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Research Article

EVALUATION AND CHARACTERISATION OF ANTIBACTERIAL POTENTIAL OF NOVEL SCHIFF BASES OF BENZIMIDAZOLE

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ABSTRACT

It is a great challenge for a chemist to develop a novel antibiotic because of microbial resistance. Benzimidazole is an important class of heterocyclic compounds which possess good antimicrobial activity. This convinced us to synthesise some novel antimicrobial agents having benzimidazole nucleus. According to earlier investigation, Schiff base also possess very good antimicrobial activity. In this research, work we have synthesized various Schiff bases of benzimidazole. *o*-phenylenediamine reacted with substituted benzoic acid to form of 2-phenyl substituted benzimidazole, which upon reaction with ethylchloroacetate produce ethyl-2-(2-phenyl-1*H*-benzimidazole-1-yl)acetate. This was further treated with hydrazine hydrate in the presence of ethanol to form 2-(2-phenyl benzimidazol-1-yl)acetohydrazide. Finally, aromatic aldehydes were reacted with synthesized acetohydrazide to give Schiff bases of benzimidazole. The purity of synthesized derivatives were checked with thin layer chromatography and structure of compounds were elucidated using IR, ^{1}HNMR and mass spectrometry. Cup and plate method were used to check the *in vitro* antibacterial activity using Gram positive (*S. aureus* and *B. subtilis*) and Gram-negative strains (*E. coli* and *P. aeruginosa*) bacteria. All the synthesized Schiff bases of benzimidazoles showed moderate to strong activity against the above-mentioned microbes. Maximum antibacterial activity shown by compounds JA-3.1, JA-3.2, AG-3.1, AG-3.2, AR-3.1 and AR-3.2 as compared to the standard ciprofloxacin.

Keywords: Benzimidazole, Schiff Base, Hydrazone, Antimicrobial, Antibacterial

INTRODUCTION

Infectious disease caused by microorganisms is one of the most common reason for illness and death in developing countries. In 20th century, development of new and effective antibiotic reduced the threat of infectious diseases. Development of resistant to antimicrobial agents by microbes worsen the condition worldwide[1]. Due to this serious problem, 'the theme of World Health Day 2011, Antimicrobial resistance: no action today, no cure tomorrow' was adopted. Now a day's chemist focused on development of new antimicrobial agents which will resolve the resistant issue to produce good anti-infective agents[2–5]. Azole fused with benzene ring, such as benzimidazoles and benzoxazole containing 2 or 3 hetero atoms possess various medicinal properties[6-20].

It is reported that benzimidazole is an important class of heterocyclic compound which are associated with various pharmacological activities e.g: antioxidant[21], anticancer[22], anthelmintic[23], antihypertensive[24], antiviral[25], anti-inflammatory[26], antihistaminic[27], analgesic[28], antiprotozoal[29], antiulcer[30], anticoagulant[31], anticonvulsant[32], antifungal[33], antihepatitis B Virus[34], and antibacterial activity[35].

Schiff base is obtained by reacting carbonyl compounds with primary amines[38-40]. These compounds have broader spectrum of activity in medicinal and pharmaceutical fields like antitubercular, anti-inflammatory, analgesic, anticonvulsant, anticancer[41], antioxidant, anthelmintic[42], and antimicrobial[43]. It may believe that Schiff base inhibit bacterial cell growth by interacting with the cell constituents[44,45]. Nitrofurantoin, furazolidone, furacilin, nitrofurazone, ftivazide, nifuroxazide are some of the drugs which contain Schiff base and have antibacterial activity[46-48].

Literature study shows that both benzimidazole and Schiff base possess antimicrobial activity. In present work, attempt was made to join both pharmacophores to produce novel and effective antibacterial agents. *In vitro* antibacterial activity of synthesized derivatives was determined by Cup and plate method against gram-negative (*E. coli* and *P. aeruginosa*) and gram positive (S. *aureus* and *B. substilis*) bacteria.

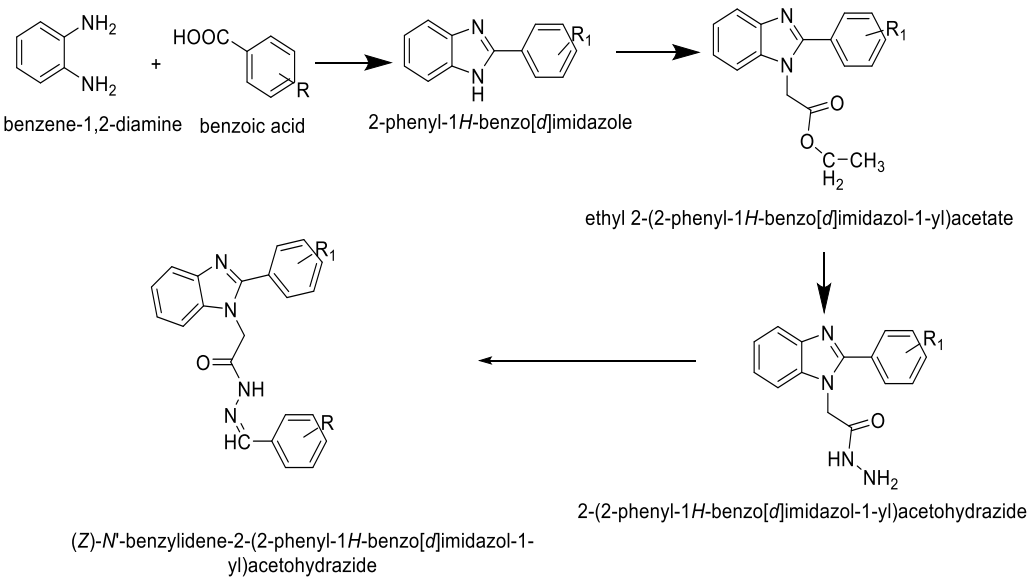
MATERIALS AND METHODS

Chemistry

The chemical used for synthesis of Schiff base of benzimidazole were purchased from Mumbai, Loba Chemie Pvt. Ltd., Mumbai, India, Merck, Electron LLS India Pvt. Ltd., Qualikems Fine Chem Pvt. Ltd. Vadodara, India. and Thermo Electron LLS India Pvt. Ltd. Mumbai.

Digital melting point apparatus (Popular, India) was used to determine the melting point by open capillary method. Shimadzu 8400 FTIR was used to scan IR spectra of the samples using pellets of Potassium Bromide (KBr). Bruker Avance II 400 NMR spectrometer was used to record ^{1}H-NMR spectra. Waters Q-Tof micromass spectrometer was used to record Mass spectra. The elements like C, H and N were analysed using Thermo Flash 2000 analyser. The progress of reaction was monitored through Thin Layer Chromatography (TLC) analysis using pre-coated aluminium plates (Silica gel 60 F254 Merck-Germany).

Synthetic Strategy



Scheme: Synthesis of Schiff base of benzimidazole derivatives.

General Procedure

An equimolar quantity of o-phenylenediamine reacted with substituted benzoic acid in the presence of polyphosphoric acid to form 2-phenyl substituted benzimidazole, which on reaction with ethylchloroacetate and potassium carbonate solution in dry acetone produced ethyl-2-(2-phenyl-1H-benzimidazole-1-yl)acetate. The later was mixed with hydrazine hydrate using ethanol as solvent to form 2-(2-phenyl benzimidazol-1-yl)acetohydrazide. The final product as Schiff base was produced by condensing hydrazide produced in above reaction with substituted aromatic aldehydes.

