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SYNTHESIS AND *IN-VITRO* ANTI BACTERIAL ACTIVITY OF *N*'-{4-[2-(1*H*-BENZIMIDAZOL-2-YL)-2-OXOETHYL] PHENYL}-2 HYDROXYACETOHYDRAZIDE AND IT'S DERIVATIVES

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ABSTRACT

Benzimidazoles are a class of heterocyclic, aromatic compounds which share a fundamental structural characteristic of six-membered benzene fused to five-membered imidazole moiety. Molecules having benzimidazole motifs showed promising application in biological and clinical studies. Benzimidazole and its derivatives having versatile nitrogen containing heterocyclic compounds which have long been known as a promising class of biologically active compounds possessing wide variety of biological and pharmacological activities like antibacterial, anti-inflammatory, anti-ulcer, anti-diabetic etc. Many Scientists have declared that Benzimidazole system possesses the variable sites like position 2 and 5 which can be suitably modified to yield potent therapeutic agents. The present review covers the chemistry and pharmacological activities of substituted benzimidazoles In this research we use Formic acid; Acetyl Chloride; Hydrazine; Benzene-1, 2-diol; Glycolic Acid; Benzoyl Chloride; Methyl Chloride; Ethyl Chloride; Benzamide etc and method is TLC, IR spectra, ^{1}H-NMR and MS. The synthesize compounds were establish to be BA to BK. The compound BA, BC, BJ, BI and BK were established to be the most potent compound through compare to standard drugs phenytoin. Synthesized newer benzimidazole derivatives were screened for Anti-bacterial activity. It was seen that in biological activity; derivatives containing 2-nitro aniline and 3- nitro aniline having significant biological activity than other benzimidazole derivatives.

KEYWORDS

Benzimidazole, Hydroxy acetic 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.

The benzimidazoles are also known as Benzoglyoxalines. A compound containing benzimidazole and benzene rings have been used extensively for pharmaceutical purpose since 1960. 1-H-Benzimidazole rings, which exhibit remarkable basic characteristics due to their nitrogen content, comprise the active substances for several drugs[3-5].

It is main focus on investigation of new antibacterial agents. 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[6-8]. There is biological relevance of many heterocyclic building blocks is due to the structural similarity with purine nucleobase and as benzimidazole derivative also which selectively inhibits the endothelial cell growth[9] and then suppresses the process of angiogenesis *in- vitro* as well as *in-vivo* biological activity.

MATERIAL AND METHODS

Materials

Formic acid; Acetyl Chloride; Hydrazine, 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). 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 1A and Scheme 1B.

Experimental work

Synthesis of Benzimidazole Derivatives

Synthesis of Benzimidazole (BA): (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 25 ml of cold water, and then recrystallization with Hot water.

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

In a round-bottomed flask take 2gm of 1H benzimidazole and 2ml 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.

Synthesis of 1-(1*H*-benzimidazol-2-yl)-2-(4-hydrazinylphenyl) ethanone (BC): (Scheme 1A)

In a round-bottomed flask take 2gm of 1-(1-H benzimidazol-2-yl) ethanone and 2gm Benzene-1, 2-diol and 10ml of hydrazine was 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-(1*H*-benzimidazol-2-yl)-2-(4-hydrazinylphenyl) ethanone.

Synthesis of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxy aceto hydrazide (BD): (Scheme 1A)

In a round-bottom flask take 2gm of 1-(1*H*-benzimidazol-2-yl)-2-(4-hydrazinylphenyl)ethanone and 2ml Hydroxy Acetic Acid was heated and 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 N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxy aceto hydrazide.

Synthesis of {N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyaceto hydrazide (BE): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 5ml benzoyl chloride was heated for 4hrs. 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 {N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide.

Synthesis of N'- {4- [2- (1H-benzimidazol-2yl) -2-oxoethyl] phenyl} – 2 –methoxy aceto hydrazide (BF): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 5ml Methyl Chloride 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 N'- {4- [2- (1H-benzimidazol-2yl) -2-oxoethyl] phenyl} – 2 – methoxyacetoydrazide.

