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Microwave-Assisted Synthesis of 2-(5-(5-(4-Substituted phenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)alkyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione Derivatives and their Antimicrobial Activity

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A method for the synthesis of several imidazoles containing isoquinoline scaffolds under conventional and microwave irradiation methods. In the microwave irradiation method gives higher yields with in shorter reaction time as compared to conventional heating method, using green solvents and eco-friendly reaction conditions. All the synthesized derivatives were characterized by IR, NMR and Mass spectral analysis. Furthermore, the title compounds were screened for their *in vitro* antimicrobial activity against bacteria such as *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumonia* as well as fungi such as *Aspergillus niger, Aspergillus flavus* and *Fusarium oxysporum*. The compounds **8a, 8d**, **8e** and **8h** exhibited better antimicrobial activity against all organisms.

Keywords: Imidazole, Isoquinoline, Microwave irradiation, Antimicrobial activity.

INTRODUCTION

In current year, efforts for discovery and design of novel antimicrobial drugs have developed in the world. The delinquent of antimicrobial drug resistance to antibiotics as β-lactam antibiotics and macrolides is extensively known [1]. There is still now an increase in humanity, illness and antibiotics treatment failure due to a diversity of infectious conditions affected by resistant microbial [2,3]. Therefore, there is a need to develop effective new antimicrobial agents to overcome these disorder. The heterocyclic compounds have been core structural in medicinal chemistry and similarly they are commonly found in large percent in biomolecules as enzyme, vitamins, naturally occurring compounds and biological active compounds [4].

One of the best naphthalimide heterocyclic scaffolds were first discovered by Brana *et al.* [5], have been known as exhibited high anticancer against several cell lines and DNA intercalators [6-8]. The naphthalimide-based protective compounds, such as amonafide and mitinafide have confirmed remarkable potency in clinical trials (Fig. 1). Nevertheless, the results in trials were associated with severe side effects [9]. The structure activity relationship exposed that naphthalimide core should be intact although adding other functional groups may decrease the systemic toxicity. The naphthalimide core fused aromatic rings such as benzene, pyrazine, thiophene, imidazole and others core moiety to improve anticancer activity and decrease side effects. Some of them achieved compound exhibits significant improvement in cellular cytotoxic activity over amonafide [10-13].

On the other hand, imidazole scaffolds has attracted extraordinary attention in chemistry, biochemistry and these compounds exhibited various pharmaceutical properties such as antibacterial [14,15], antifungal [10], antiinflammatory [16], analgesic [17], antitubercular [18,19], antidepressant [20], antiviral [14] and anticancer [21] activities. Furthermore, some of them have found applications as fluorescent whitening agents. The clotrimazole, fluconazole, miconazole (Fig. 1) are having imidazole derivatives exhibited as antifungal activity.

In the background of green chemistry, microwave irradiation method provides an alternative to conventional heating methods. It uses the capability of mobile electric charge present in liquid or conducting ions in solid to convert electromagnetic energy into heat. The microwave-assisted reactions are well-known to afford improved rate of reaction and enhanced yield