EXPERIMENTAL

2-Phenyl Benzimidazole (JA): FT-IR (KBr, cm^{-1}): 3404(N-H str), 3047 (=C-H str), 1664 (C=N), 1589 and 1464 (C=C str), 1276 (C-N str) ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.61(d, 2H, benzene), 7.5 (t, 2H, benzene), 7.4 (t, 1H, benzene), 8.21(d, 2H, benzene), 7.45 (t, 2H, benzene), 12.8 ((s, 1H, NH), ES-MS (m/z): 194 [M+1]; Anal. for $C_{13}H_{10}N_2$: C;80.39, H;5.19, N; 14.49.

Ethyl-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetate (JA-1): FT-IR (KBr, cm^{-1}): 3047 (=C-H str), 2966 (C-H str), 1772 (C=O str), 1683 (C=N str), 1622 and 1462 (C=C str), 1276 (C-N str), 1226 (C-O-C str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.62(d, 2H, benzene), 7.49 (t, 2H, benzene), 7.39 (t, 1H, benzene), 8.23(d, 2H, benzene), 7.47 (t, 2H, benzene), 4.7 ((s, 2H, $-CH_2$), 4.3(q, 2H, $-CH_2$), 2.0 (t, 3H, $-CH_3$), ES-MS (m/z): 280 [M+1]; Anal. for $C_{17}H_{16}N_2O_2$: C;72.84, H;5.75, N; 9.99, O; 11.41.

2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-2): FT-IR (KBr, cm^{-1}): 3479 and 3416 (N-H Str), 3047 (=C-H str), 2986 (C-H str), 1637(C=N str), 1618 (C=O str). 1591 and 1475 (C=C str), 1541(N-H bend), 1276 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.61(d, 2H, benzene), 7.50 (t, 2H, benzene), 7.40 (t, 1H, benzene), 8.22(d, 2H, benzene), 7.48 (t, 2H, benzene), 4.7 (s, 2H, $-CH_2$), 9.15(t, 1H, -Sec NH), 2.15 (d, 2H, $-NH_2$), ES-MS (m/z): 266 [M+1]; Anal. for $C_{15}H_{14}N_4O$: C;67.65, H;5.30, N; 21.04, O; 6.01.

N'-benzylidine-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3): FT-IR (KBr, cm^{-1}): 3117 (N-H Str), 3047 (=C-H str), 2918 (C-H str), 1668 (C=O str), 1622 (C=N str), 1591 and 1460 (C=C str), 1274 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.62 (d, 2H, benzene), 7.49 (t, 2H, benzene), 7.41 (t, 1H, benzene), 8.20 (d, 2H, benzene), 7.45 (t, 2H, benzene), 4.6 (s, 2H, $-CH_2$), 8.11(t, 1H, -Sec NH), 8.35 (s, 1H, CH), 6.7 – 7.1 (m, 5H, benzene), ES-MS (m/z): 354 [M+1]; Anal. for $C_{22}H_{18}N_4O$: C;74.56, H;5.12, N; 15.81, O; 4.51.

N'-(3-chlorobenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide(JA-3.1): FT-IR (KBr, cm^{-1}): 3159 (N-H Str), 3047 (=C-H str), 2918 (C-H str), 1665 (C=O str), 1699(C=N str), 1626 and 1464 (C=C str), 1276 (C-N str), 985 (C-Cl bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.61 (d, 2H, benzene), 7.49 (t, 2H, benzene), 7.42 (t, 1H, benzene), 8.22 (d, 2H, benzene), 7.46 (t, 2H, benzene), 4.7 (s, 2H, $-CH_2$), 8.11(t, 1H, -Sec NH), 8.24 (s, 1H, CH), 7.85 (s, 1H, Aromatic CH), 7.55 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.20 (d, 1H, Aromatic CH) ES-MS (m/z): 388 [M+1]; Anal. for $C_{22}H_{17}ClN_4O$: C; 67.95, H;4.41, Cl; 9.12, N; 14.41, O; 4.11.

N'-(4-chlorobenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3.2): FT-IR (KBr, cm^{-1}): 3150 (N-H Str), 3047 (=C-H str), 2922 (C-H str), 1661 (C=O str), 1695(C=N str), 1623 and 1460 (C=C str), 1275 (C-N str), 990 (C-Cl bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.6 (d, 2H, benzene), 7.48 (t, 2H, benzene), 7.41 (t, 1H, benzene), 8.21 (d, 2H, benzene), 7.44 (t, 2H, benzene), 4.8 (s, 2H, $-CH_2$), 8.11(t, 1H, -Sec NH), 8.24 (s, 1H, CH), 7.8 (d, 2H, Aromatic CH), 7.52 (d, 2H, Aromatic CH), ES-MS (m/z): 388 [M+1]; Anal. for $C_{22}H_{17}ClN_4O$: C; 67.95, H;4.41, Cl; 9.12, N; 14.41, O; 4.11.

N'-(2-hydroxybenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3.3): FT-IR (KBr, cm^{-1}): 3243 (-OH broad band), 3047 (=C-H str), 2918 (C-H str), 1666 (C=O str), 1699 (C=N str), 1622 and 1462 (C=C str), 1274 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.6 (d, 2H, benzene), 7.49 (t, 2H, benzene), 7.41 (t, 1H, benzene), 8.21 (d, 2H, benzene), 7.43 (t, 2H, benzene), 4.75 (s, 2H, $-CH_2$), 8.11 (s, 1H, -Sec NH), 8.24 (s, 1H, CH), 10.8 (s, 1H, OH), 7.55 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.18 (t, 1H, Aromatic CH), 7.58 (d, 1H, Aromatic CH), ES-MS (m/z): 370 [M+1]; Anal. for $C_{22}H_{18}N_4O_2$: C;71.74, H;4.90, N; 15.13, O; 8.64.

N'-(3-hydroxybenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3.4): FT-IR (KBr, cm^{-1}): 3248 (-OH broad band), 3045 (=C-H str), 2920 (C-H str), 1652 (C=O str), 1696 (C=N str), 1620 and 1460 (C=C str), 1270 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.61 (d, 2H, benzene), 7.48 (t, 2H, benzene), 7.42 (t, 1H, benzene), 8.21 (d, 2H, benzene), 7.45 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.10 (s, 1H, -Sec NH), 8.24 (s, 1H, CH), 10.8 (s, 1H, OH), 7.85 (s, 1H, Aromatic CH), 7.54 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.20 (d, 1H, Aromatic CH), ES-MS (m/z): 370 [M+1]; Anal. for $C_{22}H_{18}N_4O_2$: C;71.74, H;4.90, N; 15.13, O; 8.64.

N'-(4-hydroxybenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3.5): FT-IR (KBr, cm^{-1}): 3252 (-OH broad band), 3045 (=C-H str), 2917 (C-H str), 1655 (C=O str), 1698 (C=N str), 1624 and 1464 (C=C str), 1271 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.6 (d, 2H, benzene), 7.48 (t, 2H, benzene), 7.4 (t, 1H, benzene), 8.2 (d, 2H, benzene), 7.43 (t, 2H, benzene), 4.8 (s, 2H, -CH_2), 8.12 (s, 1H, -Sec NH), 8.23 (s, 1H, CH), 10.81 (s, 1H, OH), 7.81 (d, 2H, Aromatic CH), 7.52 (d, 2H, Aromatic CH), ES-MS (m/z): 370 [M+1]; Anal. for $C_{22}H_{18}N_4O_2$: C;71.74, H;4.90, N; 15.13, O; 8.64.