Synthesis of N' {4- [2- (1H-benzimidazol- 2yl} – 2 - oxoethyl] phenyl} – 2 – ethoxy aceto hydrazide (BG): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 5ml chloroethane 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 N' {4- [2- (1H-benzimidazol- 2yl} – 2 - oxoethyl] phenyl} – 2 – ethoxy aceto hydrazide.

Synthesis of N'{4-[2-(1H-benzimidazol-2-yl) -2-oxoethyl] phenyl}-2-hydroxy acetyl benzamide (BH): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 2gm of benzamide 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, the solid obtained was filtered recrystalized from methanol to give N'{4-[2-(1H-benzimidazol-2-yl) -2-oxoethyl] phenyl}-2-hydroxy acetyl benzamide.

Synthesis of N'- {4- [2 - (1H – benzimidazole-2-yl) – 2 - oxoethyl] phenyl} -2-hydroxyaceto hydrazide-N-phenylacetamide (BI): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 5ml of aniline 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 N' - {4 [2, - (1H-benzimidazol-2-yl) - 2 - oxoethyl] phenyl} -2-hydroxyaceto hydrazide N- (2-nitrophenyl) acetamide (BJ): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 5ml of 2-nitroaniline 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 N' - {4 [2, -(1H-benzimidazol - 2yl) -2 - oxoethyl] phenyl} -2-hydroxyacetohydrazide N- (2-nitrophenyl) acetamide.

Synthesis of N'-{4- [2- (1H – benzimidazol-2-yl) - 2 - oxoethyl] phenyl} -2- hydroxyaceto hydrazide - N- (3-nitrophenyl) acetamide (BK): (Scheme 1B)

In a round-bottomed flask; take 2gm of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide and 5ml 3-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 N'-{4- [2- (1H – benzimidazol-2-yl) -2 - oxoethyl] phenyl} -2- hydroxyaceto hydrazide - 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 N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxy aceto hydrazide (BD) derivatives were shown in Table No.1.

Spectral Data

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

% yield: 80%; Melting point: 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); 1H NMR 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); Mol. Wt. 118.

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

% yield: 92%; Melting point: 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 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); Mol. Wt. 161.

Synthesis of 1-(1H-benzimidazole-2yl)-(3hydrazinylphenyl) ethanone (BC): (Scheme 1A)

% yield: 96%; Melting point: 270°C; Rf Value: 0.9; benzene: Ethanol (7:1); FTIR (KBr): ν cm^{-1}: 3089.97 (C-H Aromatic), 2797.24 (C-H Aliphatic), 1682.95 (C=C Aromatic), 1170.58 (C-C Aromatic), 3356.50 (N-H Aromatic), 1717.30 (C=O ketone), 1280.50 (C-N Aromatic); 1H NMR 11.9 (N-H), 11.4 (N-H), 8.2 (Ar C-H), 8.0 (Ar C-H), 7.5 (Ar C-H), 7.4 (Ar C-H), 7.3 (Ar C-H), 7.0 (Ar C-H), 6.8 (Ar C-H), 6.7 (Ar C-H), 6.4 (C-H); Mol. Wt. 161.

Synthesis of N' {4- [2 - (1H–benzimidazole–2-yl) – 2 oxoethyl] phenyl} -2-hydroxyaceto hydrazide (BD): (Scheme 1A)

% yield: 79%; Melting point: 280°C; Rf Value: 0.8; benzene: Ethanol (5:1); FTIR (KBr) ν cm^{-1} : 2977.55 (C-H Aromatic), 2881.13 (C-H Aliphatic), 1698.02 (C=C), 1247.72 (C-C), 3413.72 (N-H); 1340.28 (C-N Ar), 3026.73 (N-H Ar), 1725.98 (C=O ketone), 1193.72 (C-O Aliphatic), 3428.10(C-O Aliphatic); 1H NMR: 12.8 (N-H), 12.2 (N-H), 7.9 (Ar C-H), 7.8 (Ar C-H), 7.7 (Ar C-H), 7.5 (Ar C-H), 7.3 (Ar C-H), 6.9 (Ar C-H), 6.8 (Ar C-H), 6.6 (Ar C-H), 6.3 (C-H), 6.1 (C-H), 5.4 (O-H); GC-MS(m/z): 322; Mol. Wt. 324.