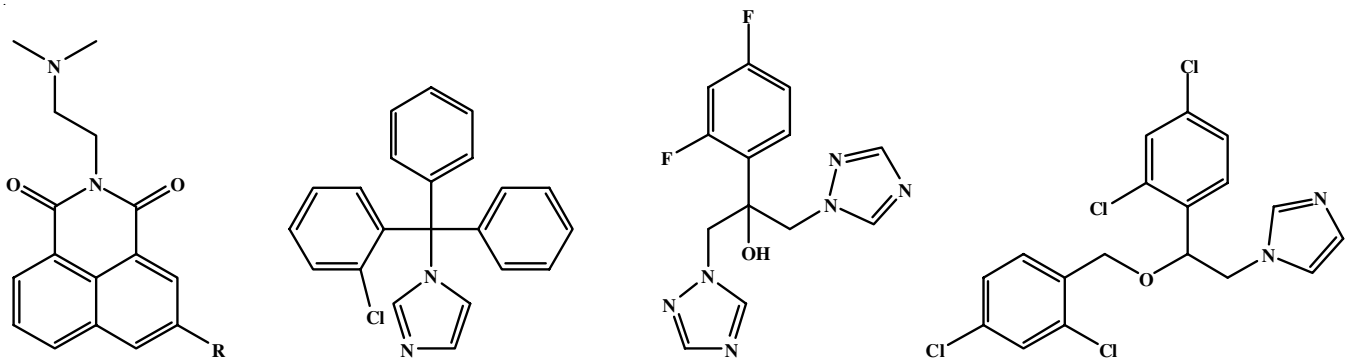


Fig. 1. Structure of some bioactive compounds containing imidazole moiety

of product in the organic synthesis and where it is quite successful in the formation of a variety of carbon-heteroatom bonds [22]. In recent years, microwave irradiation method have been extensively utilize for carrying out organic reactions and have become a useful non-conventional energy source for performance organic synthesis [23,24].

The molecular hybridization is a new research topic in drug design and development of new hybrid core by combination of two or more pharmacophore moieties to generate enhanced affinity, efficiency and decrease side effects, when compared to parental drug. Moreover, this approach can outcome result in compounds presenting modified selectivity profile, changed dual modes of action and decreasing side effects [25]. Inspire of biological activities of imidazole, naphthalimide and molecular hybridization, we decide to synthesize of design target molecules by conventional heating and microwave irradiation method. All the compounds were evaluating for their antimicrobial activity.

EXPERIMENTAL

All the reagents and solvents were purchased from Sigma-Aldrich or S.D. fine chemicals limited and used without further purification. Melting points were determined using a Cintex apparatus and were uncorrected. Elemental analysis was measured by means of Perkin Elmer 2400 CHN elemental analyzer. Purity of compounds was monitored by TLC on silica gel plates 60 F254 (Merck). Reactions under microwave irradiation were carried out in milestone multi SYNTH microwave system. IR (KBr) spectra were recorded on a Shimadzu FT-IR-8400S spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were measured on Bruker Avance II 400 MHz spectrometer (TMS internal standard). Mass spectra were recorded on SHIMADZU LCMS 2020 mass spectrometer.

General procedure for compounds 8a-h:

Conventional heating method: To a stirred solution of 2-(substituted-2*H*-chromen-3-yl)-5-aryl-1*H*-imidazoles (**5a-d**) compound **7a-b** in DMF, refluxed over anhydrous potassium carbonate for 10-14 h. After the completion of reaction mixture (as indicated by TLC) and then reaction mixture was poured onto ice-cold water, extracted with DCM and dried over Na_2SO_4 the obtained crude purified by column chromatography using hexane:ethyl acetate (5:5 v/v).

Microwave irradiation method: A mixture of 2-(substituted-2*H*-chromen-3-yl)-5-aryl-1*H*-imidazoles (**5a-d**) compound **7a-b** in DMF, refluxed over anhydrous potassium carbonate was taken in a quartz tube and inserted into a Teflon vial with screw capped and then it was subjected to microwave irradiation at 320 watts for 9-12 min with an every 30 s intervals. After the completion of reaction mixture (as indicated by TLC) and then reaction mixture was poured onto ice-cold water, extracted with DCM and dried over Na_2SO_4 the obtained crude purified by column chromatography using hexane:ethyl acetate (5:5 v/v).

