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Synthesis, characterization and biological study of new benzoxazole based sulphonamide derivatives

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ABSTRACT

Benzoxazoles are privileged organic compounds of medicinal significance, found in many natural products and are used in drug discovery programme. Eleven newly synthesized 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides derivatives were characterized by means of chromatography, IR, ^{1}H-NMR and Mass spectral analysis.4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides have significant biological activity in varied degrees. The investigation of anti-inflammatory activity revealed that the test compounds of 4-amino-N-[1,3-benzoxazole-2-yl] benzene sulphonamides showed favorable anti inflammatory activity at a dose of 30mg/kg bw. Among the titled compounds some were having potent antioxidant activity. Besides its use in medicinal chemistry, these are recognized as fluorescent probes such as anion and metal cation sensors, as photo chromatic agents and laser dyes.

Key words: Benzoxazoles, spectral analysis, anti-inflammatory activity, antioxidant and fluorescent probes.

INTRODUCTION

Biologically active benzoxazole derivatives have been known for long time, since benzoxazoles can be considered as structural isosteres of the naturally occurring nucleic bases adenine and guanine, which allow them to interact easily with polymers of living systems. Benzoxazoles possess most remarkable and a wide range of biological activities. Benzoxazole derivatives are potential synthons for building synthetically a variety of chemical systems known for their broader biological and pharmacological properties. The literature survey reveals that substituted benzoxazoles have been shown to exhibit activity against platelet aggregation, inflammation and cell proliferation[1], anti inflammatory activity[2-8,10],COX-2 inhibitory[9], screened for their gastric ulceration on potential in tested animals[11],antimicrobial activity against some gram positive and gram negative bacteria and fungi[12-15], HIV-1 reverse transcriptase inhibitor activity[16], as DNA Topoisomerase I and II Inhibitors[17] anticancer activity[18-19] and anti diabetic[20] activities.

Recent observations suggest that substituted benzoxazoles and related heterocyclics, possesses potential activity with lower toxicities in the chemotherapeutic approach in man. Although they have been known from long ago to be biologically active, their varied biological features are still of great scientific interest. A brief account of various alterations conducted on benzoxazole ring and their associated biological activities was incorporated in the present work.

It is interesting to note from the literature that the benzoxazole moiety is yet to be explored both synthetically and biologically, in spite of the extensive work reported so far on benzoxazoles. Technology now plays a major role in the field of drug discovery and drug development. Many simulation techniques are available in aid of such research.

In view of the biological prominence of the benzoxazole moiety it is planned to synthesize some new 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides.

MATERIALS AND METHODS

All chemical in the present study of synthesis of new 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides from Sigma Aldrich (LR grade) and Merck were used in the present synthesis work.

Instruments used:
The instruments such as Infrared spectra are recorded on Perkin Elmer model 283B and Nicolet 740 FT-IR instruments and values are given in cm^{-1}.Proton Nuclear Magnetic Resonance spectra are recorded on varian Gemini-200, varian Unity-200 and advance-300MHZ Bruker UX-NMR instrument. The samples are made in chloroform-d (1:1) or/and DMSO-d6 using tetra methyl silane (Me_4Si) as the internal standard.ESI Mass spectra were recorded on Micro mass Quattro LC using ESI+ software with Capillary voltage 3.98 kV and ESI mode positive ion trap detector. High-resolution mass spectra (HRMS) were recorded on a QSTAR XL Hybrid MS–MS Mass spectrometer. Elemental analysis is carried out on VARFIO EL, se Elementor**.** Analytical Thin-layer Chromatography (TLC) is performed on pre coated silica-gel-60 F254 (0.5mm) glass plates. Visualisation of the sports on TLC plates is achieved either to iodine vapour or UV light. Yields of materials judged homogenous by TLC and NMR spectroscopy. Melting points were recorded on Melter Fp-51 instrument and were uncorrected were used for the characterization of synthesized compounds.

