

# SYNTHESIS; CHARACTERIZATION AND ANTI INFLAMMATORY ACTIVITY OF “3-(2-[1H BENZIMIDAZOLE-2-YL)-2-OXETHYL] PHENYL) ACETIC ACID AND ITS DERIVATIVES”

## ABSTRACT:

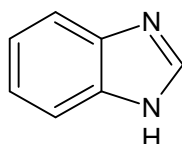
A series of five-membered heterocyclic rings like Benzimidazole were synthesized by the reaction between benzene-1, 2 diamine and formic acid to form various Benzimidazole derivatives (BD- BK) compounds and was tested for their anti-inflammatory activity determined by rat-paw- oedema method. All the synthesis compounds have been characterized by <sup>1</sup>HNMR, IR and some Mass spectral data. The compounds were purified by recrystallization method. The entire compound gives good response for the anti-inflammatory activity: Benzimidazole (AA), 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-phenylacetamide (AJ); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(2-nitrophenyl) acetamide (AK); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(3-nitrophenyl) acetamide (AL). For this anti-inflammatory activity, Indometacin was used as a standard drug and compared to new synthesized drugs. Some new synthesized drugs have shown better activities for the anti-inflammation. The synthesized compounds were established to be AA to AL. The compound AA, AC, AJ, AK and AL were established to be the most potent compound through compare to standard drugs Indomethacin.

## KEYWORDS:

Benzimidazole; Hydroxy acetic acid; Benzene-1, 2-diol; 2- Nitro Aniline; Indometacin; Anti-inflammatory activity

## INTRODUCTION:

Inflammation is an important pathogenetic factor in a variety of disorders. It is a serious issue in modern medicine. Nowadays, NSAIDs are widely used and account for 20% of the global population. They have antipyretic, analgesic, and anti-inflammatory effects. In 1944, the benzimidazole nucleus was found. It contains a fused benzene and imidazole ring. 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 Fig 1). Nowadays benzimidazole is a moiety of choice which possesses many pharmacological properties.



1H-benzimidazole

**Fig.1 Benzimidazole heterocyclic nucleus**

Benzoglyoxalines are another name for benzimidazoles. Since 1960, a molecule comprising benzimidazole and benzene rings has been widely employed in pharmaceutical applications [3-5]. The active ingredients of various medications are 1-H-benzimidazole rings, which have outstanding basic properties due to their nitrogen presence. These compounds have also been tested for anti-inflammatory

action [6-9]. Because of their physiological features, five-membered-ring aromatic systems with one heteroatom in a symmetrical position have received the most attention [10-11]. It is also well recognised that several benzimidazole derivatives have a wide range of pharmacological effects, including antibacterial, anticonvulsant, and antifungal capabilities.