2-(5-(5-(4-Fluorophenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)pentyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8a): Pale yellow coloured solid; m.p.: 250-252 °C; IR (KBr, ν_{max}, cm^{-1}): 1658 (C=O), 1570 (N=C), 1112 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.60 (d, 2H, *J* = 7.2 Hz, Ar-H), 8.22 (d, 2H, *J* = 8.2 Hz, Ar-H), 7.78-7.74 (m, 2H, Ar-H), 7.50-7.34 (m, 2H, Ar-H), 7.15-6.85 (m, 3H, Ar-H), 6.52 (d, 2H, *J* = 8.2 Hz, Ar-H) 6.43 (d, 2H, *J* = 8.2 Hz, Ar-H), 5.30 (s, 2H, -OCH_2), 4.33-4.18 (m, 4H, -CH_2), 3.82 (s, 3H, -OCH_3), 2.12-2.01 (m, 2H, -CH_2) 1.25-1.20 (m, 4H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.4, 155.9, 153.6, 144.5, 139.9, 134.2, 133.8, 133.3, 131.6, 131.5, 129.9, 128.3, 127.6, 126.4, 122.4, 120.9, 120.5, 117.9, 117.7, 111.9, 108.7, 103.5, 66.5, 55.5, 47.3, 39.8, 30.5,29.8,27.7, 24.1. MS, *m/z*: found $[M + H]^+$588; Calculated for $C_{36}H_{30}N_3O_4F$: C: 73.60; H: 5.25; F: 3.33; N: 7.28.

2-(5-(5-(4-Chlorophenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)pentyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8b): Pale yellow coloured solid; m.p.: 258-260 °C; IR (KBr, ν_{max}, cm^{-1}): 1658 (C=O), 1570 (N=C), 1112 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.61 (d, 2H, *J* = 7.2 Hz, Ar-H), 8.23 (d, 2H, *J* = 8.2 Hz, Ar-H), 7.78-7.75 (m, 2H, Ar-H), 7.50-7.35 (m, 2H, Ar-H), 7.15-6.84 (m, 3H, Ar-H), 6.53 (d, 2H, *J* = 8.2 Hz, Ar-H) 6.45 (d, 2H, *J* = 8.2 Hz, Ar-H), 5.31 (s, 2H, -OCH_2), 4.33-4.19 (m, 4H, -CH_2), 3.83 (s, 3H, -OCH_3), 2.12-2.02 (m, 2H, -CH_2) 1.26-1.20 (m, 4H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.3, 155.9, 154.7, 144.5, 139.9, 134.3, 133.8, 133.6, 131.5, 131.3, 129.8, 128.1, 127.5, 126.4, 122.6, 121.8, 120.3, 118.4, 117.6, 111.8, 108.7, 103.6, 66.3, 55.6, 47.6, 39.9, 30.4, 29.7, 26.7, 24.0. MS, *m/z*: found $[M + H]^+$604; Calculated for $C_{36}H_{30}N_3O_4Cl$: C: 71.62; H: 5.16; Cl: 5.86; N: 6.97.

2-(5-(5-(4-Bromophenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)pentyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8c): Pale yellow coloured solid; m.p.: 288-290 °C; IR (KBr, ν_{max}, cm^{-1}): 1658 (C=O), 1570 (N=C), 1112 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.57 (d, 2H, *J* = 7.2 Hz, Ar-H), 8.21 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.76-7.72 (m, 2H, Ar-H), 7.5 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.46 (d, 1H, *J* = 8.5 Hz, Ar-H), 7.11-7.01 (m, 2H, Ar-H), 6.52 (d, 2H, *J* = 8.2 Hz, Ar-H) 6.43 (d, 2H, *J* = 8.2 Hz, Ar-H), 5.20 (s, 2H, -OCH_2), 4.24-4.14 (m, 4H, -CH_2), 3.82 (s, 3H, -OCH_3), 2.00-1.53 (m, 6H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.2, 155.7, 154.6, 144.2, 139.7, 134.0, 133.9, 133.0, 131.5, 131.2, 129.7, 128.1, 126.9, 126.4, 122.5, 120.8, 120.3, 117.8, 117.6, 111.8, 108.8, 103.4, 66.4, 55.6, 47.4, 39.9, 30.4, 29.7, 26.7, 24.0. MS, *m/z*: found $[M + H]^+$ 648; Calculated for $C_{36}H_{30}N_3O_4Br$: C: 66.62; H: 4.65; Br: 12.42; N: 6.52.

