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Synthesis of Some Novel 1, 2, 4-Triazole Derivatives Bearing Benzimidazole Nucleus and Biological Evaluation of Their Possible *In Vitro* Anti Inflammatory and Antioxidant Activity.

Sahoo Ujjwal*, Seth AK, and Balaraman R.

Department of Pharmacy, Sumandeep Vidyapeeth University, Vadodara-391760, Gujarat, India.

ABSTRACT

Series of 4-[1-({5-[3-(substituted) phenyl]-4*H*-1, 2, 4-triazol-3-yl} methyl)-5- substituted -1*H*-benzimidazol-2-yl] benzonitrile **8(I-XXXI)** were synthesized. Substituted o-phenylenediamine was reacted with substituted 4-cyanobenzaldehydes in the presence of sodium metabisulfite to furnish substituted 2-(4-Cyanophenyl)-1H-benzimidazoles **(1)**. When these substituted 2-(4-Cyanophenyl)-1H-benzimidazoles were further treated with ethyl chloroacetate in KOH/DMSO, N-alkylated product (2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid ethyl esters **(2)** was formed. To synthesize 2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid hydrazides **(3)** chemical reactions were conducted between Hydrazine hydrate and the esters **(2)**. The structures of newly synthesized compounds **8(I-XXXI)** was confirmed by suitable spectroscopic techniques such as IR, ^{1}H NMR, ^{13}C NMR and m/z ratio. All the synthesized compounds were screened for its in-vitro anti-oxidant and anti-inflammatory activity. The in-vitro anti-oxidant and anti-inflammatory activity might be attributed due to the presence of more electrons withdrawing group and moiety having more lipophilicity also more electro negativity in nature.

Keywords: o-phenylenediamine, 4-cyanobenzaldehyde, 1, 2, 4-triazole, Antioxidant, Anti-inflammatory

Corresponding author

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INTRODUCTION

The structural and therapeutic diversity coupled with commercial capability of small molecules has enthralled organic and medicinal chemists. There has been significant interest in the chemistry of triazole ring systems, which is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activity. In the past few years, research for new non-steroidal anti-inflammatory agents has been reported that many compounds having a 1,2,4-triazole derivatives are known for their anti-inflammatory activity[1-6].

From the literature survey it was found that, depending on the type of substituent, the derivatives of 1, 2, 4-triazole has a high potential for biological activity, possessing a wide range of antimicrobial[7-10] and antitumor [11-14] properties. The other triazole derivatives show anti-inflammatory [15], antihypertensive [16], anticonvulsant, antiviral [17] and analgesic activities [18].

Also a number of benzimidazole derivatives were identified as potent analgesic and anti-inflammatory compounds [19,20].

Therefore, in the present paper it was planned to incorporate the benzimidazole moiety with 1, 2, 4-triazole to have better antioxidant and anti-inflammatory activity.

MATERIALS AND METHODS

Chemistry

Melting points were determined by open capillary method and were uncorrected. The IR spectra (in KBr) were recorded on a Shimadzu IR Affinity-1 spectrophotometer. ^{1}H NMR and ^{13}CNMR spectra were recorded on a Perkin–Elmer EM 300 MHz spectrometer using TMS as internal standard. The mass spectra were recorded on a JEOL JMS-D 300 spectrometer operating at 70 eV. Purity of the compounds was checked by TLC silica coated plates obtained from Merck. All characterization data are mention in Table 1.

General procedure for the preparation of4-[1-({5-[3-(substituted) phenyl]-4*H*-1, 2, 4-triazol-3-yl} methyl)-5- substituted -1*H*-benzimidazol-2-yl] benzonitrile **8(I-XXXI)**

The mixture of 2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid hydrazide **(3)** (0.1 mol) in acetic acid (20 ml), a pinch of ammonium acetate was added followed by the addition of aromatic aldehydes (0.1 mol). The mixture was stirred for 24 hr. at room temperature.

