0, 130.2, 127.6, 126.9, 124.9, 122.9, 121.5, 121.3, 117.9, 116.8, 111.9, 56.1; MS.



Scheme 1. Synthesis of Chalcones

1. R= H, R_1= H, R_2 = CN, R_3 = H
2. R= H, R_1= OCH_3, R_2 = OH, R_3 = H
3. R= H, R_1= OCH_3, R_2 = OH, R_3 = Br
4. R= H, R_1= OCH_2CH_3, R_2 = OH, R_3 = H
5. R= H, R_1= OCH_2CH_3, R_2 = OH, R_3 = Br
6. R= H, R_1= $OCH_2C_6H_5$, R_2 = OCH_3, R_3 = H
7. R= H, R_1= OCH_3, R_2 = $OCH_2C_6H_5$, R_3 = H
8. R= OH, R_1= H, R_2 = H, R_3 = H
9. R= OH, R_1= H, R_2 = H, R_3 = Cl
10. R= OH, R_1= Br, R_2 = H, R_3 = Br
11. R= OH, R_1= I, R_2 = H, R_3 = I
12. R= H, R_1= H, R_2 = OH, R_3 = H
13. R= OH, R_1= H, R_2 = OH, R_3 = H
14. R= H, R_1= H, R_2 = OCH_3, R_3 = H
15. R= H, R_1= OCH_3, R_2 = OCH_3, R_3 = Br

m/z 320 Anal. Calcd. For Formula: $C_{20}H_{16}O_4$: C, 74.99; H, 5.03; O, 19.98; Found: C, 74.97; H, 5.00; O, 19.96.

2.1.4. (E)-3-(3-Bromo-4-Hydroxy-5-Methoxyphenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1- one (3)

Orange solid; 78%; 514-516°C IR (cm^{-1}): 3360 (OH), 3070 (=CH), 2950 (CH), 1650 (C=O), 1560 (C=C), 620 (Ar-Br); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-7.08 (m, 8H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.25(broad s,1H, OH), 4.75 (broad s,1H, OH), 3.73 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 153.5, 145.1, 141.0, 136.1, 135.0, 131.6, 131.0, 130.2, 126.9, 124.9, 123.6, 121.5, 121.3, 117.9, 114.7, 110.9, 56.1; MS. m/z 398 Anal. Calcd. For Formula: $C_{20}H_{15}BrO_4$: C, 60.17; H, 3.79; Br, 20.01; O, 16.03; Found: C, 60.15; H, 3.77; Br, 20.0; O, 16.00.

2.1.5. (E)-3-(3-Ethoxy-4-Hydroxyphenyl)-1-(2-Hydroxynaphthalene-1-yl) Prop-2-en-1-One (4)

Brown solid; 82%; 453-455°C IR (cm^{-1}): 3360 (OH), 3080 (=CH), 1650 (C=O), 1580 (C=C), 1540 (C-C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-6.79 (m, 9H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35 (s, 1H, OH), 5.20 (s, 1H, OH), 4.0 (q, 2H, CH_2), 1.32 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$,75 MHz): δ = 189.7, 162.2, 148.1, 148.0, 145.1, 136.1, 135.0, 131.6, 131.0, 130.2, 127.2, 126.9, 124.9, 122.2, 121.5, 121.3, 117.9, 116.4, 112.0, 64.9, 14.8; MS. m/z 334 Anal. Calcd. For Formula: $C_{21}H_{18}O_4$: C, 75.44; H, 5.43; O, 19.14; Found: C, 75.42; H, 5.41; O, 19.12.

2.1.6. (E)-3-(3-Bromo-5-Ethoxy-4-Hydroxyphenyl)-1-(2-Hydroxynaphthalene-1-yl) Prop-2-en-1-One (5)

Brown solid; 82%; 525-527 °C IR (cm^{-1}): 3360 (OH), 3080 (=CH), 1650 (C=O), 1580 (C=C), 1540 (C-C), 610 (Ar-Br); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.41-7.08 (m, 9H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35 (s, 1H, OH), 5.30 (s, 1H, OH), 4.09 (q, 2H, CH_2), 1.32 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$,75 MHz): δ = 189.7, 162.2, 150.3, 145.1, 141.1, 136.1, 135.0, 131.6, 131.0, 130.6, 130.2, 126.9, 124.9, 122.9, 121.5, 121.3, 117.9, 114.4, 111.5, 64.9, 14.8; MS. m/z 412 Anal. Calcd. For Formula: $C_{21}H_{17}BrO_4$: C, 61.03; H, 4.15; Br, 19.33; O, 15.49; Found: C, 61.00; H, 4.13; Br, 19.31; O, 15.46.