N'-(3-Nitrobenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3.6): FT-IR (KBr, cm^{-1}): 3140 (N-H Str), 3030 (=C-H str), 2925 (C-H str), 1664 (C=O str), 1694 (C=N str), 1590 and 1465 (C=C str), 1270 (C-N str), 1545 and 1348 (N=O bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.6 (d, 2H, benzene), 7.48 (t, 2H, benzene), 7.43 (t, 1H, benzene), 8.2 (d, 2H, benzene), 7.54 (t, 2H, benzene), 4.7 (s, 2H, -CH_2), 8.10 (s, 1H, -Sec NH), 8.24 (s, 1H, CH), 7.85 (d, 1H, Aromatic CH), 7.54 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.2 (d, 1H, Aromatic CH), ES-MS (m/z): 399 [M+1]; Anal. for $C_{22}H_{17}N_5O_3$: C; 66.16, H;4.29, N; 17.53, O; 12.02.

N'-(4-nitrobenzylidine)-2-(2-phenyl-1H-benzo[d]imidazole-1-yl)acetohydrazide (JA-3.7): FT-IR (KBr, cm^{-1}): 3142 (N-H Str), 3028 (=C-H str), 2928 (C-H str), 1667 (C=O str), 1695 (C=N str), 1592 and 1468 (C=C str), 1275 (C-N str), 1542 and 1350 (N=O bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.6 (d, 2H, benzene), 7.47 (t, 2H, benzene), 7.4 (t, 1H, benzene), 8.2 (d, 2H, benzene), 7.44 (t, 2H, benzene), 4.80 (s, 2H, -CH_2), 8.11 (s, 1H, -Sec NH), 8.23 (s, 1H, CH), 7.82 (d, 2H, Aromatic CH), 7.52 (d, 2H, Aromatic CH), ES-MS (m/z): 399 [M+1]; Anal. for $C_{22}H_{17}N_5O_3$: C; 66.16, H;4.29, N; 17.53, O; 12.02.

2-(4-chlorophenyl) Benzimidazole (AG) : FT-IR (KBr, cm^{-1}): 3410(N-H str), 3040 (=C-H str), 1665 (C=N), 1590 and 1460 (C=C str), 1274 (C-N str), 995 (C-Cl str) ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.50 (d, 2H, benzene), 7.2 (d, 2H, benzene), 7.25 (t, 2H, benzene), 12.5 (s, 1H, NH), ES-MS (m/z): 288 [M+1]; Anal. for $C_{13}H_9ClN_2$: C; 68.28, H;3.97, Cl; 15.50, N; 12.25.

Ethyl-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetate (AG-1): FT-IR (KBr, cm^{-1}): 3045 (=C-H str), 2960 (C-H Str), 1770 (C=O str), 1680 (C=N), 1620 and 1460 (C=C str), 1275 (C-N str), 1222 (C-O-C str), 993 (C-Cl str) ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.51 (d, 2H, benzene), 7.21 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 4.2 (q, 2H, -CH_2), 2.0 (t, 3H, -CH_3), ES-MS (m/z): 314 [M+1]; Anal. for $C_{17}H_{15}ClN_2O_2$: C; 64.87, H;4.80, Cl;11.26, N; 8.90, O;10.17.

2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AG-2) : FT-IR (KBr, cm^{-1}):3475 (N-H broad band), 3040 (=C-H str), 2983 (C-H Str), 1620 (C=O str), 1683 (C=N), 1590 and 1473 (C=C str),1540 (N-H bend), 1275 (C-N str), 992 (C-Cl str) ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.50 (d, 2H, benzene), 7.20 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (t, 1H, Sec NH), 2.2 (d, 2H, -NH_2), ES-MS (m/z): 300 [M+1]; Anal. for $C_{15}H_{13}ClN_4O$: C; 59.91, H;4.36, Cl;11.79, N; 18.63, O;5.32.

N'-benzylidine-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AG-3): FT-IR (KBr, cm^{-1}):3118 (N-H broad band), 3048 (=C-H str), 2920 (C-H Str), 1670 (C=O str), 1620 (C=N), 1590 and 1461 (C=C str), 1275 (C-N str), 990 (C-Cl str) ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.51 (d, 2H, benzene), 7.21 (d, 2H, benzene), 7.26 (t, 2H, benzene), 4.69 (s, 2H, -CH_2), 8.15 (t, 1H, Sec NH), 8.41(s, 1H, -CH), 6.80 - 7.15 (m, 5H, benzene) ES-MS (m/z): 388 [M+1]; Anal. for $C_{22}H_{17}ClN_4O$: C; 67.95, H;4.41, Cl; 9.12, N; 14.41, O; 4.11.

N'-(3-chlorobenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydraz -ide (AG-3.1): FT-IR (KBr, cm^{-1}):3157 (N-H broad band), 3049 (=C-H str), 2964 (C-H Str), 1655 (C=O str), 1699 (C=N), 1625 and 1465 (C=C str), 1275 (C-N str), 985 (C-Cl str) ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.51 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.15 (t, 1H, Sec NH), 8.41(s, 1H, -CH), 7.85 (s, 1H, Aromatic CH), 7.55 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.20 (d, 1H, Aromatic CH) ES-MS (m/z): 422 [M+1]; Anal. for $C_{22}H_{16}Cl_2N_4O$: C; 62.42, H;3.81, Cl; 16.75, N; 13.24, O; 3.78.

N'-(4-chlorobenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydraz -ide (AG-3.2): FT-IR (KBr, cm^{-1}):3155 (N-H broad band), 3048 (=C-H str), 2965 (C-H Str), 1657 (C=O str), 1697 (C=N), 1627 and 1465 (C=C str), 1278 (C-N str), 983 (C-Cl str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.50 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (t, 1H, Sec NH), 8.40 (s, 1H, CH), 7.53 (d, 2H, Aromatic CH), 7.8 (d, 2H, Aromatic CH), ES-MS (m/z): 422 [M+1]; Anal. for $C_{22}H_{16}Cl_2N_4O$: C; 62.42, H;3.81, Cl; 16.75, N; 13.24, O; 3.78.

N'-(2-hydroxybenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydra -zide (AG-3.3): FT-IR (KBr, cm^{-1}): 3280 (-OH broad band), 3070 (=C-H str), 2955 (C-H str), 1655 (C=O str), 1695 (C=N str), 1625 and 1464 (C=C str), 1275 (C-N str), 987 (C-Cl str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.21 (d, 2H, benzene), 7.51 (d, 2H, benzene), 7.22 (d, 1H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.15 (s, 1H, -Sec NH), 8.41 (s, 1H, CH), 10.8 (s, 1H, OH), 7.55 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.18 (t, 1H, Aromatic CH), 7.58 (d, 1H, Aromatic CH), ES-MS (m/z): 404 [M+1]; Anal. for $C_{22}H_{17}ClN_4O_2$: C; 65.27, H; 4.23, Cl; 8.76, N; 13.84, O; 7.90.

N'-(3-hydroxybenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydra -zide (AG-3.4 FT-IR (KBr, cm^{-1}): 3284 (-OH broad band), 3071 (=C-H str), 2952 (C-H str), 1657 (C=O str), 1697 (C=N str), 1626 and 1465 (C=C str), 1277 (C-N str), 986 (C-Cl str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.22 (d, 2H, benzene), 7.5 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.70 (s, 2H, -CH_2), 8.16 (s, 1H, -Sec NH), 8.4 (s, 1H, CH), 10.8 (s, 1H, OH), 7.85 (s, 1H, Aromatic CH), 7.54 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.2 (d, 1H, Aromatic CH), ES-MS (m/z): 404 [M+1]; Anal. for $C_{22}H_{17}ClN_4O_2$: C; 65.27, H; 4.23, Cl; 8.76, N; 13.84, O; 7.90.

