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Design, Synthesis and Evaluation of Antimicrobial Activities of Some Chalcone & Schiff base Derivatives Clubbed with 1*H*-Benzimidazole

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ABSTRACT

A series of 2-(1H-benzo[d]imidazol-2-ylthio)-3-(substitutedphenyl)-1-(substitutedphenyl) prop-2-en-1-one ***3 (A-L)*** *derivatives have been synthesized via Claisen-schmidt reaction of different aromatic aldehydes with 2-benzimidazolyl thioacetophenone* ***2(A-D)*** *derivatives and these 2-mercaptobenzimidazolyl acetophenone derivatives which in turn synthesized by condensation of various acetophenones with 2-mercaptobenzimidazole* ***1A*** *& 6-methoxy-2-mercaptobenzimidazole* ***1B****. On the other hand desired Schiff base derivatives N-(3-chlorophenyl)-2-(1-(2-hydrazinyl-2-oxoethyl)-1H-benzo[d]imidazol-2-ylthio)acetamide* ***7(A-H)*** *have been prepared in three successive steps which comprised of synthesis of ethyl 2-(2-(2-(3-chloro phenyl amino)-2-oxoethylthio)-1H-benzo[d]imidazol-1-yl) acetate* ***5*** *its corresponding hydrazide N-(3-chloro phenyl)-2-(1-(2-hydrazinyl-2-oxoethyl)-1H-benzo[d]imidazol-2-ylthio) acetamide* ***6*** *and finally Schiff base derivatives via acid catalyzed condensation reaction of various aldehydes with this hydrazide. All the synthesized compounds were characterized by IR, ^{1}H NMR and mass spectral techniques and evaluated for their antimicrobial activity.*

Keywords: Chalcones, Schiff base, Benzimidazole, Antimicrobial activities

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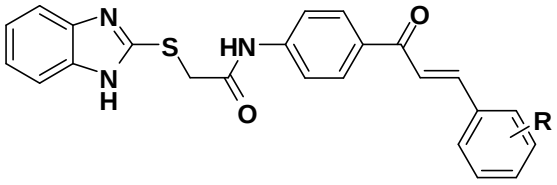
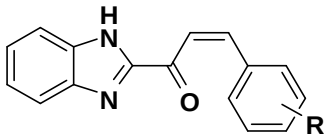
INTRODUCTION

Despite numerous attempts to search and develop new structural prototype as effective antimicrobials, benzimidazoles still remain as potential class of compounds. Recently, the chemistry and biological profiles of various pharmacophore of N-1 substituted and 2-substituted benzimidazole derivatives have been worked out [1]. Effect of substituent on the benzimidazole ring exhibited correlated structure–activity relationship [2]. Incorporation of an imidazole nucleus, a biologically active pharmacophore, in the benzimidazole molecule has made it a versatile heterocycle with wide spectrum of biological activity. Moreover, benzimidazole derivatives are structural isopterans of naturally occurring nucleotides, which allow them to interact easily with the biophores [3]. Therefore, numerous biological activities of benzimidazoles derivatives have been described; antimicrobial [4], anticancer [5] anti-inflammatory [6], antiviral [8], antiparasitic [9], antiprotozoal[10], antihelminitics [11], protein kinase inhibitors [12] and H^+/K^+ ATPase inhibitors[13]

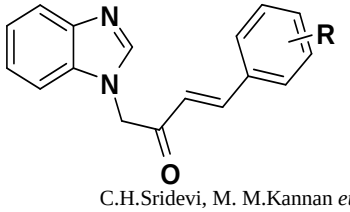
Chalcone is α, β-unsaturated ketone that forms the central core for the variety of biological important compounds. They are present in in edible plants as precursors of open chain flavonoids and isoflavonoids and their derivatives have attracted increasing attention due to numerous potential pharmacological applications. They have exhibited a broad spectrum of pharmacological activities. Modifications in their structure have offered a high degree of diversity that has led to the development of many useful new medicinal agents having improved potency and lesser toxicity. Different derivatives of chalcone clubbed with benzimidazole nucleus as a prime motif were synthesized by different authors hence we have incorporated Chalcone with another medicinally useful scaffold benzimidazole.