## **MATERIALS AND METHODS:**

### **Materials:**

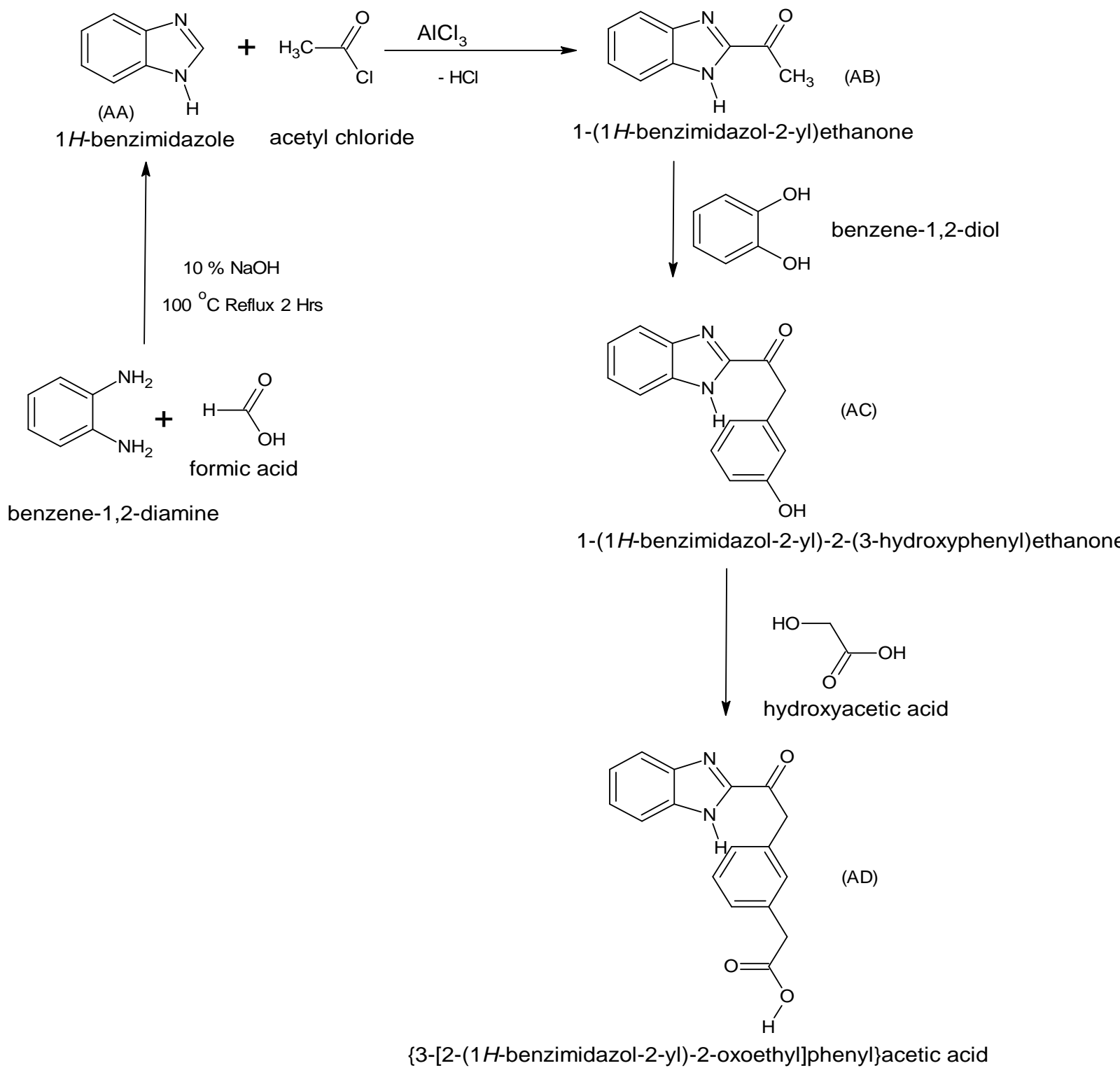
Formic acid; Acetyl Chloride; Benzene-1,2-diol; Glycolic Acid; Benzoyl Chloride; Methyl Chloride; Ethyl Chloride; Benzamide; Aniline; 2-Nitro Aniline; 3- Nitro Aniline All chemicals were of analytical grade. All chemicals were of purchased from Modern Chemicals, Nashik and Some chemicals are available 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). <sup>1</sup>H-NMR spectra were recorded on a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as internal standard in DMSO-d<sub>6</sub>/CDCl<sub>3</sub> 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 1.

## **EXPERIMENTAL WORK:**

**Chemistry: (Scheme IA)**



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



**(Scheme IB):**

UNDER PEER REVIEW

**Scheme 1B: Synthesis of 3-(2-(1H benzimidazole 2yl)-2-oxethyl) phenyl) acetic acid derivatives  
(AE- AL)**

**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 25 ml 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 reflux 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 recrystallized 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 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 recrystallized 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 recrystallized 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AE): (Scheme 1B)**

In a round-bottomed flask; take 2gm of {3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl]phenyl}acetic acid and 4 ml 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 recrystallized 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AF): (Scheme 1B)**

In a round-bottomed flask; take 2gm of {3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl]phenyl}acetic acid and benzoic acid in RBF; reaction mixture was heated under reflux 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 recrystallized 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 methyl {3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate (AG): (Scheme 1B)**

In a round-bottomed flask; take 2 gm 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 recrystallized from methanol to give methyl {3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate. Cool at room temperature; filter the product. Wash with cold water.

**Synthesis of ethyl {3-[2-(1H-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 reflux 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 recrystallized from methanol to give ethyl {3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate. Cool at room temperature; filter the product. Wash with cold water.

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

In a round-bottomed flask; take 2 gm 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 recrystallized 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 recrystallized 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 2 gm 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 recrystallized 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 2 gm 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 recrystallized from methanol to give 2- {3-(2-(1-*H* benzimidazole-2yl)2oxoethyl) phenyl}N-(3-nitrophenyl) acetamide.