2.1.7. (E)-3-(3-Benzyloxy)-4-Methoxyphenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1-One (6)

Green solid; 78%; 470-472°C IR (cm^{-1}): 3410 (OH), 3060 (=CH), 2940 (CH), 1640 (C=O), 1570 (C=C), 1490 (C-C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.31-7.01 (m, 14H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.16 (s, 2H, OCH_2-Ar), 3.83 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$,75 MHz): δ = 189.7, 162.2, 149.5, 149.0, 145.1, 136.7, 136.2, 135.0, 131.6, 131.0, 130.2, 128.9, 127.6, 127.2, 127.1, 126.3, 124.9, 122.9, 121.5, 121.3, 117.9, 114.0, 111.7, 71.1, 56.1; MS. m/z 410 Anal. Calcd. For Formula: $C_{27}H_{22}O_4$: C, 79.01; H, 5.40; O, 15.59; Found: C, 79.00; H, 5.38; O, 15.57.

2.1.8. (E)-3-(4-Benzyloxy)-3-Methoxyphenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1-One (7)

Green solid; 80%; 470-472°C IR (cm^{-1}): 3410 (OH), 3060 (=CH), 2940 (CH), 1640 (C=O), 1570 (C=C), 1490 (C-C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-6.94 (m, 14H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.10 (s, 2H, OCH_2-Ar), 3.83 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$,75 MHz): δ = 189.7, 162.2, 149.7, 145.5, 145.1, 136.7, 136.1, 135.0, 131.6, 131.0, 130.2, 128.9, 127.6, 127.3, 127.1, 126.9, 124.9, 122.5, 121.5, 121.3, 117.9, 114.8, 111.5, 71.1, 56.1; MS. m/z 410 Anal. Calcd. For Formula: $C_{27}H_{22}O_4$: C, 79.01; H, 5.40; O, 15.59; Found: C, 79.00; H, 5.38; O, 15.57.

2.1.9. (E)-1-(2-Hydroxynaphthalen-1-yl)-3-(2-Hydroxyphenyl) Prop-2-en-1-One (8)

Yellow solid; 85%; 395-397°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 1630 (C=O), 1550 (C=C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-6.96 (m, 10H, Ar-H), 8.33 (d, J=15.1Hz, 1Hβ, C=CH), 7.42 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.10 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 157.1, 141.0, 136.1, 135.0, 131.6, 131.0, 130.2, 129.3, 128.9, 126.9, 124.9, 122.6 121.5, 121.3, 121.2, 117.9, 117.6; MS. m/z 290 Anal. Calcd. For Formula: $C_{19}H_{14}O_3$: C, 78.61; H, 4.86; O, 16.53; Found: C, 78.59; H, 4.84; O, 16.51.

2.1.10. (E)-3-(5-Chloro-2-Hydroxyphenyl)-1-(2-Hydroxynaphthalen-1-Yl) Prop-2-en-1-One (9)

Yellow solid; 82%; 438-440°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 1630 (C=O), 1550 (C=C), 740 (Ar-Cl); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.71-6.84 (m, 9H, Ar-H), 8.33 (d, J=15.1Hz, 1Hβ, C=CH), 7.42 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.30 (s, 1H, OH);^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 155.1, 141.0, 136.1, 135.0, 131.6, 131.0, 130.5, 130.2, 127.8, 126.9, 126.8, 124.9, 121.5, 121.3, 118.4, 117.9; MS. m/z 324 Anal. Calcd. For Formula: $C_{19}H_{13}ClO_3$: C, 70.27; H, 4.03; Cl, 10.92; O, 14.78; Found: C, 70.25; H, 4.01; Cl, 10.90; O, 14.76.

