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SYNTHESIS AND *IN-VITRO* ANTI BACTERIAL ACTIVITY OF "3-(2-[1H BENZIMIDAZOLE-2-YL)-2-OXETHYL] PHENYL) ACETIC ACID AND ITS DERIVATIVES"

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ABSTRACT

A fundamental structural feature of benzimidazoles, a group of heterocyclic, aromatic compounds, is the fusion of a six-membered benzene ring with a five-membered imidazole moiety. The use of molecules with benzimidazole motifs in biological and medical research has shown promise. Formic acid, Acetyl chloride, Benzene-1, 2-diol, Glycolic Acid, Benzoyl chloride, Methyl chloride, Ethyl chloride, Benzamide, and other chemicals were utilized in this study. The methods employed were TLC, IR spectra, 1H-NMR, and MS. The disc diffusion method was used to conduct the pharmacological screening for antibacterial activity. It was determined that the synthetic chemicals ranged from AA to AL. When compared to common medicines like Gentamycin, the compounds Benzimidazole (AA), 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC); 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-phenylacetamide (AJ); 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(2-nitrophenyl) acetamide (AK); 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(3-nitrophenyl) acetamide (AL) were found to be the most potent.

KEYWORDS

Benzimidazole, Glycolic acid, Benzene-1, 2-diol, 2- Nitro aniline and Anti bacterial activity.

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INTRODUCTON

The benzimidazole nucleus was discovered in 1944. It contain benzene and imidazole ring fused together. Its structure is similar to purine[1]. Benzimidazole contain important heterocyclic nucleus due to its wide range of pharmacological applications. The first benzimidazole was prepared in 1872 by the scientist Hoebrecker[2]. Benzimidazoles contain a hydrogen atom which was attached to nitrogen at 1-position (see Figure

No.1). Nowadays benzimidazole is a moiety of choice which possesses many pharmacological properties.

Now a day's currently much researcher work on Antibacterial derivatives. It is main focus on investigation of new Antibacterial agents. Benzimidazole derivatives identification was conducted via in vitro screening of antibacterial activity[3]. Antibacterial activity of different derivatives depends on the presence of aryl binding site with aryl/alkyl group, hydrogen bonding domain and electron donor group, which are the essential requirements for potential Antibacterial activity[4,5]. Benzimidazole and its derivatives are important heterocyclic in organic and biochemistry. There are many Benzimidazole containing natural products such as flavones, and flavonoids etc. Fungal and bacterial infections are most commonly affecting millions of people worldwide[6-8]. Heterocyclic compounds containing N give a variety of biological activities; antimicrobial activity. Similarly, Benzimidazole moiety constitutes the basic nucleus of nucleotides, which are most important and widespread natural product of plants and display a large number of biological activities[9]. Particularly, compound having both electron withdrawing and electron donating groups attached with Benzimidazole ring showed more inhibitory potential against fungal strains and bacterial strains than standard drug. Benzimidazole gives broad spectrum activity such as Antimicrobial, Anti-inflammatory, Analgesic, Antitubercular, Antihypertensive, Anticonvulsant and Antiviral Activity[9-11].

MATERIAL AND METHODS

Materials

Formic acid; Acetyl Chloride; Benzene-1,2-diol; Glycolic Acid; Benzoyl Chloride; Methyl Chloride; Ethyl Chloride; Benzamide; Aniline; 2-Nitro Aniline; 3- Nitro Aniline All chemicals were of analytical grade. All chemicals were of purchased from Modern Chemicals, Nashik and Some chemicals are available in College.

Methods

All Benzimidazole derivatives were synthesized by conventional method. Melting points were determined by open tube capillary method. The purity of the compounds was checked on thin layer chromatography (TLC) plates (silica gel G) in Chloroform: Ethanol (6:4) and chloroform: methanol (8:2) solvent systems, the spots were located under iodine vapors and UV light. IR spectra were obtained on a Perkin Elmer Spectrum FTIR instrument (KBr pellets). ^{1}H-NMR spectra were recorded on a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as internal standard in DMSO-d_6/$CDCl_3$ and mass spectra was obtained on JEOL GCMATE II MS is presented as m/z. The synthetic route for the title compounds is shown in Scheme No.1.

Experimental work

Synthesis of Benzimidazole Derivatives

Synthesis of Benzimidazole (AA): (Scheme 1A)

In a round-bottomed flask 2gm of o-phenylenediamine was react with 7ml of 90%formic acid. The mixture was heated in a water bath at 100° for two hours. After cooling, 10% sodium hydroxide solution was added slowly, until the mixture is just alkaline to litmus. Ice-cold water was used to rinse all solid out of the reaction flask. The crude product was pressed thoroughly on the filter paper, washed with about 25ml of cold water, and then recrystallization with Hot water.