The mother liquor on neutralization with sodium bi-carbonate solution gave a solid, which was filtered and recrystallized from ethanol.

Biological Evaluation

Radical scavenging assays by the DPPH

This experimental procedure was adapted from [21]. In an ethanol solution of 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical, test compounds at different concentrations were added. The reaction mixtures were shaken vigorously and then kept in the dark for 30 min. The absorbance of the resulting solutions was measured in 1 cm cuvettes, using a UV/VIS spectrophotometer at 328nmagainst blank without DPPH. Decreasing of DPPH solution absorbance indicates an increase of DPPH radical scavenging activity. This activity is given as % DPPH radical scavenging that is calculated in the equation:

$$\text{Percentage inhibition} = \frac{\text{Absorbance of control - Absorbance of test}}{\text{Absorbance of control}} \text{ X } 100$$

The DPPH solution without sample solution was used as control. All tests were run in triplicate and averaged. Ascorbic acid was used as positive control in Table 2 and Figure 2.

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In vitro anti-inflammatory activity by inhibition of protein denaturation method

Test solution (0.5 mL) consists of 0.45 mL of BSA (5% w/v aqueous solution) and 0.05 mL of different concentration of test solutions (50, 100, 150, 200 µg/mL). Test control solution (0.5 mL) consists of 0.45 mL of BSA (5% w/v aqueous solution) and 0.05 mL of distilled water. Product control solution (0.5 mL) consists of 0.45 mL of distilled water and 0.05 mL of different concentration of test solutions (50, 100, 150, 200 µg/mL). Standard solution (0.5 mL) consists of 0.45 mL of BSA (5%w/v aqueous solution) and 0.05 mL different concentration of Diclofenac Sodium's (50, 100, 150, 200 µg/ mL). All the above solutions were adjusted to pH 6.3 using 1N hydrochloric acid. The samples were incubated at 37^0C for 20 min and the temperature was increased to keep the samples at 57^0C for 3 min. After cooling, 2.5 mL of phosphate buffer saline was added to the above solutions. The absorbance was measured using UV Visible spectrophotometer at 416 nm [22]. The percentage inhibition of protein denaturation was calculated as,

$$\text{Percentage inhibition} = \frac{\text{O. D of Test Solution - O. D of Product Control}}{\text{O. D of Test Control}} \text{ X } 100$$

The results were compared with Diclofenac Sodium in Table 3 and Figure 3.

RESULTS AND DISCUSSION

For the synthesis of the target compounds the reaction sequences outlined in Scheme 1,werefollowed.4-[1-({5-[3-(substituted) phenyl]-4*H*-1, 2, 4-triazol-3-yl} methyl)-5- substituted -1*H*-benzimidazol-2-yl] benzonitrile **8(I-XXXI)**were synthesized employing conventional techniques. Substituted o-phenylenediamine was reacted with appropriately substituted 4-cyanobenzaldehydes in the presence of sodium metabisulfite to furnish substituted 2-(4-Cyanophenyl)-1H-benzimidazoles **(1)**. These substituted 2-(4-Cyanophenyl)-1H-benzimidazoles were further treated with ethyl chloroacetate in KOH/DMSO gave the N-alkylated product, (2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid ethyl esters **(2)**. To endow2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid hydrazide **(3)** reaction were occurred between Hydrazine hydrate and the esters **(2)** in Figure 1.