Synthesis of new 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides was carried out starting from 4-chorophenol and 4-hydroxy phenylacetate to 1,3- benzoxazole-2-amine was shown in step-1 of the synthetic scheme. In step-2 and 3, 2-amino benzoxazole and acetanilide transformed into N-[4-(1, 3-benzoxazol-2-ylsulfomoyl) phenyl] acetamide intermediate, which was later converted into 4-amino-N -(1, 3-benzoxazole-2-yl) benzene sulfonamide via hydrolysis and was finally transformed into the tilted compounds of interest by the reaction of 4-amino-N -(1, 3-benzoxazole-2-yl) benzene sulfonamide(XII_{1-3}) with various aldehydes gives corresponding derivatives **(**$XIII_{4-27}$**)** .

Synthesis of titled compounds XII_{1-3} and $XIII_{4-27}$:
Synthesis of 4-amino-N-(1,3-benzoxazole-2-yl) benzene sulfonamide(XII_{1-3}) with various aldehydes gives corresponding derivatives **(**$XIII_{4-27}$**)** consisits of several steps and the details of steps were described as following. To a solution of aluminum nitrate (40g) in acetic acid: acetic anhydride (1:1, v/v) mixture (160ml) 40g of 4-chlorophenol **(I)** was added in small portions, while cooling and shaking occasionally. The reaction mixture was left at room temperature for 2hrs while shaking the contents intermittently to complete the nitration. The resulting brown solution was diluted with ice cold water (500ml) and acidified with conc.HNO_3 (40ml) to get a bulky yellow precipitate of 4-chloro-2-nitrophenol(**II**) (yield82%) and recrystallized from methanol, m.p 85 $^{\circ}$C.

4-Chloro-2-nitrophenol (**II**,40g) was dissolved in boiling ethanol (400ml) and sodium dithionate was added to this boiling alcohol solution until it becomes almost colorless. Then the solvent was reducedto1/3$^{rd\ of}$ its volume by distillation and the residual liquid was triturated with ice cold water. The resulting colorless shiny 2-amino-4-chlorophenol (**III**) was filtered, washed with cold water and dried. It is recrystallized from methanol (yield 80%), m.p 141 $^{\circ}$C.

To a solution of aluminum nitrate (40g) in acetic acid: acetic anhydride (1:1, v/v) mixture (160ml) 40g of 4-hydroxy phenyl acetate(**IV**) was added in small portions, while cooling and shaking occasionally. The reaction mixture was left at room temperature for 2hrs while shaking the contents intermittently to complete the nitration. The resulting pink solution was diluted with ice cold water (500 ml) and acidified with conc. HNO_3 (40 ml) to get a bulky colorless precipitate of 4-hydroxy-3-nitrophenyl acetate(**V)** yield 82%) and recrystallized from methanol, m.p 85°C.
4-Hydroxy-3-nitro phenyl acetate (**V**, 40g) was dissolved in boiling ethanol (400 ml) and sodium dithionate was added to this boiling alcohol solution until it becomes almost colorless. Then the solvent was reduced to1/3rd of its volume by distillation and the residual liquid was triturated with ice cold water. The resulting colorless shiny product namely 3-amino-4-hydroxyphenyl acetate (**VI**) was filtered, washed with cold water and dried. It is recrystallized from methanol (yield 85%), m.p 141 ^{0}C.

To a solution of 2-aminophenol (**VII**)/ 4-Chloro-2-aminophenol (**III**)/3- amino-4-hydroxy phenyl acetate (**VI**, 0.1mol) in CCl_4/toluene was added to a solution of Cyanogen bromide (0.2mol) in CCl_4/toluene with continuous

stirring. The addition of reactants must be under low temperature (5 °C-10 °C) and the stirring was continued for 12hrs. The completion of the reaction was monitored by TLC. The solid separated was filtered and washed with carbon tetrachloride (CCl_4) and air dried to give solid product such as 2-amono benzoxazole/5-chloro-2-amino benzoxazole/5-acetyl-2-amino benzoxazole (**VIII**).