2-(5-(2-(5-Methoxy-2*H*-chromen-3-yl)-5-(4-methoxyphenyl)-1*H*-imidazol-1-yl)pentyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8d): Pale yellow coloured solid; m.p.: 262-264 °C; IR (KBr, ν_{max}, cm^{-1}): 1658 (C=O), 1570 (N=C), 1112 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.59 (d, 2H, *J* = 7.2 Hz, Ar-H), 8.23 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.76-7.72 (m, 2H, Ar-H), 7.51 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.48 (d, 1H, *J* = 8.5 Hz, Ar-H), 7.11-7.01 (m, 2H, Ar-H), 6.53 (d, 2H, *J* = 8.2 Hz, Ar-H) 6.43 (d, 2H, *J* = 8.2 Hz, Ar-H), 5.21(s, 2H, -OCH_2), 4.25-4.14 (m, 4H, -CH_2), 3.85 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 2.00-1.53 (m, 6H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.4, 155.9, 154.8, 144.6, 139.9, 134.4, 134.2, 133.1, 131.6, 131.4, 129.9, 128.3, 127.4, 126.3, 122.2, 120.9, 120.5, 118.4, 117.3, 112.4, 108.4, 103.9, 66.4, 55.8, 47.6, 40.9, 39.2, 30.2, 29.8, 27.7, 24.0. MS, *m/z*: found $[M + H]^+$ 600; Calculated for $C_{37}H_{33}N_3O_5F$: C: 74.22; H: 5.65; N: 7.15.

2-(6-(5-(4-Fluorophenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)hexyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8e): Pale yellow coloured solid; m.p.: 288-290 °C; IR (KBr, ν_{max}, cm^{-1}): 1659 (C=O), 1572 (N=C), 1114 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.59-8.55 (m, 2H, Ar-H), 8.20-8.18 (m, 2H, Ar-H), 7.74-7.68 (m, 4H, Ar-H), 7.19 (s, 1H, Ar-H), 7.05-6.97 (m, 3H, Ar-H), 6.63 (s, 1H, Ar-H), 6.43-6.41 (m, 2H, Ar-H), 5.19 (s, 2H, -OCH_2), 4.22-4.09 (m, 4H, -CH_2), 3.77 (s, 3H, -OCH_3), 2.03-1.25 (m, 8H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.2, 155.7, 154.6, 144.2, 139.7, 134.0, 133.3, 132.2, 131.2, 130.2, 129.4, 128.2, 128.1, 127.1, 126.9, 126.5, 126.4, 122.5, 116.8, 115.4, 115.2, 107.7, 101.5, 67.0, 55.4, 47.2, 39.7, 32.3, 30.4, 27.5, 24.0. MS, *m/z*: found $[M + H]^+$ 602; Calculated for $C_{37}H_{32}N_3O_4F$: C: 73.92; H: 5.45; F: 3.24; N: 6.89.

2-(6-(5-(4-Bromophenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)hexyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8f): Pale yellow coloured solid; m.p.: 277-279 °C; IR (KBr, ν_{max}, cm^{-1}): 1657 (C=O), 1574 (N=C), 1115 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.59-8.55 (m, 2H, Ar-H), 8.20-8.18 (m, 2H, Ar-H), 7.72-7.68 (m, 4H, Ar-H), 7.18 (s, 1H, Ar-H), 7.05-6.96 (m, 3H, Ar-H), 6.65 (s, 1H, Ar-H), 6.45-6.41 (m, 2H, Ar-H), 5.21 (s, 2H, -OCH_2), 4.24-4.09 (m, 4H, -CH_2), 3.79 (s, 3H, -OCH_3), 2.04-1.25 (m, 8H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.4, 155.9, 154.8, 144.4, 139.9, 134.2, 133.5, 132.2, 131.4, 129.4, 128.5, 128.3, 128.0, 127.5, 126.3, 126.2, 124.1, 123.4, 122.6, 116.9, 115.5, 114.9, 107.9, 101.4, 67.3, 55.6, 47.3, 39.9, 32.5, 30.6, 27.9, 24.5. MS, *m/z*: found $[M + H]^+$ 662; Calculated for $C_{37}H_{32}N_3O_4Br$: C: 67.15; H: 4.89; Br:12.35; N: 6.45.