Synthesis of N'-{4- [2 - (1H – benzimidazol-2-yl) - 2 - oxoethyl] phenyl} -2- hydroxyaceto hydrazide (BE): (Scheme 1B)

% yield: 80%; Melting point (^{0}C): 290°C; Rf Value: 0.7; Benzene: Ethanol (9:1); FTIR (KBr) ν cm^{-1}: 3031.55 (C-H Ar), 2986.23 (C-H Aliphatic), 1696.09 (C=C Ar), 1046.19 (C-C Ar), 1294.00 (C-N Ar), 3344.93 (N-H Ar), 1718.26 (C=O Ketone), 1014.90 (C-O Aliphatic); 1H NMR: 12.3 (N-H), 12.0 (N-H), 11.7 (N-H), 9.3 (Ar C-H), 9.2 (Ar C-H), 9.0 (Ar C-H), 8.9 (Ar C-H), 8.7 (Ar C-H), 8.6 (Ar C-H), 8.3(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. 412.

Synthesis of N'- {4- [2- (1-H – benzimidazol-2-yl) -2 -oxoethyl] phenyl} -2-methoxyaceto hydrazide (BF): (Scheme 1B)

% yield: 95%; Melting point (^{0}C): 320°C; Rf Value: 0.9; Benzene: Ethanol (7:1); FTIR (KBr) ν cm^{-1}: 3048.91 (C-H Ar), 2820.38 (C-H Aliphatic), 1633.41 (C=C Ar), 1137.06 (C-C Ar), 1267.97 (C-N Ar), 3497.27 (N-H Ar), 1708.62 (C=O) ketone, 1249.20 (C-O Aliphatic); 1H NMR: 12.3 (N-H), 11.6 (N-H), 11.3 (N-H), 8.0 (Ar C-H), 7.8 (Ar C-H), 7.7 (Ar C-H), 7.4 (Ar C-H), 7.3 (Ar C-H), 7.2 (Ar C-H), 6.9 (Ar C-H), 6.8 (Ar C-H), 6.4 (C-H), 6.1 (C-H), 2.4 (Methyl C-H); Mol. Wt. 338.

Synthesis of N' {4- [2- (1H – benzimidazol-2-yl} - 2 -oxoethyl] phenyl} - 2-ethoxyaceto hydrazide (BG): (Scheme 1B)

% yield: 90%; Melting point (^{0}C): 290°C; Rf Value: 0.7; Benzene: Ethanol (8:1); FTIR (KBr) ν cm^{-1}: 3067.23 (C-H Ar), 2820.38 (C-H Aliphatic), 1632.20 (C=C Ar), 1139.72 (C-C Ar), 3363.39 (N-H Aliphatic), 1232.20 (C-N Ar), 3236.93 (N-H Ar), 1718.26 (C=O) ketone, 1070.30 (C-O aliphatic), 1157.39 (Ether R-O-R Aliphatic); 1H NMR: 12.3 (N-H), 11.8 (N-H), 11.4 (N-H), 8.6 (Ar C-H), 8.5 (Ar C-H), 8.4 (Ar C-H), 8.3 (Ar C-H), 8.0 (Ar C-H), 7.9 (Ar C-H), 7.8 (Ar C-H), 7.3 (Ar C-H), 6.7 (C-H), 6.4 (C-H), 6.1 (C-H), 3.0 Methyl (C-H); GC-MS(m/z): 354; Mol. Wt. 352.

Synthesis of N' {4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxy acetyl benzamide (BH): (Scheme 1B)

% yield: 85%; Melting point (^{0}C): 250°C; Rf Value: 0.6; Benzene: Ethanol (9:1); FTIR (KBr) ν cm^{-1}: 3051.26 (C-H Ar), 2874.38 (C-H Aliphatic), 1671.98 (C=C Ar), 1139.72 (C-C Ar), 1332.57 (C-N Ar), 3406.64 (N-H Ar), 1718.26 (C=O) ketone, 1167.70 (C-O); 1H NMR: 12.0 (N-H), 11.7 (N-H), 11.3 (N-H), 10.8 (N-H), 8.8 (Ar C-H), 8.7 (Ar C-H), 8.6 (Ar C-H), 8.5 (Ar C-H), 8.4 (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), 7.0 (Ar C-H), 6.4 (C-H), 6.3 (C-H); Mol. Wt. 427.