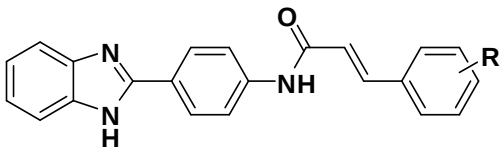
Deepkumar Joshi *et al*.[14]



Mahama Ouattara *et al*.[15]



C.H.Sridevi, M. M.Kannan *et al*.[16]

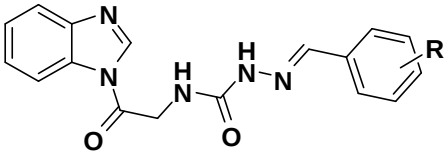


B. A. Baviskar *et al*.[17]

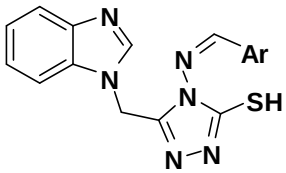
Figure-1

The compounds having structure of –C= N- (azomethine group) are well-known as Schiff bases, which are generally synthesized from the condensation of primary amines and active carbonyl groups. They are important class of compounds in medicinal and pharmaceutical field. They show diverse biological properties including antibacterial, antifungal antitumor, analgesic and anti-inflammatory activity. Presence of –C=N- and other functional groups forms more stable complexes as compared to Schiff bases having only –C=N- coordinating moiety[18].

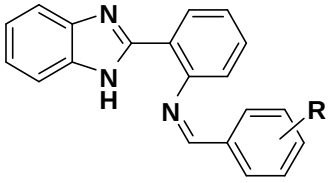
Schiff's bases comprising heterocyclic skeletons have been known to possess a wide range of biological and pharmacological activities for a long time [19]. In recent years, they have increased significant interest in the area of drug research and development owing to their broad bioactivities. Many authors have synthesized and evaluated Schiff base derivatives bearing benzimidazole scaffold, which promoted us to synthesize some novel Schiff base derivative containing benzimidazole moiety.



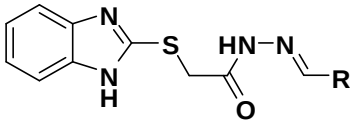
Sheeja Devi K. *et al*.[20]



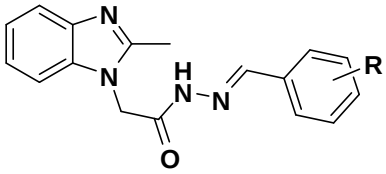
Sanahanbi. N. *et al*.[21]



Pradeep kumar *et al*.[22]



Ramesh Dhani *et al*.[23]



Rakesh Somani *et al*.[24]

Figure-2

MATERIALS AND METHODS

All chemicals and solvents were supplied by Merck, S.D. Fine Chem limited. All the solvents were distilled and dried before use. The reactions were monitored with the help of thin-layer chromatography using pre-coated aluminum sheets with GF254 silica gel, 0.2 mm layer thickness (E. Merck). Various solvent systems used for developing the chromatograms were (a) chloroform/methanol (9:1), (b) chloroform/ methanol (9.5:0.5), (c) ethyl acetate/hexane (5:5). Melting points of the synthesized compounds were recorded on the Veego (VMP-MP) melting point apparatus and not corrected. IR spectrum was acquired on a Shimadzu Infrared Spectrometer, (model FTIR-8400S). 1H NMR spectra of the synthesized compounds were performed in DMSO with IR spectra were recorded on Shimadzu FT-IR-8400 instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in DMSO-d6 solvent on a Bruker AC 400 MHz spectrometer.

EXPERIMENTAL

General procedure for the synthesis of 2-benzimidazolylthioacetophenones 2(A-D)[24]

A mixture of 2-mercaptobenzimidazole or 2-mercapto-6-methoxybenzimidazole (**1A** or **B,** 10 gm, 0.066mole) and substituted acetophenones (0.099mole) was refluxed in acetic acid (50ml) containing 3ml of con.H_2SO_4 for 3h. The

reaction mixture was cooled and neutralized with NH_4OH solution. The resulting precipitate was collected by filtration, washed several times with water, dried well and crystallized from ethanol or methanol to give the corresponding 2-benzimidazolylthioacetophenone derivatives **2(A-D)** as crystals in 85-90% yield