2-(6-(5-(4-Chlorophenyl)-2-(5-methoxy-2*H*-chromen-3-yl)-1*H*-imidazol-1-yl)hexyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8g): Pale yellow coloured solid; m.p.: 270-272 °C; IR (KBr, ν_{max}, cm^{-1}): 1656 (C=O), 1571 (N=C), 1116 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.59-8.54 (m, 2H, Ar-H), 8.20-8.19 (m, 2H, Ar-H), 7.74-7.68 (m, 4H, Ar-H), 7.18 (s, 1H, Ar-H), 7.05-6.98 (m, 3H, Ar-H), 6.62 (s, 1H, Ar-H), 6.43-6.41 (m, 2H, Ar-H), 5.18 (s, 2H, -OCH_2), 4.22-4.08 (m, 4H, -CH_2), 3.79 (s, 3H, -OCH_3), 2.02-1.25 (m, 8H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.5, 155.9, 154.8, 144.4, 139.9, 134.2, 133.4, 131.4, 128.2, 128.1, 126.9, 126.7, 126.4, 122.5, 116.8, 115.5, 115.2, 107.9, 101.4, 67.0, 55.4, 47.4, 39.9, 32.3, 30.6, 27.5, 24.1. MS, *m/z*: found $[M + H]^+$ 618; Calculated for $C_{37}H_{32}N_3O_4Cl$: C: 71.95; H: 5.35; Cl: 5.95; N: 6.95.

2-(6-(2-(5-Methoxy-2*H*-chromen-3-yl)-5-(4-methoxyphenyl)-1*H*-imidazol-1-yl)hexyl)-1*H*-benzo[de]isoquinoline-1,3(2*H*)-dione (8h): Pale yellow coloured solid; m.p.: 281-283 °C; IR (KBr, ν_{max}, cm^{-1}): 1656 (C=O), 1576 (N=C), 1118 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz): 8.59-8.55 (m, 2H, Ar-H), 8.20-8.18 (m, 2H, Ar-H), 7.74-7.68 (m, 3H, Ar-H), 7.18 (s, 2H, Ar-H), 7.05-6.99 (m, 3H, Ar-H), 6.65 (s, 1H, Ar-H), 6.43-6.41 (m, 2H, Ar-H), 5.17 (s, 2H, -OCH_2), 4.23-4.09 (m, 4H, -CH_2), 3.78 (s, 3H, -OCH_3), 3.62 (s, 3H, -OCH_3), 2.03-1.28 (m, 8H, -CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.4, 155.9, 154.8, 144.5, 14.1, 139.7, 134.3, 133.1, 131.2, 128.4, 128.1, 126.8, 126.5, 126.5, 122.5, 116.7, 115.5, 115.3, 107.9, 101.4, 67.2, 55.5, 47.2, 39.7, 38.5, 32.3, 30.5, 27.5, 24.3. MS, *m/z*: found $[M + H]^+$ 614; Calculated for $C_{38}H_{35}N_3O_5$: C: 74.45; H: 5.85; N: 6.92.