N'-(4-hydroxybenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydra -zide (AG-3.5): FT-IR (KBr, cm^{-1}): 3285 (-OH broad band), 3073 (=C-H str), 2955 (C-H str), 1655 (C=O str), 1695 (C=N str), 1625 and 1465 (C=C str), 1275 (C-N str), 985 (C-Cl str), ^{1}H-NMR (400MHz, $CDCl_3$ δ

ppm): 8.22 (d, 2H, benzene), 7.50 (d, 2H, benzene), 7.21 (d, 1H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.40 (s, 1H, CH), 10.81 (s, 1H, OH), 7.54 (d, 2H, Aromatic CH), 7.81 (d, 2H, Aromatic CH), ES-MS (m/z): 404 [M+1]; Anal. for $C_{22}H_{17}ClN_4O_2$: C; 65.27, H; 4.23, Cl; 8.76, N; 13.84, O; 7.90.

N'-(3-nitrobenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazid -e (AG-3.6): FT-IR (KBr, cm^{-1}): 3140 (N-H Str), 3030 (=C-H str), 2930 (C-H str), 1664 (C=O str), 1690 (C=N str), 1590 and 1468 (C=C str), 1270 (C-N str), 1543 and 1350 (N=O bend), 983 (C-Cl str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.21 (d, 2H, benzene), 7.51 (d, 2H, benzene), 7.23 (d, 2H, benzene), 7.26 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.41 (s, 1H, CH), 7.85 (d, 1H, Aromatic CH), 7.55 (d, 1H, Aromatic CH), 7.32 (t, 1H, Aromatic CH), 7.21 (d, 1H, Aromatic CH), ES-MS (m/z): 433 [M+1]; Anal. for $C_{22}H_{16}ClN_5O_3$: C;60.91, H; 3.72, Cl; 8.17, N; 16.14, O;11.06.

N'-(4-nitrobenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazi -de (AG-3.7): FT-IR (KBr, cm^{-1}): 3142 (N-H Str), 3031 (=C-H str), 2932 (C-H str), 1665 (C=O str), 1692 (C=N str), 1592 and 1467 (C=C str), 1272 (C-N str), 1542 and 1350 (N=O bend), 983 (C-Cl str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 8.21 (d, 2H, benzene), 7.51 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.26 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.40 (s, 1H, CH), 7.54 (d, 2H, Aromatic CH), 7.81 (d, 2H, Aromatic CH), ES-MS (m/z): 433 [M+1]; Anal. for $C_{22}H_{16}ClN_5O_3$: C;60.91, H; 3.72, Cl; 8.17, N; 16.14, O;11.06.

2-(4-nitrophenyl) Benzimidazole (AR): FT-IR (KBr, cm^{-1}): 3412 (N-H str), 3045 (=C-H str), 1663 (C=N), 1592 and 1462 (C=C str), 1275 (C-N str), 1542 and 1350 (N=O Bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.22 (d, 2H, benzene), 7.21 (d, 2H, benzene), 7.25 (t, 2H, benzene), 12.2 (s, 1H, NH), ES-MS (m/z): 239 [M+1]; Anal. for $C_{13}H_9N_3O_2$: C;65.27, H; 3.79, N; 17.56, O;13.38.

Ethyl-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetate (AR-1) : FT-IR (KBr, cm^{-1}): 3045 (=C-H str), 2961 (C-H Str), 1772 (C=O str), 1681 (C=N), 1622 and 1462 (C=C str), 1540 and 1351 (N=O Bend), 1273 (C-N str), 1220 (C-O-C str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.81 (d, 2H, benzene), 8.21 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.26 (t, 2H, benzene), 4.70 (s, 2H, -CH_2), 4.21 (q, 2H, -CH_2), 2.0 (t, 3H, -CH_3), ES-MS (m/z): 325 [M+1]; Anal. for C;65.27, H; 3.79, N; 17.56, O;13.38: C;62.76, H; 4.65, N; 12.92, O;19.67.

2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-2): FT-IR (KBr, cm^{-1}):3473 (N-H broad band), 3045 (=C-H str), 2985 (C-H Str), 1625 (C=O str), 1637 (C=N), 1592 and 1475 (C=C str), 1544 (N-H bend), 1542 and 1350 (N=O Bend), 1276 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.21 (d, 2H, benzene), 7.21 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.7 (s, 2H, -CH_2), 8.14 (t, 1H, Sec NH), 3.57 (d, 2H, -NH_2), ES-MS (m/z): 311 [M+1]; Anal. for $C_{15}H_{13}N_5O_3$: C;57.87, H; 4.21, N; 22.50, O;15.42.

N'-benzylidine-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-3): FT-IR (KBr, cm^{-1}):3120 (N-H broad band), 3050 (=C-H str), 2922 (C-H Str), 1672 (C=O str), 1623 (C=N), 1591 and 1460 (C=C str), 1540 and 1352 (N=O Bend), 1278 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.83 (d, 2H, benzene), 8.22 (d, 2H, benzene), 7.20 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.14 (t, 1H, Sec NH), 8.40 (s, 1H, -CH), 6.75 – 7.15 (m, 5H, benzene) ES-MS (m/z): 399 [M+1]; Anal. for $C_{22}H_{17}N_5O_3$: C; 66.16, H;4.29, N; 17.53, O; 12.02.

N'-(3-chlorobenzylidine)-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-3.1): FT-IR (KBr, cm^{-1}):3156 (N-H broad band), 3050 (=C-H str), 2918 (C-H Str), 1657 (C=O str), 1697 (C=N), 1624 and 1464 (C=C str), 1542 and 1354 (N=O Bend), 1274 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.22 (d, 2H, benzene), 7.21 (d, 2H, benzene), 7.26 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.14 (t, 1H, Sec NH), 8.41 (s, 1H, -CH), 7.85 (s, 1H, Aromatic CH), 7.55 (d, 1H, Aromatic CH), 7.31 (t, 1H, Aromatic CH), 7.1 (d, 1H, Aromatic CH) ES-MS (m/z): 433 [M+1]; Anal. for $C_{22}H_{16}ClN_5O_3$: C; 60.91, H; 3.72, Cl; 8.17, N;16.14, O;11.06.

N'-(4-chlorobenzylidine)-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-3.2): FT-IR (KBr, cm^{-1}):3156 (N-H broad band), 3046 (=C-H str), 2918 (C-H Str), 1655 (C=O str), 1699 (C=N), 1625 and 1467 (C=C str), 1543 and 1355 (N=O Bend),1279 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.21 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.14 (t, 1H, Sec NH), 8.40 (s, 1H, CH), 7.54 (d, 2H, Aromatic CH), 7.65 (d, 2H, Aromatic CH), ES-MS (m/z): 433 [M+1]; Anal. for $C_{22}H_{16}ClN_5O_3$: C; 60.91, H; 3.72, Cl; 8.17, N;16.14, O;11.06.

N'-(2-hydroxybenzylidine)-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-3.3): FT-IR (KBr, cm^{-1}): 3280 (-OH broad band), 3075 (=C-H str), 2952 (C-H str), 1657 (C=O str), 1694 (C=N str), 1627 and 1465 (C=C str), 1544 and 1357 (N=O Bend), 1276 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.81 (d, 2H, benzene), 8.21 (d, 2H, benzene), 7.22 (d, 1H, benzene), 7.25 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.41 (s, 1H, CH), 10.81 (s, 1H, OH), 7.55 (d, 1H, Aromatic CH), 7.33 (t, 1H, Aromatic CH), 7.17 (t, 1H, Aromatic CH), 7.59 (d, 1H, Aromatic CH), ES-MS (m/z): 415 [M+1]; Anal. for $C_{22}H_{17}N_5O_4$: C; 63.61, H; 4.13, N; 16.86, O;15.41.