**Characterization:**

**Table 1: Physical Data of 3-(2-[1*H* benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD) derivatives**

SR. NO.	Compounds	Colors Of Compounds	Molecular Formula	Melting Point	% yields	Molecular Weight
1	AA	WHITE	C <sub>7</sub> H <sub>6</sub> N <sub>2</sub>	170°C	80%	118
2	AB	YELLOWISH	C <sub>9</sub> H <sub>9</sub> N <sub>2</sub> O	180°C	92%	161
3	AC	WHITE	C <sub>15</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	181°C	51%	236
4	AD	BROWN	C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	192°C	82%	278
5	AE	WHITE	C <sub>24</sub> H <sub>18</sub> N <sub>2</sub> O <sub>4</sub>	198°C	82%	398
6	AF	YELLOWISH	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub>	200°C	75%	338
7	AG	WHITE	C <sub>19</sub> H <sub>18</sub> N <sub>2</sub> O <sub>3</sub>	195°C	89%	308
8	AH	WHITE	C <sub>24</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub>	197°C	95%	322
9	AI	WHITE	C <sub>23</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub>	201°C	89%	397
10	AJ	YELLOWISH	C <sub>23</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub>	202°C	65%	369
11	AK	GREY	C <sub>23</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub>	205°C	72%	414
12	AL	WHITE	C <sub>23</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub>	202°C	72%	354

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-[1*H* benzimidazole-2-yl)-2-oxethyl] phenyl) acetic acid (AD) derivatives were shown in Table 1.

**Spectral Data:****Synthesis of Benzimidazole (AA) :( Scheme 1 A):**

% yield:80%; Melting point ( $^{\circ}\text{C}$ ) : 170 $^{\circ}\text{C}$ ; Rf Value :0.9; Benzene :Ethanol (4:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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);  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  ppm: 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 ( $\text{M}^+$ ), 118 ( $\text{M}^++1$ ) Mol.Wt. 118.

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

% yield:92%; Melting point ( $^{\circ}\text{C}$ ) : 230 $^{\circ}\text{C}$ ; Rf Value :0.8; Benzene :Ethanol (9:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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);  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  ppm: 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 ( $\text{M}^+$ ), 161 ( $\text{M}^++1$ ); Mol.Wt. 161.

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

% yield:51%; Melting point ( $^{\circ}\text{C}$ ) : 187 $^{\circ}\text{C}$ ; Rf Value :0.5; Chloroform: Methanol (7:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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);  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  ppm: 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 ( $\text{M}^+$ ), 236 ( $\text{M}^++1$ );Mol.Wt. 236

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

% yield:82%; Melting point ( $^{\circ}\text{C}$ ) : 192 $^{\circ}\text{C}$ ; Rf Value :0.8; Chloroform :Ethanol (7:3); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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;  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  ppm: 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AE): (Scheme 1 B)**

% yield: 75%; Melting point ( $^{\circ}\text{C}$ ) : 198 $^{\circ}\text{C}$ ; Rf Value: (0.6);Chloroform: Ethanol (9:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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);  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  ppm: 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetic benzoic anhydride (AF): (Scheme 1 B)**

% yield: 89; Melting point ( $^{\circ}\text{C}$ ) : 200 $^{\circ}\text{C}$ ; Rf Value: 0.8; Chloroform: Ethanol 7:3); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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;  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetate (AG): (Scheme 1 B)**

% yield: 95%; Melting point ( $^{\circ}\text{C}$ ) : 199 $^{\circ}\text{C}$ ; Rf Value: 0.7; chloroform: Ethanol (8:2); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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);  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  ppm: 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-(1H-benzimidazol-2-yl)-2-oxoethyl]phenyl}acetate (AH): (Scheme 1 B)**

% yield: 95%; Melting point ( $^{\circ}\text{C}$ ) : 202 $^{\circ}\text{C}$ ; Rf Value: 0.6; Chloroform: Ethanol( 9:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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);  $^1\text{H NMR}$  (500 MHz)  $\text{CDCl}_3$   $\delta$  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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl} acetyl) Benzamide (AI): (Scheme 1 B)**

% yield: 89%; Melting point ( $^{\circ}\text{C}$ ) : 204 $^{\circ}\text{C}$ ; Rf Value: 0.7; Chloroform: Ethanol (8:2); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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)  $\text{CDCl}_3$   $\delta$  ppm: 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-phenylacetamide (AJ): (Scheme 1 B)**

% yield: 65%; Melting point ( $^{\circ}\text{C}$ ) : 206 $^{\circ}\text{C}$ ; Rf Value: 0.6; Chloroform: Ethanol (9:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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)  $\text{CDCl}_3$   $\delta$  ppm: 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(2-nitrophenyl) acetamide (AK): (Scheme 1B)**