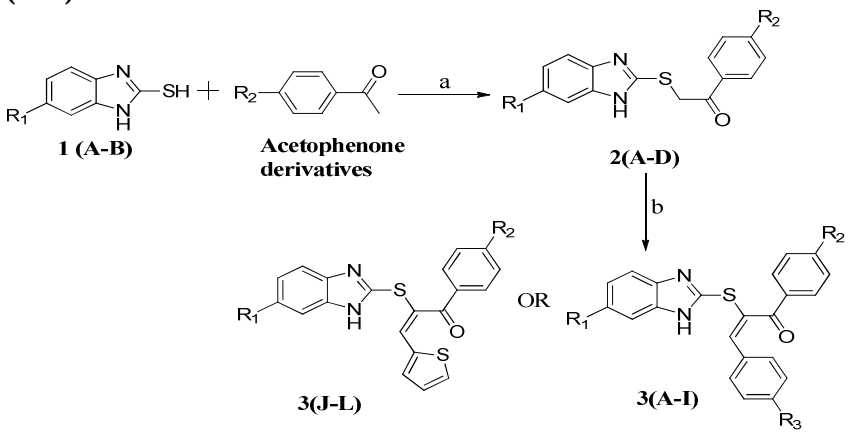
General procedure for the synthesis of compounds 3(A-L)
A mixture of 2-benzimidazolylthioacetophenones **2(A-D)** (1gm, 0.0033mole) and substituted aldehydes (0.0033mole) were stirred in methanol containing NaOH (0.0066mole) at room temperature for 4-5 h (Reaction was monitored by TLC). The reaction mixture was then poured into crushed ice. The aqueous solution was extracted with EtOAc (2 x 25). The combined organic layer washed with 1N HCl, brine solution, dried over Na_2SO_4 and concentrated under vacuum to yield 2-(1*H*-benzo[*d*]imidazol-2-ylthio)-3-(subsitutedphenyl)-1-(substituted phenyl) prop-2-en-1-one & 1-(substituted phenyl)-2-(6-methoxy-1*H*-benzo[*d*]imidazol-2-ylthio)-3-(substituted phenylprop-2-en-1-one 3(A-L) **.** All the compounds were purified by column chromatography (Hexane/EtOAc, 6:4).

Procedure for the synthesis of 2-(1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-(3-chlorophenyl) acetamide (4)
The starting material 2-(1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-(3-chlorophenyl)acetamide **4** has been synthesized according to method described in literature[25].

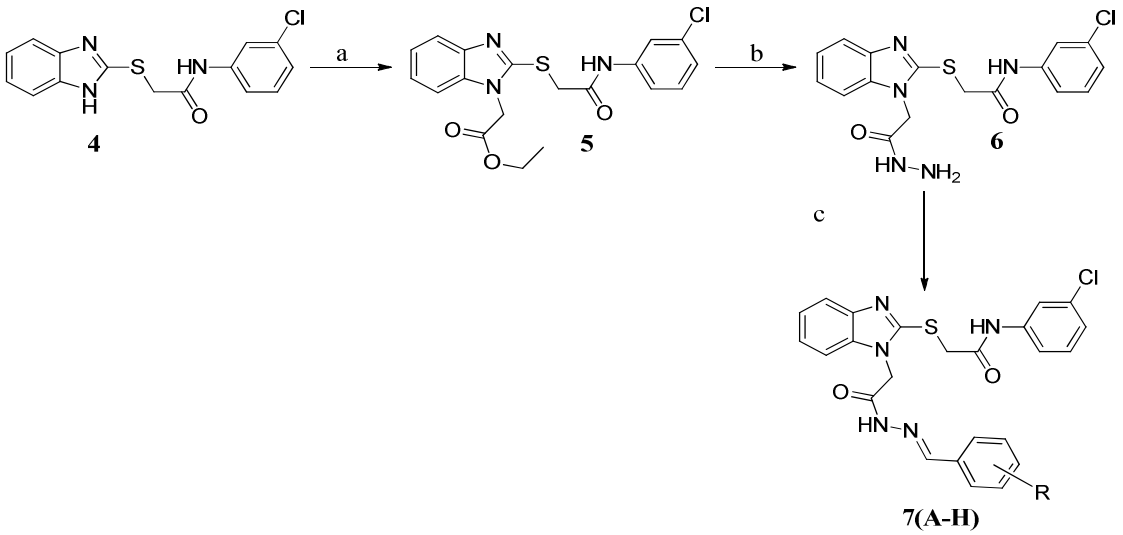
Procedure for the synthesis of ethyl 2-(2-(2-(3-chloro phenyl amino)-2-oxoethylthio)-1*H*-benzo[*d*]imidazol-1-yl) acetate (5)
A suspension of 2-(1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-(3chlorophenyl) acetamide **4** (10.0gm, 0.031mole), ethyl bromoacetate (0.031mole) and sodium carbonate (0.062mole) in acetonitrile was heated at 60^{o}C for 2 h. The reaction mixture was cooled and poured into crushed ice and resulting solid was filtered, washed with water, dried well. The dry solid was purified with methanol to get desired product in 75% yield.