N'-(3-hydroxybenzylidine)-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-3.4): FT-IR (KBr, cm^{-1}): 3282 (-OH broad band), 3072 (=C-H str), 2954 (C-H str), 1655 (C=O str), 1699 (C=N str), 1627 and 1466 (C=C str), 1545 and 1360 (N=O Bend), 1228 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.22 (d, 2H, benzene), 7.21 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.40 (s, 1H, CH), 10.81 (s, 1H, OH), 7.85 (s, 1H, Aromatic CH), 7.55 (d, 1H, Aromatic CH), 7.33 (t, 1H, Aromatic CH), 7.14 (d, 1H, Aromatic CH), ES-MS (m/z): 415 [M+1]; Anal. for $C_{22}H_{17}N_5O_4$: C; 63.61, H; 4.13, N; 16.86, O;15.41.

N'-(4-hydroxybenzylidine)-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydraz -ide (AR-3.5): FT-IR (KBr, cm^{-1}): 3285 (-OH broad band), 3073 (=C-H str), 2957 (C-H str), 1657 (C=O str), 1697 (C=N str), 1627 and 1467 (C=C str), 1546 and 1357 (N=O Bend), 1228 (C-N str), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.83 (d, 2H, benzene), 8.22 (d, 2H, benzene), 7.21 (d, 1H, benzene), 7.25 (t, 2H, benzene), 4.71 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.41 (s, 1H, CH), 10.81 (s, 1H, OH), 7.55 (d, 2H, Aromatic CH), 7.81 (d, 2H, Aromatic CH), ES-MS (m/z): 415 [M+1]; Anal. for $C_{22}H_{17}N_5O_4$: C; 63.61, H; 4.13, N; 16.86, O;15.41.

N'-(3-nitrobenzylidine)-2-[2-(4-nitrophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazide (AR-3.6): FT-IR (KBr, cm^{-1}): 3142 (N-H Str), 3033 (=C-H str), 2932 (C-H str), 1665 (C=O str), 1689 (C=N str), 1592 and 1469 (C=C str), 1272 (C-N str), 1543 and 1350 (N=O bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.23 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.26 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.40 (s, 1H, CH), 7.85 (d, 1H, Aromatic CH), 7.55 (d, 1H, Aromatic CH), 7.33 (t, 1H, Aromatic CH), 7.15 (d,

1H, Aromatic CH), ES-MS (m/z): 444 [M+1]; Anal. for $C_{22}H_{16}N_6O_5$: C; 59.46, H; 3.63, N; 18.91, O;18.00.

N'-(4-nitrobenzylidine)-2-[2-(4-chlorophenyl)-1H-benzo[d]imidazole-1-yl]acetohydrazi -de (AR-3.7): FT-IR (KBr, cm^{-1}): 3144 (N-H Str), 3034 (=C-H str), 2934 (C-H str), 1667 (C=O str), 1688 (C=N str), 1274 (C-N str), 1594 and 1470 (C=C str), 1544 and 1354 (N=O bend), ^{1}H-NMR (400MHz, $CDCl_3$ δ ppm): 7.82 (d, 2H, benzene), 8.23 (d, 2H, benzene), 7.22 (d, 2H, benzene), 7.25 (t, 2H, benzene), 4.72 (s, 2H, -CH_2), 8.14 (s, 1H, -Sec NH), 8.40 (s, 1H, CH), 7.54 (d, 2H, Aromatic CH), 7.80 (d, 2H, Aromatic CH), ES-MS (m/z): 444 [M+1]; Anal. for $C_{22}H_{16}N_6O_5$: C; 59.46, O;18.00, H; 3.63, N; 18.91.
The physiochemical characterization of synthesized derivatives is given in table 1.

Anti-microbial activity

The anti-bacterial potential of synthesized Schiff bases of benzimidazole were assessed *in vitro* against gram negative *(Escherichia coli, Pseudomonas aeruginosa)* and gram positive (*Staphylococcus aureus, Bacillus subtilis)* with cup plate method[49]. Antibacterial activity of synthesized compounds was checked at three different concentrations (25, 50 and 100 µg/ml). The standard drug used to check antibacterial activity was Ciprofloxacin. Result of antibacterial activity has been detailed in table 2 and comparison of antibacterial activity of synthesized compounds at different concentrations are represented in graph.1,2 and 3.

RESULT AND DISCUSSION

o-phenylenediamine was reacted with substituted benzoic acid in the presence of polyphosphoric acid to produce 2-(Substituted phenyl)-1H-benzimidazole. The synthesized compounds were further reacted with ethylchloroacetate in dry acetone gave ethyl-2-[2-(substituted phenyl)-*1H*- benzimidazol-1-yl]acetate. Then, the later was treated with hydrazine hydrate to form 2-[2-(substituted phenyl)-*1H*- benzimidazol-1-yl]acetohydrazide In the end substituted acetohydrazide were treatment with substituted aldehydes to produce Schiff base of benzimidazole.

Elemental analysis is used to confirm the formula of the synthesised compounds. Structures were confirmed with the help of IR, ^{1}H NMR and ES-MS spectra. In the IR spectra, all the vibrational bands appeared in the expected regions. A single band appeared in the region of 3045-3404 cm^{-1} confirmed the presence of sec. N-H functional group. For ester and amide C=O str. Vibrations were appeared at 1735-1749 and 1610-1620 cm^{-1}. The ^{1}H NMR spectra used to identify the different types of protons in the synthesized derivatives. M+1 peak of the synthesized compounds was in agreement with their molecular formula.

The synthesized Schiff base of benzimidazole showed good antibacterial potential *in vitro* against both Gram negative and Gram-positive bacteria. Among these JA-3.1, JA-3.2, AG-3.1, AG-3.2, AR-3.1, AR-3.2, AR-3.6 and AR-3.7 have better antibacterial activity as compared to standard drug ciprofloxacin. At concentration of 25µg/ml compound A-3.1 shows maximum activity against *S. aureus* (Zone of inhibition 23mm) and AR-3.7 against *E. Coli* (Zone of inhibition 22mm) which better as compared to standard drug (Ciprofloxacin). JA-3.1 and AR-3.1 shows good activity against B. Subtalis (28mm), AR-3.6 against *S. aureus* (Zone of inhibition 28mm), AR-3.7 against *E. Coli and P. aeruginosa* (Zone of inhibition 30 and 29mm) at 50µg/ml. AR-3.1 and AR 3.7 have strongest antibacterial activity against all strains of bacteria at a concentration of 100µg/ml.