Synthesis of 1-(1H-benzimidazole-2-yl) ethanone (AB): (Scheme 1A)

In a round-bottomed flask take 2gm of 1H benzimidazole and 2 ml of Acetyl chloride and the reaction mixture was heated under reflex condition till (after 2 hrs) completion of reaction (Checked by TLC).After completion of reaction the contents were allowed to cool obtain reaction mixture , the solid obtained was filtered recrystalized from methanol to give 1-(1H-benzimidazol-2-yl)ethanone. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC): (Scheme 1A)

In a round-bottomed flask take 2gm of 1-(1-H benzimidazol-2-yl) ethanone and 2gm Benzene-1,

2-diol and heated under reflex condition till (after 4 hrs) completion of reaction (Checked by TLC). After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of 3-(2-[1H benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD): (Scheme 1A)

In a round-bottom flask take 2gm of 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone and 2ml Glycolic acid. Reflux for 2hr.cool the completion of reaction Checked by TLC). After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give 3-(2-[1H benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid Cool at room temperature, filter the product. Wash with cold water. Filter the product.

Synthesis of {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AE): (Scheme 1B)

In a round-bottomed flask; take 2gm of {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}acetic acid and 4ml benzoyl chloride and then heated for 2hr. Completion of reaction (Checked by TLC). After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give 3-2(1H benzimidazol-2-yl)-2-oxoethyl phenyl) acetic benzoic anhydride. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AF): (Scheme 1B)

In a round-bottomed flask; take 2gm of {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic acid and benzoic acid in RBF; reaction mixture was heated under reflex condition at 100° till (after 2 hrs) completion of reaction (Checked by TLC). After completion of reaction the contents were allowed to cool obtain reaction mixture; the solid obtained was filtered recrystalized from methanol to give {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of methyl {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate (AG): (Scheme 1B)

In a round-bottomed flask; take 2gm of {3-2(1-H benzimidazole-2-yl)-2-oxoethyl) phenyl} acetic acid and chloromethane was heated together under reflux condition till (after 4 hrs) completion of reaction (Checked by TLC).After completion of reaction the contents were allowed to cool obtain reaction mixture , the solid obtained was filtered recrystalized from methanol to give methyl {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of ethyl {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}acetate (AH): (Scheme 1B)

In a round-bottomed flask; take 2 gm of {3-2(1-H benzimidazole-2-yl)-2-oxoethyl) phenyl} acetic acid and chloroethane was heated under reflex condition till (after 2 hrs) completion of reaction (Checked by TLC).After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give ethyl {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate. Cool at room temperature; filter the product. Wash with cold water**.**

Synthesis of *N*-({3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetyl) Benzamide (AI): (Scheme 1B)

In a round-bottomed flask; take 2gm of {3-2(1-H benzimidazole-2-yl)-2-oxoethyl) phenyl} acetic acid and Benzamide was. Heated under reflux for 4hr (Checked by TLC). After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give *N*-({3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetyl) Benzamide.

Synthesis of 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-phenylacetamide (AJ): (Scheme 1B)

In a round-bottomed flask; take 2 gm of {3-2(1-H benzimidazole-2-yl)-2-oxoethyl) phenyl} acetic acid and 2ml aniline was heated under reflux condition for 2hr cool at room temperature, (Checked by TLC). After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-phenylacetamide. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(2-nitrophenyl) acetamide (AK): (Scheme 1B)

In a round-bottomed flask; take 2gm of {3-2(1-H benzimidazole-2-yl)-2-oxoethyl) phenyl} acetic acid and 2ml 2-nitroaniline was heated under reflux condition for 4 hr (Checked by TLC).After completion of reaction the contents were allowed to cool obtain reaction mixture , the solid obtained was filtered recrystalized from methanol to give 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(2-nitrophenyl)acetamide. Cool at room temperature; filter the product. Wash with cold water.

Synthesis of 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(3-nitrophenyl) acetamide (AL): (Scheme 1B)

In a round-bottomed flask; take 2gm of{3-2(1-H benzimidazole-2-yl)-2-oxoethyl) phenyl} acetic acid and 3-nitro aniline was heated under reflux condition for 3 hr, cool in ice bath ,cool at room temperature, (Checked by TLC).After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid obtained was filtered recrystalized from methanol to give 2- {3-(2-(1-H benzimidazole-2yl)2oxoethyl) phenyl}N-(3-nitrophenyl) acetamide.