2.1.11. (E)-3-(3, 5-Dibromo-2-Hydroxyphenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1-One (10)

Yellow solid; 82%; 540-542°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 1630 (C=O), 1550 (C=C), 640 (Ar-Br);^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-7.08 (m, 8H, Ar-H), 8.33 (d, J=15.1Hz, 1Hβ, C=CH), 7.42 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.10 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 157.3, 141.0, 136.1, 135.3, 135.0, 131.6, 131.0, 130.3, 130.2, 126.9, 124.9, 121.5, 121.3, 120.9, 117.9, 115.9, 113.3; MS. m/z 447 Anal. Calcd. For Formula: $C_{19}H_{12}Br_2O_3$: C, 50.93; H, 2.70; Br, 35.66; O, 10.71; Found: C, 50.91; H, 2.68; Br, 35.64; O, 10.69.

2.1.12. (E)-3-(2-Hydroxy-3, 5-Diiodophenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1-One (11)

Yellow solid; 85%; 536-538°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 1630 (C=O), 1550 (C=C), 490 (Ar-I); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.31-7.04 (m, 8H, Ar-H), 8.33 (d, J=15.1Hz, 1Hβ, C=CH), 7.42 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.10 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 156.3, 144.5, 141.0, 136.1, 135.0, 134.1, 131.6, 131.0, 130.2, 126.9, 124.9, 121.5, 121.3, 119.7, 117.9, 88.4, 83.6; MS. m/z 542 Anal. Calcd. For Formula: $C_{19}H_{12}I_2O_3$: C, 42.10; H, 2.23; I, 46.82; O, 8.85; Found: C, 42.08; H, 2.21; I, 46.80; O, 8.83.

2.1.13. (E)-1-(2-Hydroxynaphthalen-1-yl)-3-(4-Hydroxyphenyl) Prop-2-en-1-One (12)

Yellow solid; 85%; 395-397°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 1630 (C=O), 1550 (C=C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-6.65 (m, 10H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.25 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 157.7, 145.1, 136.1, 135.0, 131.6, 131.0, 130.6, 130.2, 127.8, 126.9, 124.9, 121.5, 121.3, 117.9, 115.8; MS. m/z 290 Anal. Calcd. For Formula: $C_{19}H_{14}O_3$: C, 78.61; H, 4.86; O, 16.53; Found: C, 78.59; H, 4.84; O, 16.51.

2.1.14. (E)-3-(2, 4-Dihydroxyphenyl)-1-(2-Hydroxynaphthalen-1-yl) Prop-2-en-1-One (13)

Yellow solid; 83%; 507-509°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 1630 (C=O), 1550 (C=C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-6.14 (m, 9H, Ar-H), 8.33 (d, J=15.1Hz, 1Hβ, C=CH), 7.42 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 5.30 (s, 1H, OH), 5.25 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 160.0, 159.1, 141.0, 136.1, 135.0, 131.6, 131.2, 131.0, 130.2, 126.9, 124.9, 121.5, 121.3, 117.9, 115.6, 108.4, 103.5; MS. m/z 306 Anal. Calcd. For Formula: $C_{19}H_{14}O_4$: C, 74.50; H, 4.61; O, 20.89; Found: C, 74.48; H, 4.59; O, 20.87.

2.1.15. (E)-1-(2-Hydroxynaphthalen-1-yl) 3-(4-Methoxyphenyl) prop-2-en-1-One (14)

Yellow solid; 78%; 330-332°C IR (cm^{-1}): 3320 (OH), 3060 (=CH), 2940 (CH), 1630 (C=O), 1550 (C=C), 740 (Ar-Cl); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.31-6.94 (m, 10H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 3.83 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 159.8, 145.1, 136.1, 135.0, 131.6, 131.0, 130.2, 127.5, 126.9, 124.9, 121.5, 121.3, 117.9, 114.2, 55.8; MS. m/z 304 Anal. Calcd. For Formula: $C_{20}H_{16}O_3$: C, 78.93; H, 5.30; O, 15.77; Found: C, 78.91; H, 5.28; O, 15.75.