Table 1: Physiochemical characteristics JA-3 toJA-3.7, AG-3 to AG-3.7and JA-3 to JA-3.7

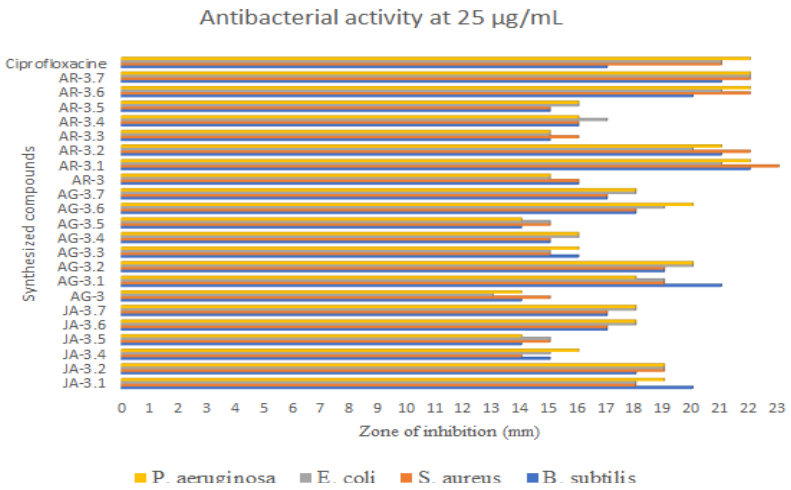
Compound Number	R	R^1	Molecular Formula	Molecular weight	M. P [°C]	R_f [value][a]	Yield (%)
JA	-	-	$C_{13}H_{10}N_2$	194	209-210	0.74	84
JA-1	-	-	$C_{17}H_{16}N_2O_2$	280	240-242	0.82	77
JA-2	-	-	$C_{15}H_{14}N_4O$	266	224-226	0.79	75
JA-3	-H	-H	$C_{22}H_{18}N_4O$	354	294 -296	0.73	80
JA-3.1	-H	-3-Cl	$C_{22}H_{17}ClN_4O$	388	277 -279	0.75	75
JA-3.2	-H	-4-Cl	$C_{22}H_{17}ClN_4O$	388	280 - 282	0.68	76
JA-3.3	-H	-2-OH	$C_{22}H_{18}N_4O_2$	370	276-278	0.78	81
JA-3.4	-H	-3-OH	$C_{22}H_{18}N_4O_2$	370	278- 280	0.77	80
JA-3.5	-H	-4-OH	$C_{22}H_{18}N_4O_2$	370	275 - 277	0.76	82
JA-3.6	-H	-3-NO_2	$C_{22}H_{17}N_5O_3$	399	288 – 290	0.77	78
JA-3.7	-H	-4-NO_2	$C_{22}H_{17}N_5O_3$	399	289 - 291	0.81	74
AG	-4-Cl	-	$C_{13}H_9ClN_2$	288	251-253	0.73	78
AG-1	-4-Cl	-	$C_{17}H_{15}ClN_2O_2$	314	268-270	0.84	79
AG-2	-4-Cl	-	$C_{15}H_{13}ClN_4O$	300	265-266	0.79	80
AG-3	-4-Cl	-H	$C_{22}H_{17}ClN_4O$	388	268 - 270	0.80	76
AG-3.1	-4-Cl	-3-Cl	$C_{22}H_{16}Cl_2N_4O$	422	271 - 272	0.71	81
AG-3.2	-4-Cl	-4-Cl	$C_{22}H_{16}Cl_2N_4O$	422	265 - 267	0.76	80
AG-3.3	-4-Cl	-2-OH	$C_{22}H_{17}ClN_4O_2$	404	284- 286	0.81	72
AG-3.4	-4-Cl	-3-OH	$C_{22}H_{17}ClN_4O_2$	404	265 - 267	0.83	71
AG-3.5	-4-Cl	-4-OH	$C_{22}H_{17}ClN_4O_2$	404	285 - 287	0.77	78
AG-3.6	-4-Cl	-3-NO_2	$C_{22}H_{16}ClN_5O_3$	433	279-280	0.80	74
AG-3.7	-4-Cl	-4-NO_2	$C_{22}H_{16}ClN_5O_3$	433	278 - 279	0.85	78
AR	-4-NO_2	-	$C_{13}H_9N_3O_2$	239	235-237	0.86	80
AR-1	-4-NO_2	-	$C_{17}H_{15}N_3O_4$	325	274-276	0.79	86
AR-2	-4-NO_2	-	$C_{15}H_{13}N_5O_3$	311	266-268	0.75	75
AR-3	-4-NO_2	-H	$C_{22}H_{17}N_5O_3$	399	290 – 292	0.79	76
AR-3.1	-4-NO_2	-3-Cl	$C_{22}H_{16}ClN_5O_3$	433	294 – 295	0.71	72
AR-3.2	-4-NO_2	-4-Cl	$C_{22}H_{16}ClN_5O_3$	433	292-293	0.72	80
AR-3.3	-4-NO_2	-2-OH	$C_{22}H_{17}N_5O_4$	415	281 – 282	0.85	74
AR-3.4	-4-NO_2	-3-OH	$C_{22}H_{17}N_5O_4$	415	283 – 285	0.83	73
AR-3.5	-4-NO_2	-4-OH	$C_{22}H_{17}N_5O_4$	415	275 – 277	0.86	75
AR-3.6	-4-NO_2	-3-NO_2	$C_{22}H_{16}N_6O_5$	444	294 – 295	0.74	76
AR-3.7	-4-NO_2	-4-NO_2	$C_{22}H_{16}N_6O_5$	444	290 - 291	0.72	74

[a]TLC mobile phase: hexane: Ethyl acetate (7.5:2.5)

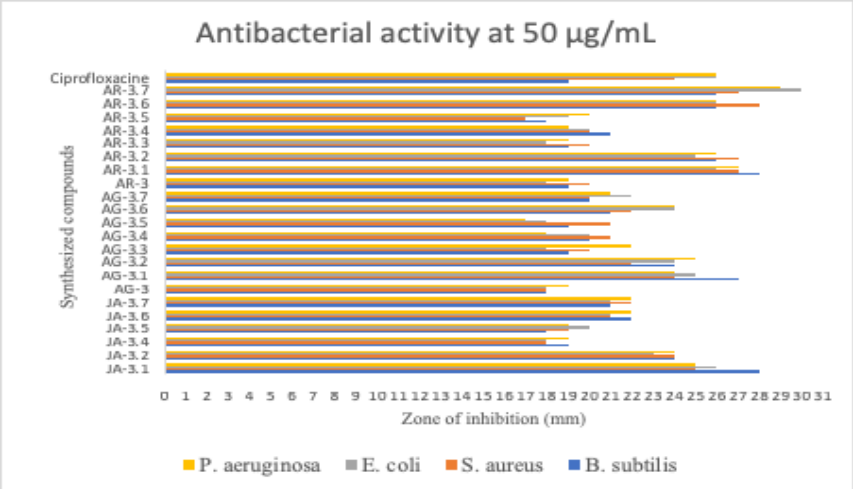
Table 2: Anti-bacterial evaluation of benzimidazole-Schiff base derivatives

Bacterial strain	*B. subtilis*			*S. aureus*			*E. coli*			*P. aeruginosa*		
Conc. (µg/ml)	25	50	100	25	50	100	25	50	100	25	50	100
Compound Number	**Zone of inhibition (mm*)**											
JA-3.1	**20**	**28**	**30**	**18**	**25**	**28**	**18**	**26**	**29**	**19**	**25**	**28**
JA-3.2	**18**	**24**	**27**	**19**	**24**	**28**	**19**	**23**	**26**	**19**	**24**	**27**
JA-3.4	15	19	23	14	18	20	15	18	21	16	19	22
JA-3.5	14	18	21	15	19	22	15	20	23	14	19	22
JA-3.6	17	22	24	17	21	24	18	21	23	18	22	24
JA-3.7	17	21	25	17	22	24	18	21	23	18	22	25
AG-3	14	18	20	15	18	21	13	18	20	14	19	21
AG-3.1	**21**	**27**	**29**	**19**	**24**	**26**	**19**	**25**	**27**	**18**	**24**	**27**
AG-3.2	**19**	**24**	**27**	**19**	**22**	**24**	**20**	**24**	**28**	**20**	**25**	**28**
AG-3.3	16	19	22	15	20	23	15	18	20	16	22	24
AG-3.4	15	20	22	15	21	23	16	20	21	16	18	20
AG-3.5	14	19	22	15	21	23	15	18	20	14	17	19
AG-3.6	18	21	24	18	22	25	19	24	26	20	24	26
AG-3.7	17	20	24	17	20	23	18	22	25	18	21	22
AR-3	16	19	21	16	20	22	15	18	20	15	19	22
AR-3.1	**22**	**28**	**32**	**23**	**27**	**33**	**21**	**26**	**30**	**22**	**27**	**32**
AR-3.2	**21**	**26**	**30**	**22**	**27**	**31**	**20**	**25**	**29**	**21**	**26**	**30**
AR-3.3	15	19	24	16	20	23	15	18	23	15	19	22
AR-3.4	16	21	24	16	20	23	17	20	24	16	19	22
AR-3.5	15	18	23	15	17	20	16	19	22	16	20	22
AR-3.6	**20**	**26**	**29**	**22**	**28**	**31**	**21**	**26**	**30**	**22**	**26**	**29**
AR-3.7	**21**	**26**	**28**	**22**	**27**	**30**	**22**	**30**	**33**	**22**	**29**	**32**
Ciprofloxacin	17	19	22	21	24	26	21	26	29	22	26	28