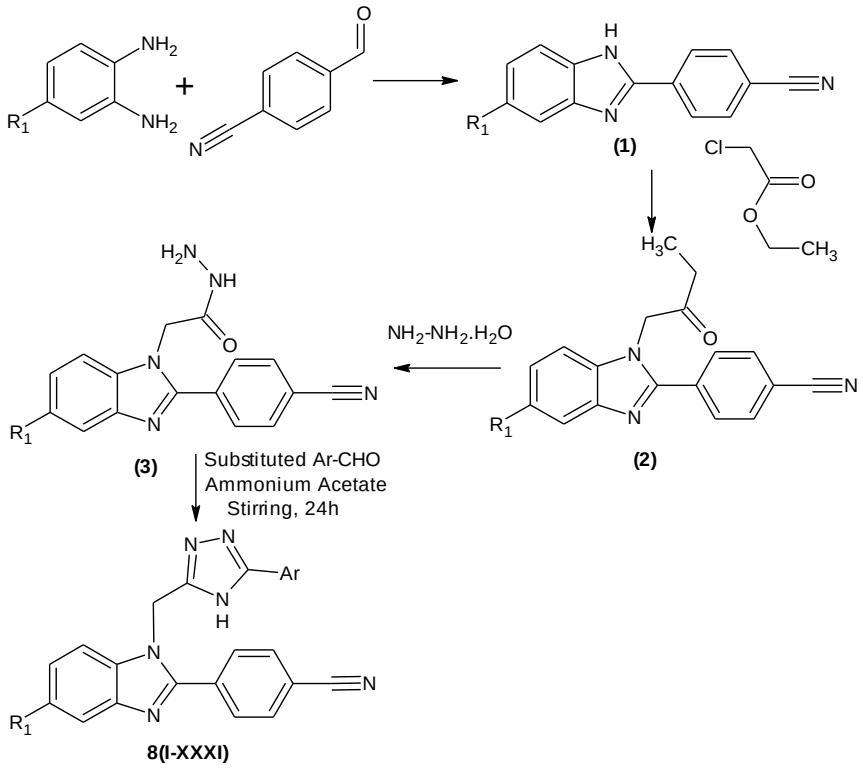

Figure 1: Scheme 2 Synthetic route for the preparation of the compounds

8. III: 4-(1-{[5-(2-methoxylphenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 32%; m.p.: 214-216; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 1145 (C-O-C)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.431 (s, 2H, $-CH_2$), 3.87 (s, 3H, $-CH_3$), 6.69-8.57 (m, 11H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 55, 109, 111, 112, 114, 117, 119, 122, 126, 130, 133, 134, 136, 141, 145, 151, 155, 157, 168; MS: m/z 451 (M^+)

8. VI: 4-(1-{[5-(4, 5-difluoro-2-hydroxyphenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 27%; m.p.: 273-275; IR (Cm^{-1}): 3467 (O-H), 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 1333 (C-F)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 6.48-8.43 (m, 9H, aromatic protons), 6.166 (s, 1H, NH), 6.166 (s, 1H, OH), ^{13}C: 50, 108, 110, 111, 112, 114, 117, 119, 130, 134, 136, 141, 144, 145, 151, 153, 154, 156, 168; MS: m/z 473 (M^+)

8. VII: 4-(1-{[5-(3, 5-dichlorophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 21%; m.p.: 242-244; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.36-8.43 (m, 9H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 112, 114, 119, 128, 129, 130, 133, 134, 136, 139, 141, 144, 145, 151, 152, 168; MS: m/z 490 (M^+)

8. VIII: 4-(5-chloro-1-{[5-(2-chloro-4-nitrophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-1*H*-benzimidazol-2-yl) benzonitrile
Yield 28%; m.p.: 274-276; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.23-8.29 (m, 10H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 114, 119, 122, 123, 124, 125, 127, 129, 130, 134, 137, 140, 145, 148, 151, 152, 168; MS: m/z 490 (M^+)

8. IX: 4-[1-({5-[2-bromo-4-(trifluoromethyl) phenyl]-4*H*-1, 2, 4-triazol-3-yl} methyl)-5-nitro-1*H*-benzimidazol-2-yl] benzonitrile
Yield 32%; m.p.: 210-212; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 1333 (C-F), 567 (C-Br)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.36-8.43 (m, 10H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 112, 114, 119, 121, 124, 127, 128, 129, 130, 134, 135, 136, 141, 144, 145, 149, 151, 168; MS: m/z 568, 570 (M^+)