2.1.16.(E)-3-(3-Bromo-4,5-Dimethoxyphenyl)-1-(2-Hydroxynaphthalen-1-yl)Prop-2-en-1-One (15)

Orange solid; 84%; 448-450°C IR (cm^{-1}): 3350 (OH), 3080 (=CH), 1640 (C=O), 1580 (C=C), 2990 (CH), 620 (Ar-Br); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.31-7.08 (m, 8H, Ar-H), 8.06 (d, J=15.1Hz, 1Hβ, C=CH), 7.59 (d, J=15.1Hz, 1Hα, CH=C), 5.35(s, 1H, OH), 3.83 (s, 6H, OCH_3); ^{13}C NMR ($CDCl_3$): δ = 189.7, 162.2, 151.9, 150.5, 145.1, 136.1, 135.0, 131.6, 131.0, 130.7, 130.2, 126.9, 124.9, 123.2, 121.5, 121.3, 117.9, 113.1, 110.5, 60.9, 56.1; MS. m/z 413 Anal. Calcd. For Formula: $C_{21}H_{17}BrO_4$: C, 61.03; H, 4.15, Br, 19.33; O, 15.49; Found: C, 61.00; H, 4.13; Br, 19.31; O, 15.47.

2.2. Procedure of Antibacterial Activity

The synthesized compounds were screened for antibacterial activity against *Bacillus licheniformis, Bacillus species, Escherichia coli and Staphylococcus aureus* using the well diffusion method. Microbial suspension of 100 *u*L containing 10^8 cfu mL^{-1} of bacteria on Mueller-Hinton Agar (MHA) medium was used. The extracts were diluted in 100% dimethyl Sulphoxide at the concentrations of 5mg/ml. The Mueller Hinton agar was melted and cooled to 48-50°C and standardized inoculums (1.5 X 10^8 cfu/ml, 0.5 McFarland) were added aseptically to the molten agar and poured into sterile petri dishes to yield solid plates. Wells were prepared in the seeded agar plates. To check the activity, the compound was introduced in the well (6mm). The plates were incubated in the incubator overnight at 37°C. The antibacterial spectrum of the extract was determined for the bacterial species in term of zone sizes around each well. The diameters of zone of inhibition produced by the compound were compared with standard Ciprofloxacin [35, 36]. The results are tabulated in (Table **1**).

2.3. Procedure of Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentration of compound was obtained by Broth dilution method. In this the concentration of the synthesized compound was maintained at8mg/mL in the first tube containing 1mL of broth. The tubes were vortexed to make the initial standard concentration. This was serially diluted in other tubes and finally 1mL was discarded from the last tube to make the dilution of 1, 0.5, and 0.25 mg/mL, respectively. To all these tubes, 0.1 mL of the long phase culture of target microorganisms was added separately and incubated at 37°C for 24-48 hrs for bacterial growth [37, 38].

3. RESULTS AND DISCUSSION

3.1. Chemistry

This paper describes simple method for effective synthesis of chalcones from 2-hydroxy-1-acetonaphthone and different substituted aldehydes in which 2-hydroxy-1-acetonaphthone were dissolved in ethyl alcohol. In warmed solution, substituted aldehydes were added. The reaction mixture was kept in bulb oven overnight, poured in ice cold water and neutralized by dil. HCl. The synthesized compounds were filtered through buckner funnel and recrystallized from ethanol Scheme **1**.

The structure of chalcone derivatives was characterized by recording their IR, ^{1}HNMR and Mass spectra. All the chalcones showed an absorption band in region 1650-1590 cm^{-1} due to carbonyl(C=O) stretching vibration. ^{1}HNMR spectra serve as the best analyzing tool for the structural elucidation. ^{1}HNMR spectra showed two doublets in the region of 7.42-8.33 δ ppm with J=15.1Hzs indicating the presence of trans olefinic protons (-CH=CH-) and also showed a singlet at 5.35 δ ppm due to the hydroxyl group. ^{13}CNMR spectra of chalcones were recorded in $CDCl_3$ and were in good agreement with theoretic structure ^{13}CNMR spectra proposed for all chalcones.

3.2. Antibacterial Activity

Although no definite structure-activity relationship could be determined, some conclusions on the structural changes that may influence the antibacterial activity can be drawn by the comparison among the structure of the compound with a different activity.