% yield: 95%; Melting point ( $^{\circ}\text{C}$ ) : 199 $^{\circ}\text{C}$ ; Rf Value: 0.8; chloroform: Ethanol (9:1); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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)  $\text{CDCl}_3$   $\delta$  ppm: 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-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(3-nitrophenyl) acetamide (AL): (Scheme 1B)**

% yield: 92; Melting point ( $^{\circ}\text{C}$ ) : 200 $^{\circ}\text{C}$ ; Rf Value: 0.8; Chloroform: Ethanol 7:3); FTIR (KBr)  $\nu$   $\text{cm}^{-1}$  : 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)  $\text{CDCl}_3$   $\delta$  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-inflammatory activity. Total 12 compounds (4 Step Products + 8 Benzimidazole Derivatives) were evaluated for their biological screening. The following section describes, in brief the Anti-inflammatory activity.

**Anti-inflammatory activity:**

Anti-inflammatory activity of all synthesized benzimidazole derivatives was determined by the carrageen an- induced rat paw oedema model. Wister rats (100-200 g) were divided into 3 groups as control, test and standard [12-15]. In each group there are six animals per group. During experiment; overnight fasted animals were used and during that period only distilled water was given to animals. Generally, Indomethacin was used as standard drug. Both test and standard drugs were suspended in 1% carboxymethyl cellulose (CMC) and administered orally through the Gavage needle. 1% of Carboxymethyl cellulose (CMC) was administered in control group [16-18]. After 1 hr of administering the compound, we induced the carrageen an (1%) by the sub planner surface of the right hind paws of animals. The initial paw volume and also the paw volume after 3 and 6 h of administrating carrageen a were measured. Percent paw oedema inhibition was calculated for benzimidazole derivatives [19-20].

**Table 2: Anti-inflammatory activities of compounds AA to AK**

Code	Dose Mg/Kg	Inhibition of paw oedema after 3 h (%)1	Inhibition of paw oedema after 6 h (%)2
AA	30 mg/Kg	4.28 $\pm$ 0.28	88.24
AB	30 mg/Kg	2.48 $\pm$ 0.23	68.48
AC	30 mg/Kg	4.46 $\pm$ 0.22	51.16
AD	30 mg/Kg	2.62 $\pm$ 0.27	78.98
AE	30 mg/Kg	4.26 $\pm$ 0.241	69.48
AF	30 mg/Kg	3.22 $\pm$ 0.281	53.98
AG	30 mg/Kg	1.52 $\pm$ 0.271	79.54

AH	30 mg/Kg	3.48 ± 0.23	59.24
AI	30 mg/Kg	4.26 ± 0.241	76.48
AJ	30 mg/Kg	3.22 ± 0.281	61.16
AK	30 mg/Kg	4.52 ± 0.271	70.98
AL	30 mg/Kg	5.26 ± 0.241	79.48
Control	-	0.36 ± 0.28	-
Indomethacin	40	2.78 ± 0.340	67.44

1: Dose for 1-7: 30 mg/Kg; 2: Dose for indomethacin 40 mg/Kg b.wt; mean ± SEM; n+6

## RESULT 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. <sup>1</sup>H-NMR spectra were recorded on a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as an internal standard in DMSO-d<sub>6</sub>/CDCl<sub>3</sub> and mass spectra was obtained on JEOL GCMATE II. At the end of the experiment, it has been concluded that the compounds synthesized in the project have good yield value. The synthesized oxadiazole compounds were identified and characterized by IR, <sup>1</sup>H NMR and MASS spectra. Then, the pharmacological activity was done. The entire compound had a good response for Anti-inflammatory activity: Benzimidazole (AA), 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-phenylacetamide (AJ); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(2-nitrophenyl) acetamide (AK); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(3-nitrophenyl) acetamide (AL).. The results of Anti-inflammatory activity testing of the prepared compounds were shown in Table 2.

## 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 Anti-inflammatory activity was taken by using Wistar rats and it having body weight 150-200 gm. In this research; benzimidazole derivatives had stronger Anti-inflammatory activity against inflammation. Synthesized compounds exhibited more activity when compared to other benzimidazole. Hence, it can be concluded that the benzimidazole derivatives can be potentially developed into useful anti-convulsant agents. The synthesized compounds were established to be AA to AL. The compound Benzimidazole (AA), 1-(1H-benzimidazol-2-yl)-2-(3-hydroxyphenyl) ethanone (AC); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-phenylacetamide (AJ); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(2-nitrophenyl) acetamide (AK); 2-{3-[2-(1H-benzimidazol-2-yl)-2-oxoethyl] phenyl}-N-(3-nitrophenyl) acetamide (AL). were established to be the most potent compound as compared to standard drugs Indomethacin.

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