Procedure for the synthesis of *N*-(3-chloro phenyl)-2-(1-(2-hydrazinyl-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio) acetamide (6)
A suspension of ethyl 2-(2-(2-(3-chlorophenylamino)-2-oxoethylthio)-1*H*-benzo[*d*]imidazol-1-yl)acetate **5**(10.0gm,0.024mole) and hydrazine hydrate (10ml) in methanol was stirred for 2h at room temperature. The precipitated solid was filtered and washed with methanol and dried well to get pure compound **6** in 80% yield.

General procedure for the synthesis of compounds 7 (A-H)
A suspension of *N*-(3-chloro phenyl)-2-(1-(2-hydrazinyl-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio) acetamide **6** (0.5gm, 0.0012mole) and substituted benzaldehydes (0.0012mole) in ethanol in the presence of catalytic amount of acetic acid was refluxed for 3h. The reaction mixture cooled to room temperature and solid was filtered, washed with ethanol and dried well to get pure *N*-(3-chlorophenyl)-2-(1-(2-hydrazinyl-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio)acetamide **7 (A-H)**



Where R_1= -H, -OCH_3, R_2= -H,-OH, -OCH_3, Ar/Het = -C_6H_5, C_6H_4F, C_6H_4Cl, C_4H_3S
Figure-3: Reaction Scheme-1: Reactants: (a) Cat.H_2SO_4, Acetic acid, reflux (b) Ar/Het-CHO, NaOH, Methanol, Room temperature



Where R= -H,-X, -OH, -OCH_3, -OC_3H_7,

Figure-4: Reaction Scheme-2: Reactants: (a) $BrCH_2COOEt$, K_2CO_3, CH_3CN, 60°C (b) Hydrazine hydrate, CH_3OH, Room temperature (c) Cat. CH3COOH, Aldehydes, Ethanol, reflux

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one (3A)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1670(-C=C–C=O,), 3068, 3024 (C–H stretching, aromatic ring), 3416 (-OH, phenolic, stretching), 1475, 1518 (C=C, aromatic ring stretching), 1600 (-C=C-, stretching,), 987 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 6.055 (s,1H), 6.437 (s,1H), 6.889 (d,2H),7.159 (s,2H), 7.189 (d,1H), 7.347 (s,2H), 7.390 (s,3H), 7.574 (d,1H),7.936 (d,2H),) ppm; MS: m/z 372.8 (M+H)+; M.P : 264-267, Yield: 50 %

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (3B)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1680(-C=C–C=O,), 3053, 2970 (C–H stretching, aromatic ring), 1421 (C-H, stretching), 1473, 1510(C=C, aromatic ring stretching), 1599 (-C=C-, stretching,), 1172 (O-C), 977 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 3.869 (s,3H), 6.044 (d,1H), 6.378 (d,1H), 7.067-7.144 (m,5H),7.284-7.397 (m,5H), 7.514 (d,1H), 8.044 (d,2H) ppm; MS: m/z 386.7 (M+H)+; M.P : 164-167, Yield: 44%.

2-(5-methoxy-1*H*-benzo[*d*]imidazol-2-ylthio)-1,3-diphenylprop-2-en-1-one (3C)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1670(-C=C–C=O,), 3068, 3023 (C–H stretching, aromatic ring), 1380 (C-H, stretching), 1472, 1512(C=C, aromatic ring stretching), 1604 (-C=C-, stretching,), 1120 (O-C), 989 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 3.738 (s,3H), 6.86 (t,1H), 7.10 (d,1H) 7.367-7.44 (m,4H),7.540-7.874 (m,8H), 8.044 (s,1H) ppm; MS: m/z 386.8 (M+H)+; M.P : 187-190, Yield: 40%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (3D)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1673(-C=C–C=O,), 3067, 3027 (C–H stretching, aromatic ring), 1485, 1510(C=C, aromatic ring stretching), 1608 (-C=C-, stretching,), 987 (-CH=C-,bending),785 (C-F).^{1}H NMR (400 MHz, DMSO-d6): δ = 6.969-7.145 (d,2H), 7.013 (t,1H), 7.145 (t,1H) 7.44-7..653 (m,11H) ppm; MS: m/z 374.8 (M+H)+; M.P : 250-255, Yield: 48%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-3-(4-fluorophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (3E).