From the screening studies (Table **1**), it is evident that the synthesized chalcones **2, 3, 4, 5, 8, 11, 12, 13** showed good

Table 1. Microbial Activity of Synthesized Compounds (in mm) (1-15).

Sr.No	Name of Organism → / Sample Name ↓	*B. Lichenifermis*	*Bacillus Sp.*	*E.coli*	*S.aureus*
01	**1**	07	11	08	16
02	**2**	14	12	10	26
03	**3**	15	13	11	27
04	**4**	15	14	09	28
05	**5**	17	16	10	28
06	**6**	07	07	08	08
07	**7**	08	08	09	09
08	**8**	18	20	10	24
09	**9**	20	22	09	25
10	**10**	19	21	09	23
11	**11**	18	21	10	24
12	**12**	24	22	18	28
13	**13**	19	18	12	22
14	**14**	09	08	08	07
15	**15**	08	07	09	08
16	**Ciprofloxacin**	27	26	20	30
17	**DMSO**	00	00	00	00

antibacterial activity against all organisms. The chalcones **4,9,10** also showed good antibacterial activity against all organisms except *Escherichia coli*. It was further observed that chalcone **1** showed good activity against *Bacillus species* and *Staphylococcus aureus*. It showed moderate activity against *Bacillus licheniformis* and *Escherichia coli.* The chalcones **6, 7, 14, 15** showed moderate activity against all organisms.

The hydroxyl group adjacent to a ketone is a very common feature of natural chalcones which is always present in the active compounds [35]. It participates to stabilize the predominant structure of the chalcones by a hydrogen bond; moreover, it is also the key element in the equilibrium chalcone-flavanone. For both these reasons, the hydroxyl substituent may be considered a crucial group for the structure stability.

A free hydroxyl group in position 2 or 4 of aldehyde ring appears to be a very important requirement in increasing the activity (**2-5** and **8-13**). When the hydroxyl group in position 4 is alkylated (**14, 15**), the chalcone is not more active. When a more complex substituent is present on aldehyde ring (**6, 7**) there is a decrease in the activity.

3.3. Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentration of the synthesized chalcones was evaluated at different concentrations *i.e.* 1.0, 0.5 and 0.25 mg/mL. The results of MIC are given in Table **2**. From Table **2**, it is clear that the chalcones **3, 4** and **12** show a good inhibition at minimum concentration (0.25 mg/mL) against all organisms. The chalcones **2, 5, 8, 9, 10** and **13** showed good inhibition at the minimum concentration of 0.25 mg/mL against *Bacillus licheniformis*, Bacillus *species* and *Staphylococcus aureus* (Gram-positive) strains. The chalcones **2, 3, 4, 5, 8, 11, 12** and **13** showed good inhibition at the minimum concentration of 0.5 mg/mL against all organisms. Chalcones **9** and **10** showed good inhibition at the minimum concentration of 0.5 mg/mL against *Bacillus licheniformis* (Gram-positive), Bacillus *species* and *Staphylococcus aureus* (Gram-positive) strain. Chalcone **1** shows a good inhibition at the minimum concentration of 0.5 mg/mL against *Escherichia coli* (Gram-negative).