8. XI: 4-(1-{[5-(2-chloro-4, 5-dimethoxyphenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 35%; m.p.: 210-212; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 1145 (C-O-C), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 3.77 (s, 6H, $-CH_3$), 6.51-8.43 (m, 9H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 56, 111, 112, 113, 114, 118, 119, 126, 130, 134, 136, 141, 144, 145, 150, 151, 152, 153, 168; MS: m/z 516 (M^+)

8. XII: 4-(1-{[5-(2-ethoxy-4-methoxyphenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 25%; m.p.: 212-214; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 1254 (C-C), 1145 (C-O-C)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 4.148-5.43 (s, 4H, $-CH_2$), 1.45-3.82 (s, 6H, $-CH_3$), 5.89-8.93 (m, 9H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 15, 50, 56, 64, 100, 106, 108, 111, 112, 114, 119, 129, 130, 134, 136, 141, 144, 145, 151, 152, 158, 164, 168; MS: m/z 495 (M^+)

8.XV: 4-(1-{[5-[3-ethoxy-4-(prop-2-yn-1-yloxy) phenyl]-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile

Yield 35%; m.p.: 196-198; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 2119 (C≡C), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 1254 (C-C), 1145 (C-O-C)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 2.41 (s, 1H, -CH), 4.09-5.43 (s, 6H, $-CH_2$), 1.488 (s, 3H, $-CH_3$), 6.52-8.60 (m, 10H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 15, 50, 57, 65, 76, 79, 111, 112, 113, 114, 118, 119, 120, 123, 130, 134, 136, 141, 144, 145, 148, 150, 151, 157, 168; MS: m/z 519(M^+)

8. XXI: 4-(5-chloro-1-{[5-(4-chlorophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-1*H*-benzimidazol-2-yl) benzonitrile
Yield 31%; m.p.: 273-275; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1341 (C-N), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.17-8.25 (m, 11H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 114, 119, 123, 124, 128, 129, 130, 131, 134, 135, 137, 145, 149, 151, 168; MS: m/z 445(M^+)

8. XXII: 4-(1-{[5-(4-bromophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-chloro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 22%; m.p.: 253-255; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1341 (C-N), 745 (C-Cl), 567 (C-Br)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.17-8.85 (m, 11H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 114, 119, 123, 124, 125, 128, 129, 130, 133, 134, 137, 145, 150, 151, 168; MS: m/z 490, 492(M^+)

8. XXVI: 4-(1-{[5-(4-chlorophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-5-nitro-1*H*-benzimidazol-2-yl) benzonitrile
Yield 23%; m.p.: 211-223; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1351 (N=O), 1341 (C-N), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.36-8.43 (m, 11H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 112, 114, 119, 128, 129, 130, 131, 134, 135, 136, 141, 144, 145, 149, 151, 168; MS: m/z 456(M^+)
8. XXVIII: 4-(5-chloro-1-{[5-(2-chlorophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-1*H*-benzimidazol-2-yl) benzonitrile
Yield 21%; m.p.: 218-220; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1341 (C-N), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.17-7.91 (m, 11H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 114, 119, 123, 124, 125, 128, 129, 130, 131, 134, 137, 145, 151, 152, 168; MS: m/z 445(M^+)

8. XXX: 4-(5-chloro-1-{[5-(3-chlorophenyl)-4*H*-1, 2, 4-triazol-3-yl] methyl}-1*H*-benzimidazol-2-yl) benzonitrile
Yield 36%; m.p.: 258-260; IR (Cm^{-1}): 3303 (N-H), 3051 (Ar-C-H), 2849 (C-H), 2217 (C≡N), 1645 (C=N), 1555, 1465, 1440 (C=C), 1341 (C-N), 745 (C-Cl)
^{1}H NMR data ($CDCl_3$) δ (ppm) and ^{13}C NMR data (ppm): 5.43 (s, 2H, $-CH_2$), 7.17-8.49 (m, 11H, aromatic protons), 7.613 (s, 1H, NH), ^{13}C: 50, 111, 114, 119, 123, 124, 126, 127, 129, 130, 134, 137, 145, 150, 151, 168; MS: m/z 445(M^+)