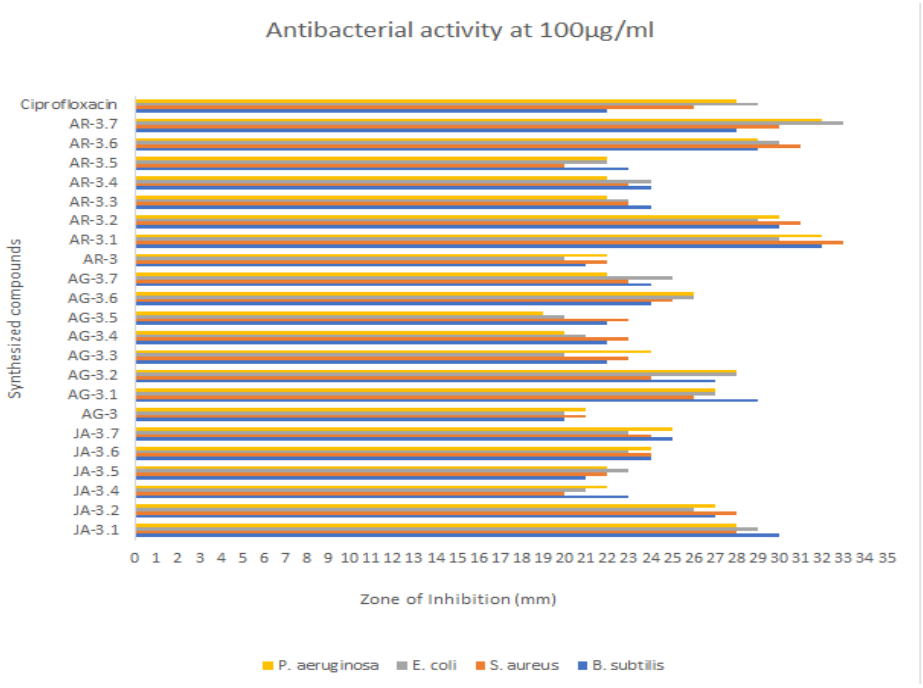
*mm= millimetre



Graph 1: Antibacterial activity of synthesized compound at 25µg/ml



Graph 2: Antibacterial activity of synthesized compound at 50µg/ml



Graph 3: Antibacterial activity of synthesized compound at 100µg/ml

CONCLUSION

A novel series of benzimidazoles were synthesized. Structure of all the synthesized compounds were elucidated using NMR, mass, IR and elemental analysis. The Schiff Bases were evaluated for *in vitro* anti-bacterial activity by cup and plate method against both gram -negative and gram-positive strains of bacteria. All the compounds exhibited good antibacterial activity but JA-3.1, JA-3.2, AG-3.1, AG-3.2, AR-3.1, AR-3.2, AR-3.6 and AR-3.7 have better antibacterial activity as compared to standard drug ciprofloxacin.

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REFERENCES

1. Ozkay Y, Tunalı Y, Karaca H, Işıkdag I. Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety. Eur J Med Chem 2010;45:3293-98.
2. Gould IM. The epidemiology of antibiotic resistance. Int.J. Antimicrob. Agents 2008;32(Suppl 1):S2–S9.
3. Wise R; BSAC Working Party on the Urgent Need: Regenerating Antibacterial Drug Discovery and Development. The urgent need for new antibacterial agents. J. Antimicrob. Chemother 2011;66:1939–1940.
4. Fischbach MA, Walsh CT. Antibiotics for emerging pathogens. Science 2009;325:1089–1093.
5. Martinez JL, Rojo F, Vila J. Are nonlethal targets useful for developing novel antimicrobials? Future Microbiol 2011;6:605–607.
6. Katritzky AR, Rogovoy BV, Kirichenko N, Vvedensky V. Solid-phase preparation of amides using N-acylbenzotriazoles. Bioorganic Med. Chem. Lett 2002;12(14):1809-11.
7. Katritzky AR, Suzuki K, Singh SK, He H-Y. Regiospecific C-acylation of pyrroles and indoles using N-acylbenzotriazoles. J. Org. Chem 2003;68(14):5720-3.
8. Wang X, Zhang Y. Low-valent titanium promoted self-coupling of N-acylbenzotriazoles and their cross-coupling with diarylketones. Synthetic communications 2003;33(15):2627-34.
9. Katritzky AR, Abdel-Fattah AA, Wang M. Expedient acylations of primary and secondary alkyl cyanides to α-substituted β-ketonitriles. J. Org. Chem 2003;68(12):4932-4.
10. Katritzky AR, Abdel-Fattah AA, Wang M. Efficient conversion of sulfones into β-keto sulfones by N-acylbenzotriazoles. J. Org. Chem 2003;68(4):1443-6.
11. Katritzky AR, Shestopalov AA, Suzuki K. A new convenient preparation of thiol esters utilizing N-acylbenzotriazoles. Synthesis 2004;(11):1806-13.
12. Katritzky AR, Cai C, Suzuki K, Singh SK. Facile syntheses of oxazolines and thiazolines with N-acylbenzotriazoles under microwave irradiation. J. Org. Chem 2004;69(3):811-4.
13. Katritzky AR, Abdel-Fattah AA, Gromova AV, Witek R, Steel PJ. α-Nitro ketone synthesis using N-acylbenzotriazoles. J. Org. Chem 2005;70(23):9211-4.
14. Katritzky AR, Suzuki K, Wang Z. Acylbenzotriazoles as advantageous N-, C-, S-, and O-acylating agents. Synlett 2005;(11):1656-65.
15. Katritzky AR, Widyan K, Kirichenko K. Preparation of polyfunctional acyl azides. The Journal of organic chemistry 2007;72(15):5802-4.
16. Lim D, Fang F, Zhou G, Coltart DM. Direct Carbon− Carbon Bond Formation via Soft Enolization: A Facile and Efficient Synthesis of 1, 3-Diketones. Organic letters 2007;9(21):4139-42.
17. Wang X, Wang W, Wen Y, He L, Zhu X. Facile and Highly Regiospecific Synthesis of 2-Aryl-Substituted Pyrazolidin-3-ones from α, β-Unsaturated N-Acylbenzotriazoles and Arylhydrazines. Synthesis 2008;(20):3223-8.
18. Zhou G, Lim D, Fang F, Coltart DM. A Practical Synthesis of β-Keto Thioesters by Direct Crossed-Claisen Coupling of Thioesters and N-Acylbenzotriazoles. Synthesis 2009;(19):3350-2.