Synthesis of N'- {4- [2- (1H–benzimidazol-2-yl) - 2 -oxoethyl] phenyl} -2-hydroxyaceto hydrazide –N - phenylacetamide (BI): (Scheme 1B)

% yield: 88%; Melting point (^{0}C): 280°C; Rf Value: 0.8; Benzene: Ethanol (8:1); FTIR (KBr) ν cm^{-1}: 3033.48 (C-H Ar), 2736.49 (C-H), 1655.59 (C=C Ar), 1077.05 (C-C Ar), 1261.30 (C-N); 3489.55 (N-H Ar), 1776.34 (C=O) ketone, 1130.32 (C-O), 1H NMR: 12.0 (N-H), 11.7 (N-H), 11.3 (N-H), 10.8 (N-H), 8.8 (Ar C-H), 8.7 (Ar C-H), 8.6 (Ar C-H), 8.5 (Ar C-H), 8.4 (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), 7.0 (Ar C-H), 6.4 (C-H), 6.3 (C-H); Mol. Wt. 399.

Synthesis of N'- {4- [2 - (1H-benzimidazol-2yl) - 2- oxoethyl] phenyl} -2-hydroxyaceto hydrazide N- (2-nitrophenyl) acetamide (BJ): (Scheme 1B)

% yield: 85%; Melting point (^{0}C): 340°C; Rf Value: 0.8; Benzene: Ethanol (4:1); FTIR (KBr) ν cm^{-1}: 3051.80 (C-H Stretch Aromatic), 2743.24 (C-H Aliphatic), 1658.55 (C=C Ar), 1008.59 (C-C Ar), 3433.24 (N-H Ar), 1268.15 (C-N Ar), 3241.70 (N-H Ar), 1729.58 (C=O) ketone, 1124.30 (C-O); 1H NMR: 11.4 (N-H), 11.3 (N-H), 11.0 (N-H), 10.9 (N-H), 8.8 (Ar C-H), 8.7 (Ar C-H), 8.6 (Ar C-H), 8.5 (Ar C-H), 8.4 (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), 7.0 (Ar C-H), 6.3 (C-H), 6.1 (C-H); Mol. Wt. 444.

Synthesis of N'- {4- [2 - (1H-benzimidazol-2yl) - 2- oxoethyl] phenyl} -2-hydroxyaceto hydrazide N- (3-nitrophenyl) acetamide (BK): (Scheme 1B)

% yield: 85%; Melting point (^{0}C): 340°C; Rf Value: 0.8; Benzene: Ethanol (4:1); FTIR (KBr) ν cm^{-1}: 3050.80 (C-H Stretch Aromatic), 2742.24 (C-H Aliphatic), 1668.55 (C=C Ar), 1008.59 (C-C Ar), 3433.24 (N-H Ar), 1268.15 (C-N Ar), 3241.70 (N-H Ar), 1729.58 (C=O) ketone, 1124.30 (C-O); 1H NMR :11.4 (N-H), 11.3 (N-H), 11.0 (N-H), 10.9 (N-H), 8.8 (Ar C-H), 8.7 (Ar C-H), 8.6 (Ar C-H), 8.5 (Ar C-H), 8.4 (Ar C-H), 8.2 (Ar C-H), 7.9 (Ar C-H), 7.7 (Ar C-H), 7.4 (Ar C-H), 7.3 (Ar C-H), 7.0 (Ar C-H), 6.3 (C-H), 6.2 (C-H); Mol. Wt. 444.

Biological evaluation

Synthesized newer benzimidazole derivatives were screened for Anti-bacterial activity. Total 11 compounds (4 Step Products + 7 Benzimidazole Derivatives) were evaluated for their biological

screening. The following section describes, in brief about antibacterial 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 37^0C. Standard: Gentamycin (100µg/mL of DMSO).