Characterization

The purity of products was monitored through TLC plates and melting point was determined through melting point apparatus. Generally, Chloroform, ethanol, methanol and Benzene solvent medium was used for checking of reaction through TLC plates. Progress of reaction was monitored by thin layer chromatography. Ultra Violet lamp was used as visualizing agent. The whole reactions were carried out in clean glassware with specific catalysts, basic or acidic conditions. All synthesized compounds were characterized by using different spectroscopic techniques such as 1H NMR; IR and MS. The physical data of 3-(2-[1H benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD) derivatives were shown in Table No.1.

Spectral Data

Synthesis of Benzimidazole (AA): (Scheme 1A)

% yield: 80%; Melting point (^{0}C): 170°C; Rf Value :0.9; Benzene: Ethanol (4:1); FTIR (KBr) ν cm^{-1} : 3051.80 (Ar C-H), 2809.78 (Ar C-H), 1699.33 (Ar C=C), 1003.77 (Ar C-C), 1216.86 (Ar C-N), 3277.83 (Ar N-H)28; 1H NMR (500 MHz) CDCl3 δppm: 12.3 (N-H), 7.2 (Ar C-H),7.5 (Ar C-H), 7.7 (Ar C-H), 7.9 (Ar C-H), 6.6 (C-H); JEOL GCMATE II MS (m/z): 117 (M^+), 118 (M^++1) Mol. Wt. 118.

Synthesis of 1-(1H-benzimidazole-2-yl) ethanone (AB): (Scheme 1A)

% yield: 92%; Melting point (^{0}C): 230°C; Rf Value: 0.8; Benzene: Ethanol (9:1); FTIR (KBr) ν cm^{-1}: 3048.91 (C-H Stretch); 2881.13 (C-H Stretch); 1694.16 (C=C); 1191.79 (C-C); 1260.25 (C-N), 3482.81 (N-H), 1718.34 (C=O ketone); 1H NMR (500 MHz) CDCl3 δppm: 11.7 (N-H), 7.6 (Ar C-H), 7.5 (Ar C-H), 7.3 (Ar C-H), 7.1 (Ar C-H), 2.3(Methyl C-H); JEOL GCMATE II MS (m/z): 160 (M^+), 161 (M^++1); Mol. Wt. 161.

Synthesis of 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC): (Scheme 1A)

% yield: 51%; Melting point (^{0}C): 187°C; Rf Value :0.5; Chloroform: Methanol (7:1); FTIR (KBr) ν cm^{-1}: 3089.97 (C-H Aromatic); 2797.24 (C-H Aliphatic); 16.8295 (C=C Aromatic); 2943.58 (C-C Aromatic); 1641.50 (N-H Aromatic); 1286.30 (C=O ketone); 1710.50 (C-N Aromatic), 3347 (C-OH), 2797 (C-H), 1340 (C-C), 3468 (N-H), 1008 (C-O); 1H NMR (500 MHz) CDCl3 δppm: 11.7 (N-H), 11.4 (N-H), 8.2 (Ar C-H), 8.0 (Ar C-H), 7.5 (Ar C-H), 7.3 (Ar C-H), 6.8 (Ar C-H), 7.0 (Ar C-H), 6.7 (Ar C-H), 6.4 (C-H), 5.3 (O-H) JEOL GCMATE II MS (m/z): 235 (M^+), 236 (M^++1); Mol. Wt. 236

Synthesis of 3-(2-[1H benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD): (Scheme 1A)

% yield: 82%; Melting point (^{0}C): 192°C; Rf Value: 0.8; Chloroform: Ethanol (7:3); FTIR (KBr) ν cm^{-1}: 3059.55 (C-H Aromatic); 2881.13 (C-H Aliphatic); 1637.02 (C=C); 1000.72 (C-C); 3352.72 (N-H); 1340.28 (C-N Ar); 3026.73 (N-H Ar); 1719.98 (C=O ketone); 3537.72; 1193.10(C-O Aliphatic); acid anhydride1751; 1H NMR (500 MHz) CDCl3 δppm: 11.7 (N-H), 8.9 (Ar C-H), 8.8 (Ar C-H), 8.7 (Ar C-H), 8.5 (Ar C-H), 8.4 (Ar C-H), 8.3 (Ar C-H), 8.1 (Ar C-H), 8.0 (Ar C-H), 7.7 (C-H), 7.5 (C-H), 7.3, 6.4(C-H), (C-H), 6.3 (C-H); Mol. Wt. 278