Antibacterial activity: The antimicrobial activity of all the synthesized compounds against Gram-positive bacterial strains such as *Bacillus subtilis* and *Staphylococcus* and Gram-negative strains such as *Klebsiella pneumonia*, *Escherichia coli* at a various concentration of 10 µg/mL and 20 µg/mL. The cultures were diluted with 5 % saline autoclaved and the ultimate volume was made with concentration almost equal 10^5–10^6 CFU/mL. All the synthesized derivatives were dissolved in DMSO for antimicrobial assays. For agar disc diffusion method, the solution form of tested compounds was saturated on the disc and then allowed to air dry to get completely saturated with tested compounds. These saturated discs were kept on the upper layer of middle evenly flooded with the bacteria. The discs were soaked in all compounds, were placed over the evenly extended bacteria nutrient media and keep them warm at 37 °C for 2-3 days for enhanced inhibition of bacteria. After 24-48 h to measure the zone of inhibition in mm. The zone of inhibition of all the synthesized compounds **8a-h** were compared with the standard antibiotic as gatifloxacin at different concentration (10 and 20 µg/mL).

Antifungal activity: The screening of antifungal activity of all the synthesized compounds **8a-h** was tested three pathogenic fungi such as *Aspergillus niger*, *Fusarium oxysporum* and *Aspergilus flavus*. For asceptic condition of the poison plate technique at a concentration of 100 µg/mL. three kinds

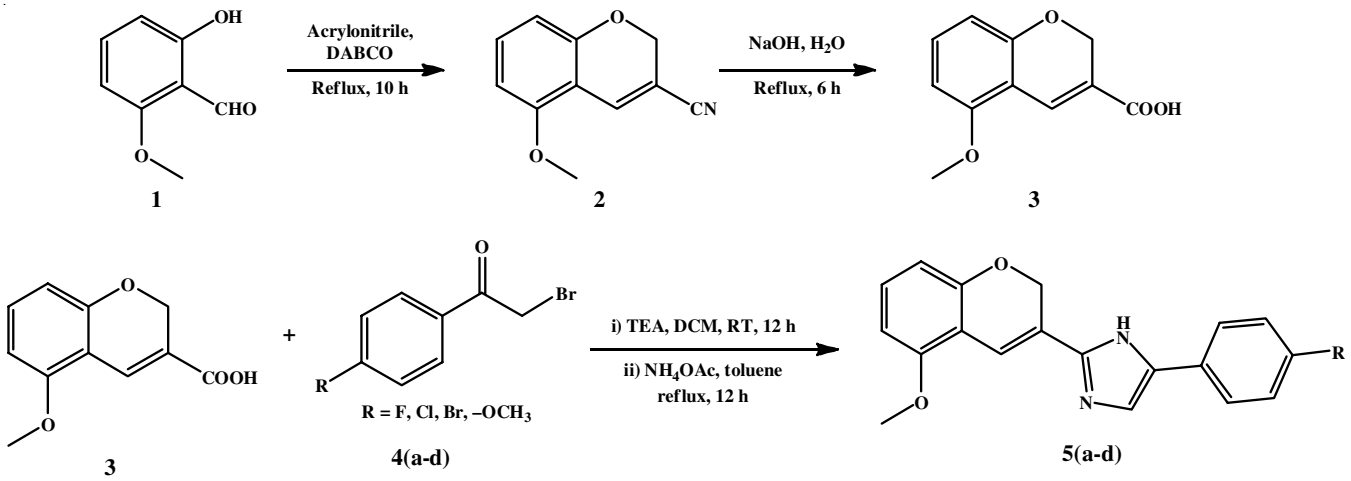
of fungi were incubated in PDA at 25 ± 1 °C for 5 days to get new mycelium for antifungal assay, then a mycelia as discs of approximately 0.45 cm diameter cut from the culture medium were picked up with a sterilized inoculation needle and inoculated in the center of PDA plate. The tested compounds were dissolved in DMSO (10 mL). the tested compounds were dissolved in DMSO (10 mL) then added to the potato dextrose agar medium (PDA, 90 mL) such that finally gets concentration of compounds in medium was 100 µg/mL. The immunized plates were incubated at 25 ± 1 °C for 5 days. The clotrimazole were used as standards for all the treatment and DMSO in sterilized water was used as control. The radical development of the fungus colonies was measured on the 4th day and the data were statistically evaluated. The *in vitro* inhibition of all the tested compounds on the fungi were calculated by CV = (A–B)/A, where A represent as the diameter of fungi growth on untreated PDA, B represents as the diameter of fungi on treated PDA and CV represents as the rate of inhibition.