The compounds **8.XV** (237±1.077) µg/ml **and 8.XXII** (214±1.17) µg/ml were highly active at low concentration and compounds **8.VI** (261±0.95) µg/ml**, 8.VII** (278±1.102) µg/ml**, 8.IX** (279±1.312) µg/ml**, 8.XI** (388±1.152) µg/ml**, 8.XII** (283±1.29) µg/ml**, 8.XXI** (278±0.95) µg/ml**, 8.XXVIII** (281±0.882) µg/ml and **8.XXX** (301±1.012) µg/ml were moderately active at higher concentration as compared to ascorbic acid (109±0.7296) µg/ml in free radical scavenging activity by 2, 2-diphenyl-1-picryl hydrazide assay method.

In vitro anti-inflammatory by inhibition of protein denaturation method the compounds **8.IX** (89.98±1.025) µg/ml**, 8.XI** (60.79±0.96) µg/ml**,8.XVI** (80.41±1.16) µg/ml**, 8.XXI** (95.49±0.96) µg/ml**,8.XXVIII** (84.07±0.8819171) µg/mland**8.XXX** (68.26±0.6896) µg/ml were found to be highly active in low concentration and compounds **8.III**(119.8±0.9614) µg/ml**,8.VI**(118.3±0.9865) µg/ml**,8.VII**(102.1±1.0425) µg/ml**,8.VIII**(137.4±0.67) µg/ml**,8.XII**(113.9±1.052) µg/mland**8.XXVI**(107.1±0.6666) µg/ml were found to be moderately active at higher concentration as compared to diclofenac sodium (57.08±0.7296) µg/ml. The results may be attributes due to the presence of more electrons withdrawing group and moiety having more lipophilicity also more electro negativity in nature.

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Table 1: Characterization Data Scheme 2