Synthesis of {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AE): (Scheme 1B)

% yield: 75%; Melting point (^{0}C): 198°C; Rf Value: (0.6);Chloroform: Ethanol (9:1); FTIR (KBr) ν cm^{-1}: 3051.85 (C-H Ar); 2797.23 (C-H Aliphatic); 1687.41 (C=C Ar); 1000.19 (C-C Ar); 1340.00 (C-N Ar); 3352.64 (N-H Ar); 1719.83(C=O Ketone); 1193.72 (C-O); 1H NMR (500 MHz) CDCl3 δppm: 11.7 (N-H); 12.0 (N-H); 8.9 (Ar C-H); 8.8 (Ar C-H); 8.7 (Ar C-H); 8.5 (Ar C-H); 8.4 (Ar C-H); 8.3 (Ar C-H); 8.1(Ar C-H); 8.0(Ar C-H); 7.7(Ar C-H); 7.5 (Ar C-H); 7.3(Ar C-H); 7.0(Ar C-H); 7.0 (Ar C-H); 6.4 (C-H); 6.3(C-H); Mol. Wt. 398.

Synthesis of {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AF): (Scheme 1B)

% yield: 89; Melting point (^{0}C) : 200°C; Rf Value: 0.8; Chloroform: Ethanol 7:3); FTIR (KBr) ν cm^{-1}: 3051.80 (C-H Ar); 2797.24 (C-H Aliphatic); 1695.12 (C=C Ar); 1178.29 (C-C Ar); 1340.28(C-N Ar); 3460.63(N-H Ar); 1725.88 (C=O) ketone; 1263.60(C-O Aliphatic); acid anhydride 1746.46; 1H NMR (500 MHz) CDCl3 δ ppm: 11.7 (N-H); 11.6 (N-H); 11.3 (N-H); 8.9 (Ar C-H); 8.8 (Ar C-H); 8.7 (Ar C-H); 8.5 (Ar C-H);8.4 (Ar C-H); 8.3 (Ar C-H); 8.1(Ar C-H); 8.0 (Ar C-H); 7.7 (C-H); 7.5 (C-H); 7.3 (Methyl C-H);7.0 (Ar C-H); 7.0 (Ar C-H);6.4 (C-H); Mol. Wt. 338.

Synthesis of methyl {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate (AG): (Scheme 1B)

% yield: 95%; Melting point (^{0}C) : 199°C; Rf Value: 0.7; chloroform: Ethanol (8:2); FTIR (KBr) ν cm^{-1}: 2975.53 (C-H Ar); 2881.30(C-H)1698C=C) Aliphatic); 1247 (C=C Ar); 1340.28 (C-C Ar); 3026.73 (N-H Aliphatic); 1725.98(C-N Ar); 1219.16 (N-H Ar); 1H NMR (500 MHz) CDCl3 δppm: 12.1 (N-H); 8.0 (Ar C-H); 8.0 (Ar C-H); 7.8 (Ar C-H); 7.6(Ar C-H); 7.4 (Ar C-H); 7.3 (Ar C-H); 7.2(Ar C-H); 6.9(Ar C-H); 6.7 (Ar C-H); 6.2(C-H); 6.4 (C-H); 2.4 Methyl (C-H); Mol. Wt. 308.

Synthesis of ethyl {3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate (AH): (Scheme 1B)

% yield: 95%; Melting point (^{0}C) : 202°C; Rf Value: 0.6; Chloroform: Ethanol (9:1); FTIR (KBr) ν cm^{-1} : 3067.23(C-H Ar); 2997.80(C-H Aliphatic); 1594.84 (C=C Ar); 1201.43 (C-C Ar); 1270.40 (C-N Ar); 3295.50(N-H Ar);1695.12 (C=O) ketone; 1000.87 (C-O); 1H NMR (500 MHz) CDCl3 δ ppm: 11.5 (N-H); 8.6 Ar C-H); 8.5(Ar C-H); 8.4 (Ar C-H); 8.2(Ar C-H); 8.1 (Ar C-H); 7.8 (Ar C-H); 7.7 (Ar C-H); 7.2(Ar C-H); 6.6 (Ar C-H); 6.4 (Ar C-H); 6.2 (Ar C-H); 3.0 (Ar C-H); Mol. Wt. 322.