RESULTS AND DISCUSSION

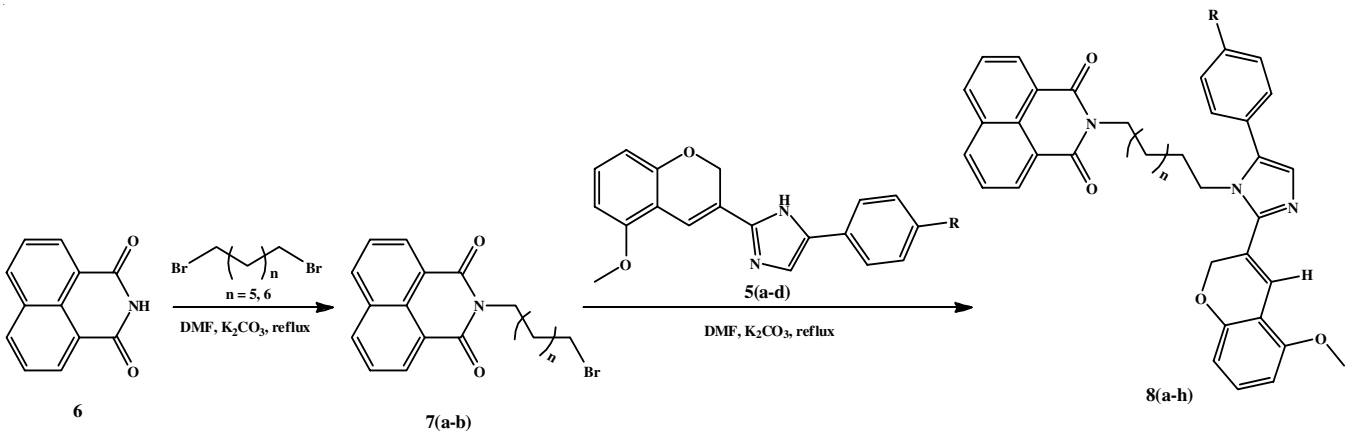
The substituted salicylaldehydes (**1**) treated with acrylonitrile and DABCO (1,4-diazabicyclo[2.2.2]octane) as catalyst in Baylis-Hillman reaction afforded a chromene-3-nitriles (**2**), after its turn in base hydrolzed to get chromene-3-carboxylic acid (**Scheme-I**). The chromene-3-carboxyic acids (**1**) were treated in DCM with different substituted acryl bromides (**4a-d**) in the presence of TFA followed by refluxing in toluene in presence of NH_4OAc to give 2-(substituted-2*H*-chromen-3-yl)-5-aryl-1*H*-imidazoles (**5a-d**). 1,8-Naphthalimide (**6**) treated with terminal dibromo alkane were refluxed in DMF over anhydrous potassium carbonate for 6 h on water bath. After the completion of reaction mixture was monitored (TLC) and purified. Further, it reacts with compounds **5a-d** in DMF to form the targeted compounds **8a-h** (**Scheme-II**).

In the synthesis of targeted compounds **8a-h** under conventional heating and microwave irradiation methods, we conformed that microwave irradiation method provides much more rate of reaction and higher yields (reaction time 9-12 min; yields 79-83 %) than conventional heating method (reaction time 10-14 h; yields 61-68 %). The comparisons of yields of the compounds **8a-h** in both the methods were depicted in Table-1.