Compound Code	R_1	Ar	Molecular Formula	Molecular Weight	Yield (%)	Melting point (^oC)	R_f value
8. I	$-NO_2$	$-C_7H_7Br$	$C_{24}H_{16}BrN_7O_2$	514.33	26	272-274	0.72
8. II	$-NO_2$	$-C_7H_8$	$C_{24}H_{17}N_7O_2$	435.43	31	269-271	0.69
8. III	$-NO_2$	$-C_7H_8O$	$C_{24}H_{17}N_7O_3$	451.43	32	214-216	0.71
8. IV	-Cl	$-C_6H_4BrNO_2$	$C_{23}H_{13}BrClN_7O_2$	534.75	31	211-213	0.69
8. V	$-NO_2$	$-C_6H_5BrO$	$C_{23}H_{14}BrN_7O_3$	516.30	35	270-272	0.72
8. VI	$-NO_2$	$-C_6H_4F_2O$	$C_{23}H_{13}F_2N_7O_3$	473.39	27	273-275	0.73
8. VII	$-NO_2$	$-C_6H_4Cl_2$	$C_{23}H_{13}Cl_2N_7O_2$	490.30	21	242-244	0.72
8. VIII	-Cl	$-C_6H_4ClNO_2$	$C_{23}H_{13}Cl_2N_7O_2$	490.30	28	274-276	0.69
8. IX	$-NO_2$	$-C_7H_4BrF_3$	$C_{24}H_{13}BrF_3N_7O_2$	568.30	32	210-212	0.71
8. X	$-NO_2$	$-C_6H_4ClNO_2$	$C_{23}H_{13}ClN_8O_4$	500.85	31	275-277	0.69
8. XI	$-NO_2$	$-C_8H_9ClO_2$	$C_{25}H_{18}ClN_7O_4$	515.90	35	210-212	0.72
8. XII	$-NO_2$	$-C_9H_{12}O_2$	$C_{26}H_{21}N_7O_4$	495.48	25	212-214	0.73
8. XIII	$-NO_2$	$-C_{10}H_{12}O_3$	$C_{27}H_{21}N_7O_5$	523.49	22	184-186	0.72
8. XIV	$-NO_2$	$-C_9H_{11}BrO$	$C_{26}H_{20}BrN_7O_3$	558.38	24	210-212	0.69
8. XV	$-NO_2$	$-C_{11}H_{12}O_2$	$C_{28}H_{21}N_7O_4$	519.51	35	196-198	0.71
8. XVI	$-NO_2$	$-C_8H_{10}O_3$	$C_{25}H_{19}N_7O_5$	497.46	33	224-226	0.69
8. XVII	-Cl	$-C_6H_4N_2O_5$	$C_{23}H_{13}ClN_8O_5$	516.85	22	253-255	0.72
8. XVIII	$-NO_2$	$-C_{14}H_{22}O$	$C_{31}H_{31}N_7O_3$	549.62	35	244-246	0.73
8. XIX	$-NO_2$	$-C_9H_{10}O$	$C_{26}H_{19}N_7O_3$	477.47	25	253-255	0.72
8. XX	$-NO_2$	$-C_9H_8N_2$	$C_{26}H_{17}N_9O_2$	487.47	34	283-285	0.69
8. XXI	-Cl	$-C_6H_5Cl$	$C_{23}H_{14}Cl_2N_6$	445.30	31	273-275	0.71
8. XXII	-Cl	$-C_6H_5Br$	$C_{23}H_{14}BrClN_6$	489.75	22	253-255	0.69
8. XXIII	-Cl	$-C_6H_6O_2$	$C_{23}H_{15}ClN_6O_2$	442.85	33	266-268	0.72
8. XXIV	$-NO_2$	$-C_6H_6O_2$	$C_{23}H_{15}N_7O_4$	453.40	36	225-227	0.73
8. XXV	$-NO_2$	$-C_6H_5Br$	$C_{23}H_{14}BrN_7O_2$	500.30	18	210-212	0.72
8. XXVI	$-NO_2$	$-C_6H_5Cl$	$C_{23}H_{14}ClN_7O_2$	455.85	23	211-223	0.69
8. XXVII	$-NO_2$	$-C_7H_8O$	$C_{24}H_{17}N_7O_3$	451.43	22	222-224	0.71
8. XXVIII	-Cl	$-C_6H_5Cl$	$C_{23}H_{14}Cl_2N_6$	445.30	21	218-220	0.69
8. XXIX	-Cl	$-C_6H_7N$	$C_{23}H_{16}ClN_7$	425.87	17	208-210	0.72
8. XXX	-Cl	$-C_6H_5Cl$	$C_{23}H_{14}Cl_2N_6$	445.30	36	258-260	0.73
8. XXXI	$-NO_2$	$-C_6H_5Cl$	$C_{23}H_{14}ClN_7O_2$	455.85	20	218-220	0.72

Table 2:The IC_{50}±SEM (Standard Error Of Mean) Values Of Ascorbic Acid And Compounds, Values Represent The Mean Of Triplicates

Compound	IC_{50}Value(µg/ml)	IC_{50}Value±SEM (µg/ml)
8.VI	261	261±0.95
8.VII	278	278±1.10
8.IX	279	279±1.31
8. XI	388	388±1.15
8. XII	283	283±1.29
8.XV	237	237±1.07
8. XXI	278	278±0.95
8. XXII	214	214±1.17
8. XXVIII	281	281±0.88
8. XXX	301	301±1.01
Ascorbic Acid	109	109±0.72

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Table 3: The IC_{50}±SEM (Standard Error Of Mean) Values Of Diclofenac Sodium And Compounds, Values Represent The Mean Of Triplicates