Synthesis of *N*-({3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetyl) Benzamide (AI): (Scheme 1 B)

% yield: 89%; Melting point (^{0}C) : 204°C; Rf Value: 0.7; Chloroform: Ethanol (8:2); FTIR (KBr) ν cm^{-1} : 3005.52 (C-H Ar); 2997.80 (C-H); 1594.84 (C=C Ar); 1201.43(C-C Ar); 3098.08 (C-N); 1337.27 (N-H Ar); 3420.59 (N-H),1707(C=O),1278.57(C-O),3352.64(N-H); 1H NMR (500 MHz) CDCl3 δppm: 12.2 (N-H); 11.6 (N-H), 9.2(Ar C-H); 9.1 (Ar C-H); 9.0 (Ar C-H); 8.8 (Ar C-H); 8.6 (Ar C-H); 8.5 (Ar C-H); 8.3(Ar C-H); 8.0 (Ar C-H); 7.8 (Ar C-H); 7.6 (Ar C-H); 7.3 (Ar C-H); 7.2 (C-H); 7.1 (C-H);6.3(C-H);6.4(C-H); Mol. Wt. 397.

Synthesis of 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-phenylacetamide (AJ): (Scheme 1 B)

% yield: 65%; Melting point (^{0}C): 206°C; Rf Value: 0.6; Chloroform: Ethanol (9:1); FTIR (KBr) ν cm^{-1}: 3074.98 (C-H Stretch Aromatic); 2997.50 (C-H

Aliphatic); 1671.98(C=C Ar); 1139.72 (C-C Ar); 3096.24 (N-H Al); 1340.28 (C-N Ar); 3236.98 (N-H Ar); 1710.55 (C=O) ketone; 1276.20 (C-O), 3304.52 (N-H); 1H NMR (500 MHz) CDCl3 δppm: 11.2 (N-H); 10.9 (N-H); 8.9 (Ar C-H); 8.8 (Ar C-H); 8.7 (Ar C-H); 8.5 (Ar C-H); 8.4 (Ar C-H); 8.3 (Ar C-H); 8.2 (Ar C-H); 8.0 (Ar C-H); 7.7 (Ar C-H); 7.4 (Ar C-H); 7.3(Ar C-H); 7.1 (C-H); 7.0 (C-H); 6.3(C-H),6.4(C-H), Mol. Wt. 369.

Synthesis of 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(2-nitrophenyl) acetamide (AK): (Scheme 1B)

% yield: 95%; Melting point (^{0}C) : 199°C; Rf Value: 0.8; chloroform: Ethanol (9:1); FTIR (KBr) ν cm^{-1} : 2975.53 (C-H Ar); 2881.30(C-H)1698C=C) Aliphatic); 1247 (C=C Ar); 1340.28 (C-C Ar); 3026.73 (N-H Aliphatic); 1735.98(C-N Ar); 1215.16 (N-H Ar); 1H NMR (500 MHz) CDCl3 δppm: 12.1 (N-H); 8.0 (Ar C-H); 8.0 (Ar C-H); 7.8 (Ar C-H); 7.6(Ar C-H); 7.4 (Ar C-H); 7.3 (Ar C-H); 7.2(Ar C-H); 6.9(Ar C-H); 6.7 (Ar C-H); 6.2(C-H); 6.4 (C-H); 2.4 Methyl (C-H); Mol. Wt. 308.

Synthesis of 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(3-nitrophenyl) acetamide (AL): (Scheme 1B)

% yield: 92; Melting point (^{0}C): 200°C; Rf Value: 0.8; Chloroform: Ethanol 7:3); FTIR (KBr) ν cm^{-1}: 3051.80 (C-H Ar); 2795.24 (C-H Aliphatic); 1696.12 (C=C Ar); 1178.29 (C-C Ar); 1340.28(C-N Ar); 3460.63(N-H Ar); 1725.88 (C=O) ketone; 1263.60(C-O Aliphatic); acid anhydride 1756.46; 1H NMR (500 MHz) CDCl3 δ ppm: 11.8 (N-H); 11.6 (N-H); 11.3 (N-H); 8.9 (Ar C-H); 8.8 (Ar C-H); 8.7 (Ar C-H); 8.4 (Ar C-H);8.4 (Ar C-H); 8.3 (Ar C-H); 8.1(Ar C-H); 8.0 (Ar C-H); 7.7 (C-H); 7.5 (C-H); 7.3 (Methyl C-H);7.0 (Ar C-H); 7.0 (Ar C-H);6.4 (C-H); Mol. Wt. 338.

Biological evaluation

Synthesized newer benzimidazole derivatives were screened for Anti-Bacterial Activity. Total 12 compounds (4 Step Products + 8 Benzimidazole Derivatives) were evaluated for their biological screening. The following section describes, in brief the Anti-Bacterial Activity.