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1672(-C=C–C=O,), 3067, 3020 (C–H stretching, aromatic ring), 3420 (-OH, phenolic, stretching), 1473, 1520(C=C, aromatic ring stretching), 1604 (-C=C-, stretching,), 790 (C-F), 984 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 6.12 (s, 1H), 6.513(s, 1H), 6.980 (d, 2H) 7.24 (s, 2H), 7.447(s, 2H), 7.52(s, 3H), 7.66(d, 1H), 8.03(d, 2H) ppm; MS: m/z 390.8 (M+H)+; M.P: 261-264, Yield: 57%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-3-(4-fluorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (3F)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1668(-C=C–C=O,), 3043, 3001 (C–H stretching, aromatic ring), 1357 (C-H, stretching), 1471, 1514(C=C, aromatic ring stretching), 1595 (-C=C-, stretching,), 1120 (O-C), 798 (C-F), 985 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ =

3.91(s, 3H), 6.749 (d,1H), 7.03 (d,3H), 7.167 (t,1H),7.24 (d,2H), 7.564 (s,4H), 8.044 (d,2H), 8.06 (s,1H) ppm; MS: m/z 404.8 (M+H)+; M.P: 152-155, Yield: 45%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-3-(4-chlorophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (3G)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1670(-C=C–C=O,), 3068, 3024 (C–H stretching, aromatic ring), 3416 (-OH, phenolic, stretching), 1475, 1518(C=C, aromatic ring stretching), 1600 (-C=C-, stretching,), 810 (C-Cl), 987 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 6.05 (s, 1H), 6.507(s, 1H), 6.960 (d, 2H) 7.19 (s, 2H), 7.41(s, 2H), 7.49(s, 3H), 7.59(d, 1H), 8.014(d, 2H) ppm; MS: m/z 404.8 (M+H)+; M.P : 234-237, Yield: 57%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-3-(4-chlorophenyl)-1-(4-methoxyphenyl) prop-2-en-1-one (3H)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1678(-C=C–C=O,), 3077, 3028 (C–H stretching, aromatic ring), 1370 (C-H, stretching), 1477, 1508(C=C, aromatic ring stretching), 1610 (-C=C-, stretching,), 1120 (O-C), 797 (C-Cl), 987 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 3.835 (s, 3H), 6.725(d, 1H), 6.985 (d, 3H) 7.112 (t, 1H), 7.187(d, 1H), 7.502(s, 4H), 7.968(d, 2H), 8.042(s, 1H) ppm; MS: m/z 420.8 $(M+H)^+$; M.P: 151-154, Yield: 49%.

3-(4-chlorophenyl)-2-(5-methoxy-1*H*-benzo[*d*]imidazol-2-ylthio)-1-phenylprop-2-en-1-one (3I)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1680(-C=C–C=O,), 3070, 3019 (C–H stretching, aromatic ring), 1374 (C-H, stretching), 1471, 1512(C=C, aromatic ring stretching), 1607 (-C=C-, stretching,), 1126 (O-C), 784 (C-Cl), 989 (-CH=C-,bending),^{1}H NMR (400 MHz, DMSO-d6): δ = 3.606 (s, 1H), 3.699(d, 2H), 6.784 (t, 1H) 6.943 (s, 1H), 7.413-7.536(m, 11H),8.457(s, 1H) ppm; MS: m/z 420.8 (M+H)+; M.P: 184-187, Yield: 52%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-1-phenyl-3-(thiophen-2-yl)prop-2-en-1-one (3J)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1} : 1672(-C=C–C=O,), 3060, 3027 (C–H stretching, aromatic ring),1485, 1525(C=C, aromatic ring stretching), 1610 (-C=C-, stretching,), 976 (-CH=C-,bending),^{1}H NMR(400MHz,DMSO-d6):δ=6.354-6.765(m,2H),7.074-7.439(m,8H),7.635-7.975 (m,2H), 8.256(s,1H) ppm; MS: m/z 420.8 (M+H)+; M.P. : 182-185, Yield: 45%.

2-(1*H*-benzo[*d*]imidazol-2-ylthio)-1-(4-hydroxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one (3K)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1} : 1672(-C=C–C=O,), 3060, 3027 (C–H stretching, aromatic ring),1485, 1525(C=C, aromatic ring stretching), 1610 (-C=C-, stretching,), 976 (-CH=C-,bending), 3425 (-OH, phenolic, stretching),^{1}H NMR (400 MHz, DMSO-d6): δ = 6.739-6.966(m,3H), 7.043-7.102(m,3H),7.162-7.285(m,3H), 7.721-7.800(m,3H) 7.981(s,1H) ppm; MS: m/z 378.7 (M+H)+; M.P. : 210-213, Yield: 49%.