RESULTS AND DISCUSSION

The syntheses of benzimidazole derivatives from BE to BK were undertaken as per the scheme 1B. The required N' {4- [2 - (1H–benzimidazole–2-yl) – 2 oxoethyl] phenyl} -2-hydroxyaceto hydrazide (BD) was prepared by mixture of 2gm of 1-(1H-benzimidazole-2yl)-(3hydrazinylphenyl) ethanone and 2ml Hydroxy acetic acid reflux for 2hr. After completion of reaction the contents were allowed to cool obtains reaction mixture, the solid product was obtained. N' {4- [2 - (1H–benzimidazole–2-yl) – 2 oxoethyl] phenyl} -2-hydroxyaceto hydrazide react with different reagent so it gives different benzimidazole derivatives. 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 BD, BE and BJ having the side chain showed higher activity than BF and BG 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 BH, BI and BJ 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 BH, BI and BJ showed highly active compound against *E. coli, Staphylococcus aureus* and *Pseudomonas aureus.* BH showed moderately active compound against *E. coli* and *S. aureus.* BI and BJ showed moderately active compound against *E. coli* and *S. aureus*. Standard (Gentamycin) showed highly active against *E. coli, Pseudomonas aeruginosa* and *S. aureus*.

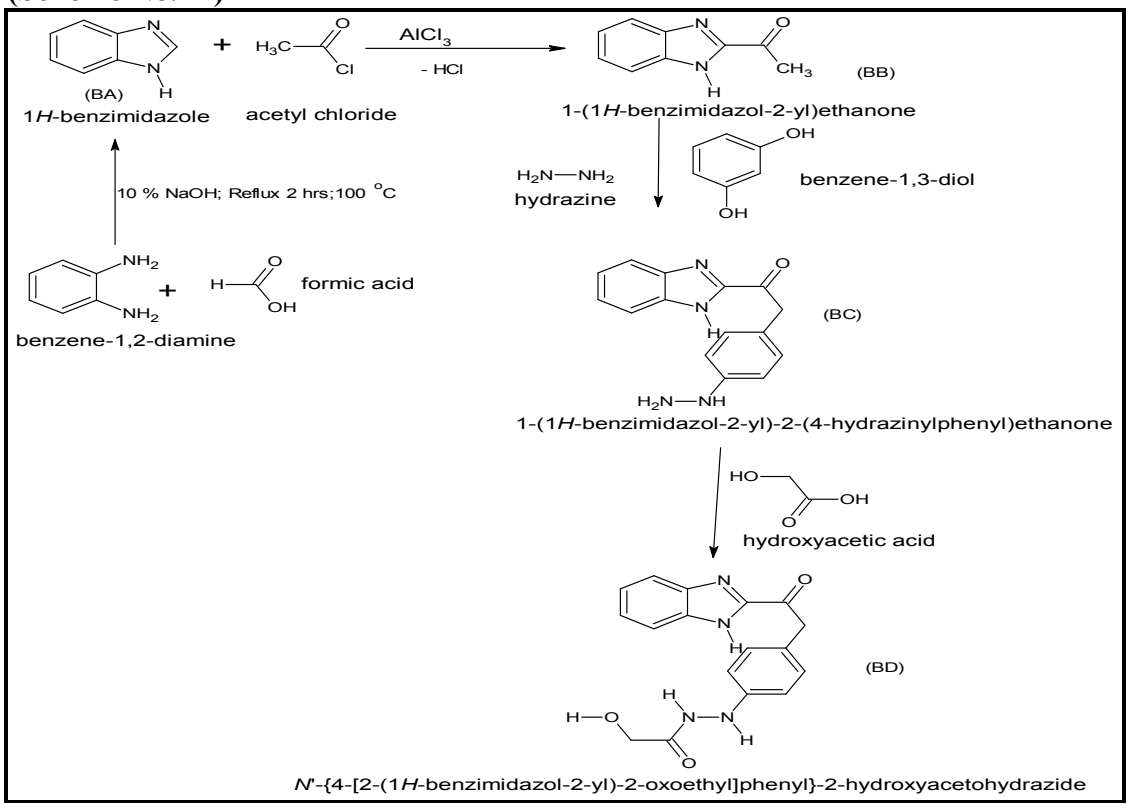
Table No.1: Physical Data of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxy aceto hydrazide (BD) derivatives