Antibacterial activity: All the newly synthesized **8a-h** were screenings for their antibacterial activity against Gram-positive strains such as *Bacillus subtilis* (MTCC 121), *Staphylococcus aureus* (MTCC 96) and Gram-negative strains such as *Escherichia coli*, (MTCC 43), *Klebsiella pneumonia* (MTCC 530) at various concentration 10 and 20 µg/mL and the zone of inhibition was measured in mm. The result of all the compounds were compared with gatifloxacin was used as standard drug



Scheme-I



Scheme-II

TABLE-1
REACTION TIME AND YIELDS OF THE SYNTHESIZED COMPOUNDS **8a-h**

Comp. No.	Conventional		MWI	
	Time (h)	Yield (%)	Time (min)	Yield (%)
8a	14	64	9	81
8b	10	61	11	79
8c	11	68	10	84
8d	12	67	12	82
8e	14	61	9	79
8f	13	67	9	83
8g	14	68	10	83
8h	12	67	12	82

and result are shown (Table-2). The compounds **8a**, **8d**, **8e** and **8h** were showed high potential activity against all bacterial strains. The reaming compounds **8b**, **8c**, **8f** and **8g** were moderately active against all bacterial strains. The results also demonstrated that the activity of these compounds **8a-h** is influenced by their structures. In conclusion, **8a**, **8d**, **8e** and **8h** showed potential antibacterial activity against tested organisms.

Antifungal activity: All the newly synthesized compounds **8a-h** were tested for antifungal activity against three fungal organisms such as *Aspergillus niger*, *Aspergillus flavus* and *Fusarium oxysporum* at the concentration 50 µg/mL and the obtained result were compared with clotrimazole as standard drug and result of antifungal activity data showed in Table-2. The result evaluated that, among the entire synthesized compound **8a**, **8d**, **8e** and **8h** were shown better activity against all the three pathogenic fungi. The compounds **8f** and **8g** were showed maximum activity against *Fusarium oxysporum*, compounds **8c** and **8f** were shown to promising activity against *Aspergillus niger* and the compound **8c** shown better activity against *Aspergillus flavus.* Most of the compounds exhibits good activity against all the tested fungal strains.

Conclusion

In conclusion, a new series of compounds **8a-h** under microwave irradiation method and conventional heating method synthesized. The microwave irradiation method give higher yield with in shorter reaction time as compared conventional heating. The compounds were evaluated for their *in vitro* antimicrobial activity. In which some of the compounds **8a**, **8d**, **8e** and **8h** exhibited promising antibacterial activity and compounds **8a**, **8d**, **8e and 8h** were shows potential antifungal activity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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TABLE-2
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES DATA OF ALL THE SYNTHESIZED COMPOUNDS **8a-h**

Compound	Zone of inhibition (mm)										
	Antibacterial activity								Antifungal activity		
	Gram-positive bacteria				Gram-negative bacteria						
	S. aureus		*B. subtilis*		*K. pneumoniae*		*E. coli*		*A. niger*	*A. flavus*	*F. oxysporum*
	10 µg/mL	20 µg/mL	10 µg/mL	20 µg/mL	10 µg/mL	20 µg/mL	10 µg/mL	20 µg/mL	50 µg/mL	50 µg/mL	50 µg/mL
8a	12	22	14	26	13	20	14	22	16.8	16.5	17.8
8b	9	15	6	15	10	18	10	16	12.2	13.4	14.2
8c	8	16	7	14	8	15	8	12	16.5	15.2	13
8d	13	22	12	19	11	21	13	19	16.4	16.5	18.5
8e	14	24	11	18	13	18	14	21	16.5	15.9	17.9
8f	9	16	7	16	10	16	11	18	15.4	13.7	16.4
8g	10	17	8	15	9	19	10	17	12.7	14.3	17.4
8h	14	23	13	22	13	17	13	24	17.1	16.7	18.1
Gatifloxacin	13	23	12	25	12	20	13	21	–	–	–
Clotrimazole	–	–	–	–	–	–	–	–	17.3	16.7	18.2

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