2-(5-methoxy-1*H*-benzo[*d*]imidazol-2-ylthio)-1-phenyl-3-(thiophen-2-yl) prop-2-en-1-one (3L)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1} : 1660(-C=C–C=O,), 3069, 3033 (C–H stretching, aromatic ring), 1475, 1535(C=C, aromatic ring stretching), 1620 (-C=C-, stretching,), 980 (-CH=C-,bending), 1136 (O-C),^{1}H NMR (400 MHz, DMSO-d6): δ = 3.599(d,3H), 6.409-6804(m,2H), 7.163-8.010 (m,10H) , 8.414(s,1H) ppm; MS: m/z 392.7 (M+H)+; M.P. : 185-188, Yield: 49%.

2-(1-(2-(2-benzylidenehydrazinyl)-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-(3-chlorophenyl) acetamide (7A)
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1680(–C=O, aryl), 3297, 3060 (C–H stretching, aromatic ring),1430, 1122(C=C, stretching, aromatic ring),735(-C-H, bending ,aromatic), 875(C-X) ^{1}HNMR(400MHz, DMSO-d6): δ= 4.315(s, 2H),5.496(s,2H),7.11(d,2H),7.14-7.21 (m ,2H),7.34(t,1H),7.42-7.58(m,8H), 7.79(s,1H),8.09(s,1H), 10.672(s,1H),11.89(bs,1H), MS:m/z 478.1 $(M+H)^+$; M.P. 192-194, Yield:81%.

***N*-(3-chloro phenyl)-2-(1-(2-(2-(4-fluorobenzylidene) hydrazinyl)-2-oxoethyl)-1*H*-benzo[d]-imidazole-2-ylthio) acetamide (7B)**
This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1680(–C=O, aryl), 3197, 3064 (C–H stretching, aromatic ring),1441, 1166(C=C stretching, aromatic ring), 735(-C-H bending, aromatic), 7873(C-X), ^{1}HNMR(400MHz, DMSO-d6): δ=4.34(s,2H), 5.50(s,2H), 7.19-7.23(m,3H), 7.39-7.46 (m ,3H),7.49-7.59(m,3H), 7.82(d,2H), 8.11(s,1H), 10.67(s,1H), 11.90(bs,1H), MS: m/z 493.9 $(M+H)^+$; M.P. : 190-192, Yield:83%.

2-(1-(2-(2-(4-chlorobenzylidene)hydrazinyl)-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio-*N*-(3-chlorophenyl) acetamide (7C)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1681(–C=O, aryl), 3207, 3078 (C–H stretching, aromatic ring),1449, 1176(C=C, aromatic ring stretching),739(-C-H, bending ,aromatic),780(C-X). ^{1}H NMR (400MHz, DMSO-d6): δ=4.32(s,2H), 5.48(s,2H), 7.17-7.(m,3H), 7.37 (dd,1H), 7.47-7.57(m,5H) ,7.80(d,2H) ,8.09(s,1H),10.65(s,1H),11.88(bs,1H), MS: m/z 512.1 $(M+H)^+$; M.P. : 193-195, Yield: 78%.

2-(1-(2-(2-(4-bromobenzylidene)hydrazinyl)-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-(3-chlorophenyl) acetamide (7D)

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1680(–C=O, aryl), 3201, 3070 (C–H stretching, aromatic ring),1442, 1173(C=C, aromatic ring stretching),736(-C-H, bending ,aromatic),782(C-X).^{1}HNMR (400MHz, DMSO-d6): δ=4.32(s,2H),5.48(s,2H),7.15-7.20(m,3H),7.35(dd,1H),7.45-7.56 (m,5H), 7.78(d,2H), 8.08(s,1H), 10.60(s,1H), 11.85(bs,1H), MS: m/z 558.2 $(M+H)^+$; M.P. : 197-200, Yield: 75%.

***N*-(3-chlorophenyl)-2-(1-(2-(2-(4-hydroxybenzylidene)hydrazinyl)-2-oxoethyl)-1*H*-benzo[*d*]imidazol-2-ylthio) acetamide (7E)**

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1678(–C=O, aryl), 3320(-OH, phenolic),3107, 3072 (C–H stretching, aromatic ring),1440, 1156(C=C, aromatic ring stretching),732(-C-H, bending ,aromatic),782(C-Cl).^{1}HNMR(400MHz,DMSO-d6): δ=4.29(s,2H),5.43(s,2H),7.05(d,2H), 7.15-7.22(m,3H), 7.33 (dd,1H),7.42-7.53(m,3H), 7.80(d,2H), 8.06(s,1H),10.57(s,1H),11.83 (bs,1H), MS: m/z 495.2 $(M+H)^+$; M.P. : 203-2005, Yield:77%.