19. Li J, Sun Y, Chen Z, Su W. A Novel and Efficient Reaction of Imidazolidin-2-one and N-Acylbenzotriazoles: A Facile Synthesis of 1-Acylimidazolidin-2-one. Synth. Commun 2010;40(24):3669-77.
20. Xia Z, Lv X, Wang W, Wang X. Regioselective addition of thiophenol to α, β-unsaturated N-acylbenzotriazoles. Tetrahedron lett 2011;52(38):4906-10.
21. Goshev I et al., Antioxidant activity of some benzimidazole derivatives to definite tumor cell lines J. Cancer Res. Ther 2013;1(2):87-9.
22. Yadav S, Narasimhan B, Kaur H, Perspectives of Benzimidazole Derivatives as Anticancer Agents in the New Era. Anticancer Agents Med Chem 2016;16(11):1403-1425.
23. Longo M, Zanoncelli S, Colombo PL, Harhay MO, Scandale I, Mackenzie C, Geary T, Madrill N, Mazue G. Effects of the benzimidazole anthelmintic drug flubendazole on rat embryos in vitro, Reproductive Toxicology 2013;36:78-87.
24. Khan MT, Razi MT, Jan SU, Mukhtiar M, Gul R, Ullah I, Hussain A, Hashmi AM, Ahmad MT, Shahwan NA and Rabbani I. Synthesis, characterization and antihypertensive activity of 2-phenyl substituted benzimidazole, Pak. J. Pharm. Sci 2018;31:1067-1074.
25. Budow S, Kozlowska M, Gorska A, Kazimierczuk Z, Eickmeier H, Colla PL, Gosselin G, and Seela F. Substituted benzimidazoles: antiviral activity and synthesis of nucleosides. ARKIVOC 2009;225-250.
26. Gaba M, Gaba P, Uppal D, Dhingra N, Bahia MS, Silakari O, Mohan C. Benzimidazole derivatives: search for GI-friendly anti-inflammatory analgesic agents. Acta Pharmaceutica Sinica B 2015; 5(4):337-342.
27. Wang XJ, Xi MY, Fu JH, Zhang FR, Cheng GF, Yin DL, You QD. Synthesis, biological evaluation and SAR studies of benzimidazole derivatives as H1-antihistamine agents. Chin. Chem. Lett 2012;23(6): 707-710.
28. Gaba M, Singh S, Mohan C. Benzimidazole: An emerging scaffold for analgesic and anti-inflammatory agents. Eur. J. Med. Chem 2014;76: 494-505.
29. Flores-Carrillo P, Velázquez-López JM, Aguayo-Ortiz R, Hernández-Campos A, Trejo-Soto PJ, Yépez-Mulia L *et al*. Antiprotozoal activity, and chemoinformatic analysis of 2-(methylthio)-1H-benzimidazole-5-carboxamide derivatives: Identification of new selective giardicidal and trichomonicidal compounds. Eur J Med Chem 2017;137:211-220.
30. Noor A, Qazi NG, Nadeem H, Khan AU, Paracha RZ, Ali F, Saeed A. Synthesis, characterization, anti-ulcer action and molecular docking evaluation of novel benzimidazole-pyrazole hybrids. Chem Cent J 2017;11: 85.
31. Yang, Haoran & Ren, Yujie & Gao, Xiaodong & Gao, Yonghong. Synthesis and Anticoagulant Bioactivity Evaluation of 1,2,5-Trisubstituted Benzimidazole Fluorinated Derivatives. Chemical Research in Chinese Universities. 32. 10.1007/s40242-016-6205-4.
32. Dangi G, Kumar N, Sharma CS, Chauhan LS. Synthesis, Anticonvulsant Activity of Some Novel Benzimidazole Acetohydrazides. Journal of Drug Delivery & Therapeutics 2014;4(2): 182-185.
33. Fatmah A. S. Alasmary, Anna M. Snelling, Mohammed E. Zain, Ahmed M. Alafeefy, Amani S. Awaad and Nazira Karodia. Synthesis and Evaluation of Selected Benzimidazole Derivatives as Potential Antimicrobial Agents. Molecules 2015;20:15206-15223.
34. Yun FL, Wang GF, He PL, Huang WG, Zhu FH, Gao HY *et al*. Synthesis and Anti-Hepatitis B Virus Activity of Novel Benzimidazole Derivatives. J. Med. Chem 2006; 49: 4790-4.
35. Padalkar BS, Borse BN, Gupta BD, Phatangare KR, Patil VS, Umape PG *et al*. Synthesis and antimicrobial activity of novel 2- substituted benzimidazole, benzoxazole and benzothiazole derivatives. Arab J Chem 2016; 9(Suppl 2),S1125-S1130.
36. Singh G, Kaur M, Mohan C. Benzimidazole: A Latest information On Biological Activity. International Research Journal of Pharmacy 2013;4(1): 82-87.
37. Rathee PS, Dhankar R, Bhardwaj S, Gupta M and Kumar R. Synthesis and antimicrobial studies of substituted 2-phenylbenzimidazole derivatives. J Appl Pharm Sci 2011;1(10):140-142.
38. Cimerman Z, Miljanić S, and Galić N. Schiff bases derived from aminopyridines as spectrofluorimetric analytical reagents. Croatica Chemica Acta 2000;73(1):81–95.
39. Schiff H. Mittheilungen aus dem Universitätslaboratorium in Pisa: eine neue reihe organischer Basen. Justus Liebigs Annalen der Chemie 1864;131:118–119.
40. Dhar DN and Taploo CL. Schiff bases and their applications. J Sci Ind Res 1982;41(8):501–506.
41. Miri R, Razzaghi-asl N, and Mohammadi MK. QM study and conformational analysis of an isatin Schiff base as a potential cytotoxic agent. J Mol Model 2013;19(2):727–735.
42. Avaji PG, Kumar V, Patil SA, Shivananda KN, and Nagaraju C. Synthesis, spectral characterization, in-vitro microbiological evaluation and cytotoxic activities of novel macrocyclic bis hydrazone.Eur. J. Med. Chem 2009;44(9):3552–3559.
43. Venkatesh P. Synthesis, characterization and antimicrobial activity of various schiff bases complexes of Zn(II) and Cu(II) ions. Asian Journal of Pharmaceutical and Health Sciences 2011;1(1):8–11.
44. Venugopala KN and Jayashree BS. Synthesis of carboxamides of 2′-amino-4′-(6-bromo-3-coumarinyl) thiazole as analgesic and antiinflammatory agents. Indian J Heterocy Ch 12(4): 307–310.
45. Vashi K and Naik HB. Synthesis of novel Schiff base and azetidinone derivatives and their antibacterial activity. Eur. J. Med. Chem 2004; 1:272–276.
46. Popiołek Ł. Hydrazide–hydrazones as potential antimicrobial agents: overview of the literature since 2010. Med Chem Res 2017;26:287-301.
47. Rad MN, Khalafi-Nezhad A, Behrouz S. Synthesis of some novel hydrazono acyclic nucleoside analogues. Beilstein J Org Chem 2010; 6:1-8.
48. Malik MA, Al-Thabaiti SA, Malik MA. Synthesis, structure optimization and antifungal screening of novel tetrazole ring bearing acyl-hydrazones. Int J Mol Sci 2012;13:10880-98.
49. Alemam MA, Abdelkarim AM, Karrar E. Comparative evaluation of antimicrobial activity of sudanese honey samples collected from different regions. world journal of pharmacy and pharmaceutical sciences 2017;12(6):225-232

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