S.No	Compounds	Colors of Compounds	Molecular Formula	Melting Point	% yields	Molecular Weight
1	BA	White	C7H6N2	170°C	80%	118
2	BB	Brown	C9H9N2O	230°C	92%	161
3	BC	White	C15H14N4O	270°C	96%	266
4	BD	Brown	C17H16N4O3	280°C	79%	324
5	BE	White	C24H20N4O4	290°C	80%	412
6	BF	Brown	C18H18N4O3	320°C	95%	338
7	BG	White	C19H20N4O3	290°C	90%	352
8	BH	White	C24H21N5O3	250°C	85%	427
9	BI	White	C23H21n5O2	280°C	88%	399
10	BJ	Brown	C23H20N6O4	340°C	85%	444
11	BK	White	C23H20N6O4	340°C	85%	444

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

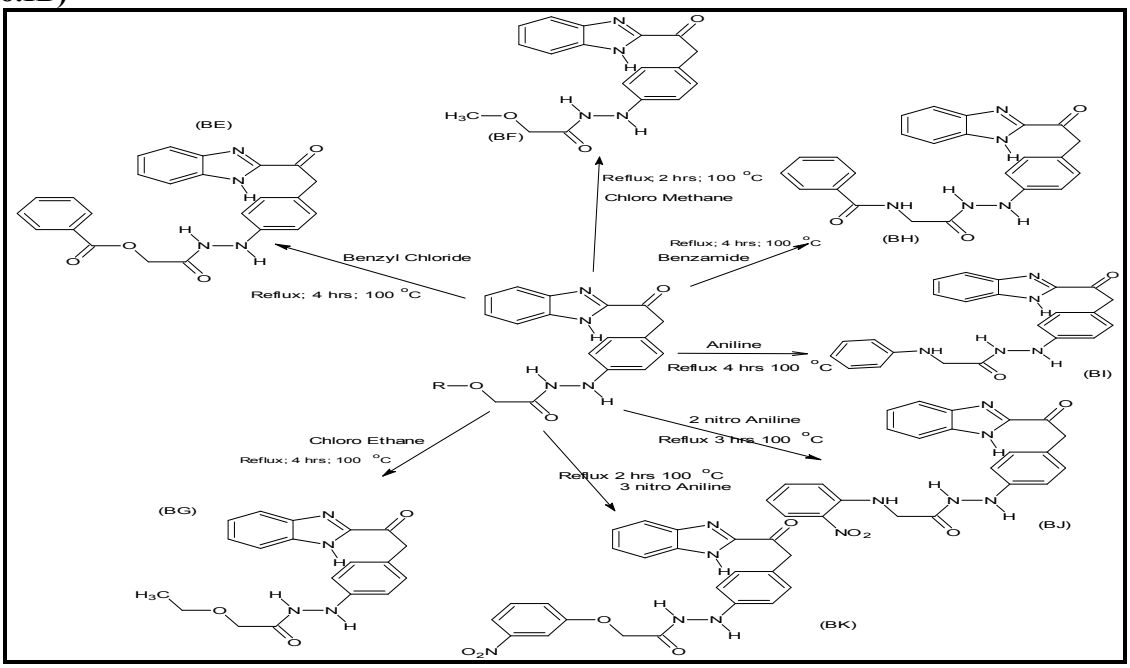
S.No	Compound No	Diameter of zone of inhibition (mm)		
		Escherichia coli	***Staphylococcus aureus***	***Pseudomonasaeruginosa***
		ATCC 25922	ATCC 25923	ATCC 27853
1	BA	12	18	10
2	BB	08	15	09
3	BC	13	20	19
4	BD	14	22	20
5	BE	14	21	21
6	BF	11	18	20
7	BG	15	19	18
8	BH	13	20	19
9	BI	12	20	20
10	BJ	11	20	21
11	BK	15	20	20
12	Gentamycin	20	36	28

Chemistry: (Scheme No.IA)