***N*-(3-chlorophenyl)-2-(1-(2-(2-(4-methoxybenzylidene)hydrazinyl)-2-oxoetthyl)-1*H*-benzo[*d*]imidazol-2-ylthio) acetamide (7F)**

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1676(–C=O, aryl), 3108, 3064 (C–H stretching, aromatic ring),1441, 1166(C=C stretching,aromatic ring),735(-C-H bending, aromatic),776(C-Cl). ^{1}HNMR 400MHz, DMSO-d6): δ= 3.86(s,3H), 4.31(s,2H), 5.49(s,2H), 7.03(d,2H)7.10-7.17(m, 3H),7. 28(dd, 1H),7.39-7.50 (m,3H), 7.77(d,2H), 8.03(s,1H), 10.55(s,1H) 11.80 (bs,1H), MS: m/z 508.1 $(M+H)^+$; M.P. : 185-187, Yield: 77%.

***N*-(3-chlorophenyl)-2-(1-(2-oxo-2-(2-(4-propoxybenzylidene)hydrazinyl)ethyl)-1*H*-benzo[*d*]imidazol-2-ylthio) acetamide (7G)**

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}:1678(–C=O, aryl), 3110, 3065 (C–H stretching, aromatic ring),1442, 1167(C=C, aromatic ring stretching),737(-C-H, bending ,aromatic),776(C-Cl). ^{1}HNMR (400MHz,DMSO-d6):δ= 0.9(t,3H), 1.74(m,2H), 3.86(s,3H), 4.02(t,2H), 4.31(s,2H), 5.47 (s,2H), 7.01(d,2H), 7.09-7.16(m,3H), 7.26(dd,1H), 7.37-7.49(m,3H), 7.75(d,,2H), 8.03(s,1H) 10.56(s,1H), 11.81(bs,1H), MS: m/z 550.2 $(M+H)^+$; M.P. : 189-191, Yield:72%.

***N*-(3-chlorophenyl)-2-(1-(2-oxo-2-(2-(thiophen-2-ylmethylene)hydrazinyl)ethyl)-1*H*-benzo[*d*]imidazol-2-ylthio) acetamide (7H)**

This compound was prepared and purified as per the above mentioned procedure. IR (KBr) Cm^{-1}: 1680(–C=O, aryl), 3115, 3044 (C–H stretching, aromatic ring),1432, 1161(C=C, aromatic ring stretching),732(-C-H, bending ,aromatic),772(C-Cl).,^{1}HNMR (300MHz, DMSO-d6): δ=4.30 (s, 2H), 5.39 (s, 2H),7.11-7.19(m,4H), 7.319(dd,1H), 7.41-7.67(m,5H), 7.78(s,1H) ,10.67(s,1H),11.86(bs,1H), MS: m/z 484.1 $(M+H)^+$; M.P. : 205-207, Yield: 71%.

Antimicrobial activity

All the synthesized compounds **3(A-L)** & **7(A-H)** were tested in vitro for their antibacterial and antifungal activity. All the glass apparatus used were sterilized before use. The broth dilution technique was used to determine the minimum inhibitory concentration (MIC) of the synthesized compounds. Bacterial strain of *Staphylococcus aureus* (MTCC737) , *Bacillus megaterium* (MTCC2444) as a gram positive, Escherichia coli (MTCC1687) *Pseudomonas aeruginosa* (MTCC3541) as a gram negative used in a present study. Fungal strains of *Aspergillus niger* (MTCC282) and *Aspergillus flavus* (MTCC418) were taken. DMSO was used as the solvent for the compounds. A blank test was carried out to check the antimicrobial activity of DMSO. ampicillin, streptomycin were used as the standard drugs for antibacterial activity and nystatin was used as the standard drug for antifungal activity.

RESULTS AND DISCUSSION

As per reported process We synthesized 2-(1H-benzo[d]imidazol-2-ylthio)-3-(subsitutedphenyl)-1-(subsitutedphenyl) prop-2-en-1-one **3(A-L)** and *N*-(3-chlorophenyl)-2-(1-(2-hydrazinyl-2-oxoethyl)-1*H*-benzo[*d*]

imidazol-2-ylthio)acetamide **7(A-H)** derivatives. All the synthesized compounds were subjected for their antimicrobial evaluation.