***In vitro* Antibacterial activity by disc diffusion method**

Antibacterial Activity

The compounds like BF to BJ were evaluated for their *in vitro* antibacterial activity against various microorganisms such as gram positive *Staphylococcus aureus*, gram-negative *Escherichia coli* and *Pseudomonas aeruginosa* by *in vitro* method like disc diffusion method was performed using Mueller Hinton Agar (M173) medium[10,11]. Each compound was tested at concentration 100µg/mL in DMSO. The zone of inhibition was measured after 24 h incubation at 37^{o}C. Standard: Gentamycin (100µg/mL of DMSO).

RESULTS AND DISCUSSION

The syntheses of benzimidazole derivatives from AE to AJ were undertaken as per the scheme 1B. The required 3-(2-[1H Benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD) was prepared by mixture. 2gm of 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone and 2ml Glycolic acid reflux for 2hr. After completion of reaction the contents were allowed to cool obtain reaction mixture, the solid product was obtained. IR spectra were obtained on a Perkin Elmer Spectrum1 FT-IR instrument (KBr pellets). Perkin Elmer Spectrum1 FT-IR instrument consists of globar and mercury vapor lamp as sources. 1H-NMR spectra were recorded on a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as an internal standard in DMSO-d6/CDCl3 and mass spectra was obtained on JEOL GCMATE II. The results revealed that most of the synthesized compounds showed varying degrees of inhibition against the tested microorganisms. In general, the inhibitory activity against the tested gram-positive bacteria was higher than that of the gram-negative bacteria. Moreover, the compounds like AD, AE and AJ having the side chain showed higher activity than AF and AG against *S. aureus* and *Pseudomonas aeruginosa.* The replacement of oxygen to nitrogen resulted in a slightly increased antimicrobial activity. Our study revealed that all the compounds had stronger antibacterial activity

against Gram-positive bacteria when compared to Gram-negative bacteria. Antimicrobial activity revealed that newly synthesized compound AH, AI and AJ showed good significant activity. The results of the preliminary antimicrobial testing of the prepared compounds, the typical broad spectrum antibacterial drug like Gentamycin was shown in Table No.2.

The synthesized compounds were screened for their antibacterial activity and Zone of Inhibition of Benzimidazole derivatives *(In vitro* Antibacterial activity by disc diffusion method) as showed in Figure No.2 and Figure No.3.

The derivatives like AH, AI and AJ showed highly active compound against *E. coli, Staphylococcus aureus* and *Pseudomonas aureus.* AH showed moderately active compound against *E. coli* and *S. aureus.* AI and AJ showed moderately active compound against *E. coli* and *S. aureus*. Standard (Gentamycin) showed highly active against *E. coli, Pseudomonas aeruginosa* and *S. aureus*.

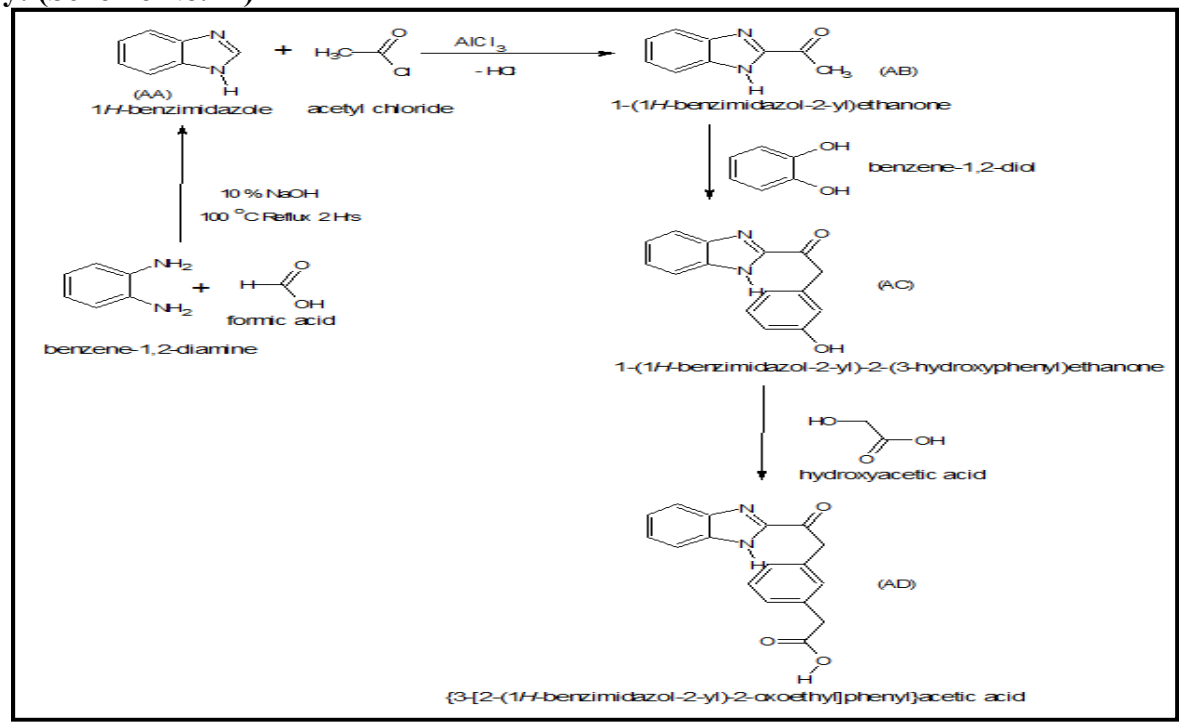
Table No.1: Physical Data of 3-(2-[1H benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD) derivatives