Scheme No.1A: Synthesis of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide (BD)

(Scheme No.IB)



Scheme No.1B: Synthesis of Synthesis of N'-{4-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-2-hydroxyacetohydrazide (BD) derivatives (BE- BK)

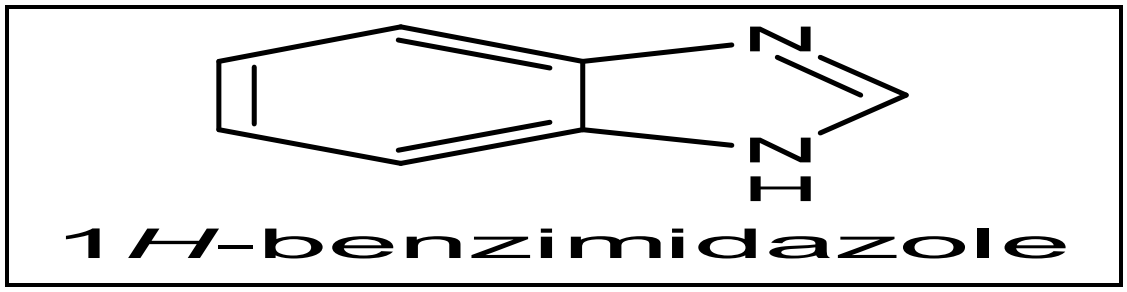


Figure No.1: Benzimidazole heterocyclic nucleus

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

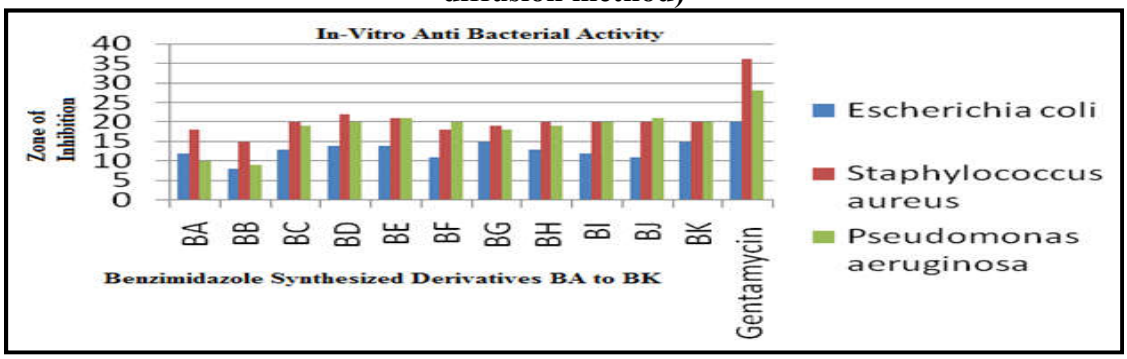


Figure No.3: Antibacterial activity graphical presentation of synthesized compound measuring the zone of inhibition in millimeter

CONCLUSION

Various benzimidazole derivatives was synthesized by N' {4- [2 - (1H–benzimidazole–2-yl) – 2 oxoethyl] phenyl} -2-hydroxyaceto hydrazide (BD}). The total 11 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 Anti-convulsant was taken by using Wistar rats and it having body weight 150-200gm. In this research; derivatives had stronger anti bacterial activity against different types of bacteria. Some of the synthesized compounds were found to have potent anti-bacterial 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 anti-convulsant agents. The synthesize compounds were establish to be AA to AL. The compound Benzimidazole (BA), 1-(1H-benzimidazole-2yl)-(3hydrazinylphenyl) ethanone (BC), N'- {4- [2 - (1H-benzimidazol-2yl) -2- oxoethyl] phenyl} -2-hydroxyaceto hydrazide

N- (3-nitrophenyl) acetamide (BK), N'- {4- [2 -(1H-benzimidazol-2yl) -2- oxoethyl] phenyl} -2-hydroxyaceto hydrazide N- (2-nitrophenyl) acetamide (BJ), N'- {4- [2- (1H–benzimidazol-2-yl) -2 -oxoethyl] phenyl} -2-hydroxyaceto hydrazide – N - phenylacetamide (BI) 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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