The MIC values (µg/ML) of **3(A-L), 7(A-H)** standard drugs against selected microbes are presented in **Table-1&2.** Microbial activities data of **3(A-L)** and **7(A-H)** revealed that, compound **3B** has been found to be quite active (62.5 µg/ML) against bacterial strains *Bacillus megaterium, Staphylococcus aureus* and fungal strain *Aspergillus flavus* with respect to standard drug ampicillin (100 µg/ML) and nystatin (100µg/ML). It also showed good antibacterial (62.5 µg/ML) and antifungal activity (125 µg/ML) against *Pseudomonas aeruginosa* and *Aspergillus niger* with respect to standard drug Streptomycin (50 µg/ML) and Nystatin (100µg/ML).whereas compound **3A** showed good antibacterial activity (62.5 µg/ML) against *Escherichia coli, Pseudomonas aeruginosa* and moderate activity (125µg/ML) against *Bacillus megaterium, Staphylococcus aureus* as compared to standard drug Streptomycin (50 µg/ML) and Ampicillin (100 µg/ML). Compound **3C** has shown good antibacterial and antifungal activities (125µg/ML) against *Bacillus megaterium, Staphylococcus aureus* and *Aspergillus niger.* Compound **3C** also exhibited mild antibacterial (125µg/ML) and antifungul (250µg/ML) activities against *Escherichia coli, Pseudomonas aeruginosa* and *Aspergillus flavus* with respect to standard drug streptomycin (50 µg/ML) and Nystatin (100µg/ML).On the other hand compound **3I** has been found mild active (250µg/ML, 125µg/ML) again bacterial strain *Bacillus megaterium, Staphylococcus aureus and Pseudomonas aeruginosa* only.

Whereas compound **7C** has been found to be mild active (250µg/ML) against bacterial strain *Bacillus megaterium* and fungal strain *Aspergillus niger.* Compounds **7F** and **7G** have bound to be mild active (250µg/ML) against bacterial strain *Bacillus megaterium* and *Staphylococcus aureus* respectively. The rest of the synthesized compounds were not much active towards either bacterial strains or fungal strains.

Table-1The minimum inhibitory concentration value of 3(A-L)

Compounds	*Bacillus megaterium*	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Aspergillus niger*	*Aspergillus flavus*
Streptomycin			50	50		
Ampicillin	100	100				
Nystatin					100	100
3A	125	125	62.5	62.5	1000	125
3B	62.5	62.5	125	62.5	125	62.5
3C	125	125	125	125	125	250
3D	250	250	250	250	500	250
3E	500	500	500	250	1000	500
3F	500	500	500	500	500	500
3G	500	500	500	250	1000	500
3H	500	500	500	500	500	500
3I	250	250	500	125	1000	1000
3J	1000	500	1000	1000	500	1000
3K	1000	1000	1000	1000	1000	1000
3L	500	500	500	500	1000	500

Table-2 The minimum inhibitory concentration value of 7(A-H)

Compounds	*Bacillus megaterium*	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Aspergillus niger*	*Aspergillus flavus*
Streptomycin			50	50		
Ampicillin	100	100				
Nystatin					100	100
7A	1000	1000	1000	1000	1000	500
7B	1000	1000	1000	1000	1000	1000
7C	250	500	250	250	250	500
7D	500	1000	500	1000	500	1000
7E	1000	1000	1000	1000	1000	1000
7F	250	500	500	500	500	500
7G	500	250	250	250	500	500
7H	500	500	250	250	500	500

CONCLUSION

Chalcones (α, β-unsaturated ketone) have displayed a wide spectrum of pharmacological activities. Modification in their structure has leaded a high degree of diversity that has proven useful for the development of new medicinal agents having improved potency and lesser toxicity. In a view to getting better therapeutic agents, it was planned to synthesize various chalcone derivatives clubbed with another therapeutically useful benzimidazole nucleus.

Schiff's bases containing heterocyclic scaffolds have been known to possess a wide range of biological and pharmacological activities for a long time and gained significant interest in the area of drug research and development. Taking in view the biological importance of Schiff's base, we have incorporated this Schiff's base with other therapeutically useful heterocyclic scaffold 2-mercaptobenzimidazol. The microbial studies showed that synthesized compounds **3(A-L) & 7(A-H)** were not as much active towards bacterial and fungal trains as we expected.

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