S.No	Compounds	Colors of Compounds	Molecular Formula	Melting Point	% yields	Molecular Weight
1	AA	White	$C_7H_6N_2$	170°C	80%	118
2	AB	Yellowish	$C_9H_9N_2O$	180°C	92%	161
3	AC	White	$C_{15}H_{14}N_2O_2$	181°C	51%	236
4	AD	Brown	$C_{17}H_{14}N_2O_2$	192°C	82%	278
5	AE	White	$C_{24}H_{18}N_2O_4$	198°C	82%	398
6	AF	Yellowish	$C_{18}H_{16}N_2O_3$	200°C	75%	338
7	AG	White	$C_{19}H_{18}N_2O_3$	195°C	89%	308
8	AH	White	$C_{24}H_{19}N_3O_3$	197°C	95%	322
9	AI	White	$C_{23}H_{19}N_3O_2$	201°C	89%	397
10	AJ	Yellowish	$C_{23}H_{18}N_4O_4$	202°C	65%	369
11	AK	Grey	$C_{23}H_{18}N_4O_4$	205°C	72%	414
12	AL	White	$C_{23}H_{18}N_4O_4$	202°C	72%	354

Table No.2: Antibacterial activity screening result of synthesized compound measuring the zone of inhibition in millimeter

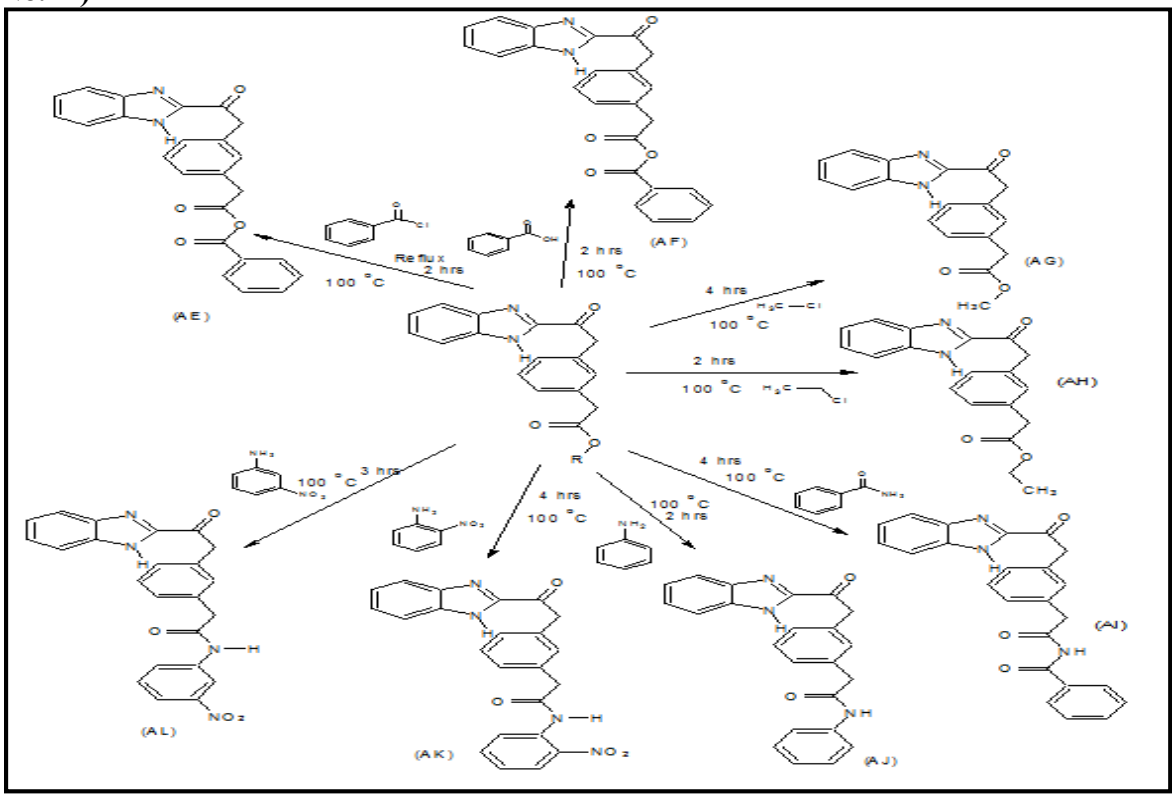
S.No	Compound No	Diameter of zone of inhibition (mm)		
		Escherichia coli	***Staphylococcus aureus***	***Pseudomonasaeruginosa***
		ATCC 25922	**ATCC 25923**	**ATCC 27853**
1	AA	12	18	10
2	AB	08	15	09
3	AC	13	20	19
4	AD	14	22	20
5	AE	14	21	21
6	AF	11	18	20
7	AG	15	19	18
8	AH	13	20	19
9	AI	12	20	20
10	AJ	11	20	21
11	AK	15	20	20
12	Gentamycin	20	36	28