Compound Code	IC_{50} Value(µg/ml)	IC_{50} Value±SEM(µg/ml)
8. III	119.8	119.8±0.96
8.VI	118.3	118.3±0.98
8.VII	102.1	102.1±1.04
8.VIII	137.4	137.4±0.67
8.IX	89.98	89.98±1.02
8. XI	60.79	60.79±0.96
8. XII	113.9	113.9±1.05
8.XVI	80.41	80.41±1.16
8. XXI	95.49	95.49±0.96
8. XXVI	107.1	107.1±0.66
8. XXVIII	84.07	84.07±0.88
8. XXX	68.26	68.26±0.68
Diclofenac Sodium	57.08	57.08±0.72

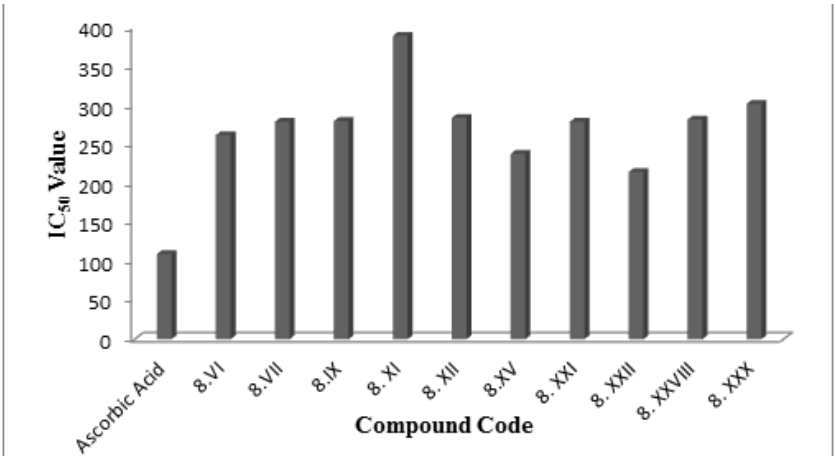

Figure 2: Comparison of IC_{50} values of compounds and ascorbic acid

The IC_{50} values of compounds and ascorbic acid (standard) in 2, 2-Diphenyl-1-Picryl Hydrazide screening of antioxidant activity, the results are (mean±SEM) of three experiments, performed in triplicate.

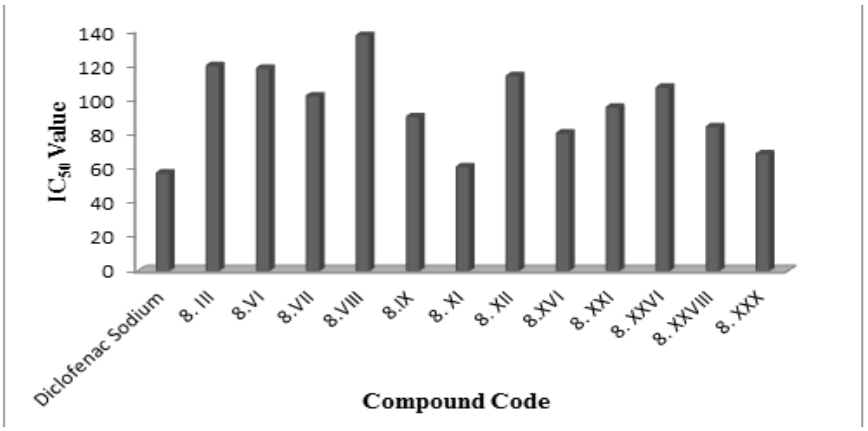

Figure 3: Comparison of IC_{50} values of compounds and diclofenac sodium

The IC_{50} values of compounds and diclofenac sodium (standard) in inhibition of protein denaturation screening of In Vitro Anti-Inflammatory activity, the results are (mean±SEM) of three experiments, performed in triplicate.

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