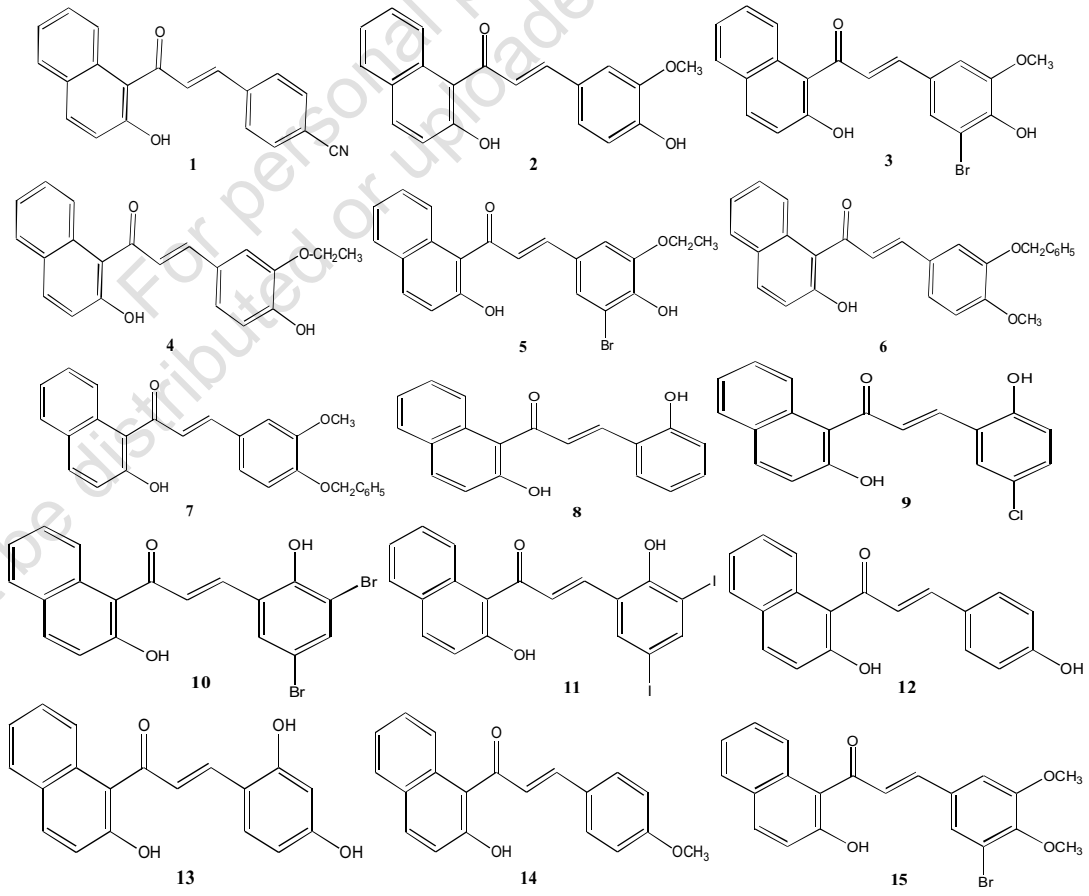
The comparative study also revealed that the electronegative substituent on the ring had a good inhibition against *Bacillus licheniformis*, *Bacillus species* and *Staphylococcus aureus* at all concentrations. The electron releasing group had a good inhibition against all bacterial strains at all concentrations [37, 38].

Table 2. Minimum Inhibitory Concentration of Synthesized Chalcones (1-15).

Comp. Name	*B. licheniformis* Conc. In Mg/mL			*Bacillus Sp.* Conc. In Mg/mL			*E. coli* Conc. In Mg/mL			*S. aureus* Conc. In Mg/mL		
	1.0	0.5	0.25	1.0	0.5	0.25	1.0	0.5	0.25	1.0	0.5	0.25
1	-	+	+	-	-	+	-	-	+	-	-	-
2	-	-	-	-	-	-	-	-	+	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	+	-	-	-
6	+	+	+	+	+	+	-	+	+	-	+	+
7	-	+	+	-	+	+	-	+	+	-	+	+
8	-	-	-	-	-	-	-	-	+	-	-	-
9	-	-	-	-	-	-	-	+	+	-	-	-
10	-	-	-	-	-	-	-	+	+	-	-	-
11	-	-	+	-	-	-	-	-	+	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	+	-	-	-
14	-	-	+	-	+	+	-	+	+	+	+	+
15	-	+	+	+	+	+	-	-	+	-	+	+
Ciproflox-acin	-	-	-	-	-	+	-	-	+	-	-	-

The Positive sign (+) indicates growth on the plates; the negative sign (-) indicates no growth on the plates

Structure of Synthesized Chalcones (1-15)



CONCLUSION

In the present work, we synthesized some novel Chalcones derived from 2-hydroxy-1-acetonaphthone and differently substituted aldehydes. The newly synthesized compounds were obtained in good yield and it was confirmed by melting points, IR, NMR and Mass spectra. It is also checked for antibacterial activity using Ciprofloxacin as a standard drug. The antibacterial data reveals that all compounds showed good to moderate activity.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Not applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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