Chemistry: (Scheme No.IA)



Scheme No.1A: Synthesis of 3-(2-1H benzimidazole 2yl) 2-oxethyl) phenyl) acetic acid (AD)

(Scheme No.IB)



Scheme No.1B: Synthesis of 3-(2-1H benzimidazole 2yl)-2-oxethyl) phenyl) acetic acid derivatives (AE-AL)

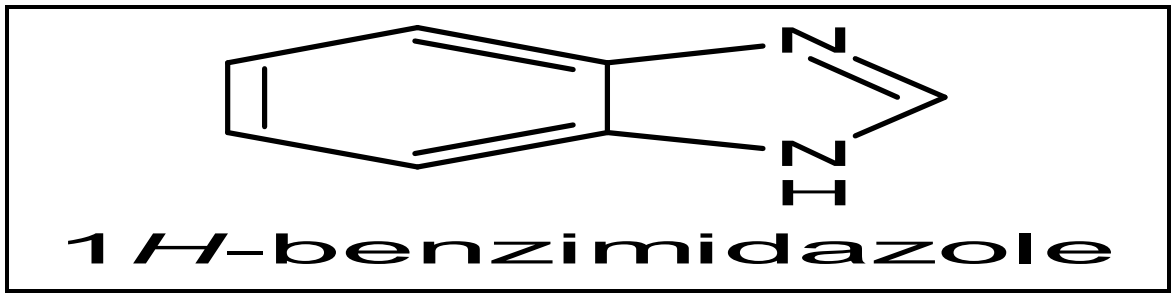


Figure No.1: Benzimidazole heterocyclic nucleus

Figure No.2: Zone of Inhibition of Benzimidazole derivatives *(In vitro* Antibacterial activity by disc diffusion method)

CONCLUSION

Various benzimidazole derivatives was synthesized by 3-(2-1H benzimidazole 2yl)-2-oxethyl) phenyl) acetic acid (AD). The total 12 benzimidazole derivatives were synthesized. All of the compounds were prepared in good yields. The structure confirmations of synthesized compounds were done by IR, NMR spectroscopy and MS. Biological activity of Antibacterial was taken by using disc diffusion method. In this research; derivatives had stronger Antibacterial activity against different types of bacteria. Some of the synthesized compounds were found to have potent Antibacterial activity. Synthesized compounds exhibited more activity when compared to other benzimidazole derivatives. Hence, it can be concluded that the benzimidazole derivatives can be potentially developed into useful Antibacterial agents. The synthesize compounds were establish to be AA to AL. The compound Benzimidazole (AA), 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC), 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-phenylacetamide (AJ), 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(2-nitrophenyl) acetamide (AK) and 2-{3-[2-(1*H*-benzimidazol-2-yl)-2-oxoethyl] phenyl}-*N*-(3-nitrophenyl) acetamide (AL) were established to be the most potent compound as compared to standard drugs Gentamycin.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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