Dry acetanilide (**IX**, 25gm, 0.185mol) in a 500ml round bottom flask and (63ml, 1 mol) of chloro sulphonic acid was added drop wise with a dropper with continuous shaking. After complete addition the reaction mixture was refluxed for one hour on water bath. Cooled to room temperature, then reaction mixture was poured onto crushed ice. Obtained precipitate was filtered and washed with water and dried. The product(**X**) was used as such in the next step.

The obtained products 2-aminobenzoxazole (**VIII**,6.7gm,5M) was added into 250ml round bottom flask with dry pyridine and dissolved, to this mixture p-acetamido benzene sulfonyl chloride **(X,**11.65gm,5M) was added and refluxed over water bath for 2hours and then the mixture was added to crushed ice while it was in hot condition. The obtained precipitate (intermediate, **XI**) was filtered and recrystallized with ethanol. (Pyridine acts as solute, and also neutralizes the released HCl from the reaction).

The compound (**XI**) was dissolved in 50ml methanol, 8ml of HCl was added and the reaction mixture was refluxed for 3hours until the solid matter got dissolved completely, reaction was monitored by TLC. After the completion of the reaction the excess acid was neutralized with 20% $NaHCO_3$.The obtained precipitate was filtered and recrystallized with ethanol to get 4-amino-*N*-(1,3-benzoxazol-2-yl)benzene sulfonamide **(XII_{1-3})** as final product. The compound was purified by recrystalisation and column chromatography (ethyl acetate: chloroform {1;3}).

The mixture of compound (**XII,** 0.02mol**)** and an appropriate aldehyde (0.02mol) was dissolved in methanol (10ml) containing 3 drops of acetic acid, and was refluxed on water bath for 3hrs. The solvent was evaporated and the reaction mixture was poured in ice cold water. The solid was separated and filtered, washed with ice cold water and dried. All the compounds were purified by recrystalisation and column chromatography (ethyl acetate: chloroform) (1:3). The compounds **($XIII_{4-27}$)** were characterized by spectral data (IR, NMR, Mass spectroscopy).

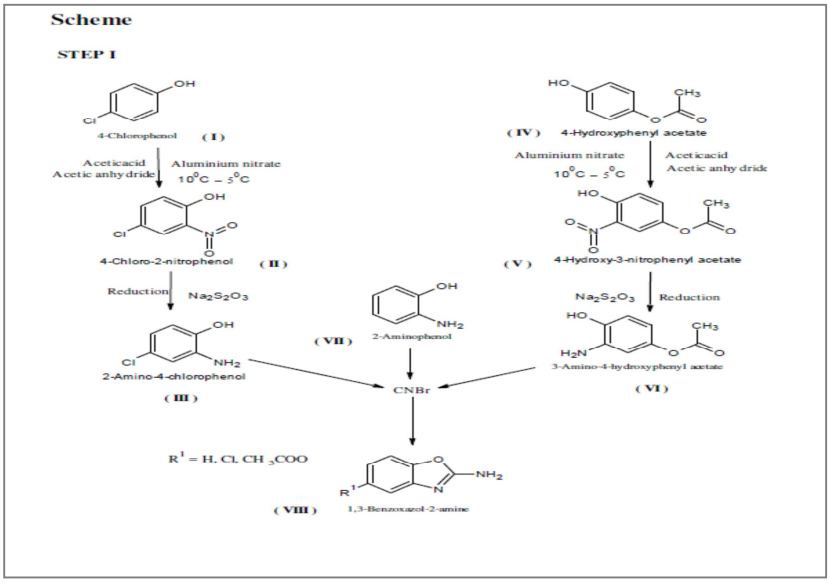

Figure 1: Synthetic scheme

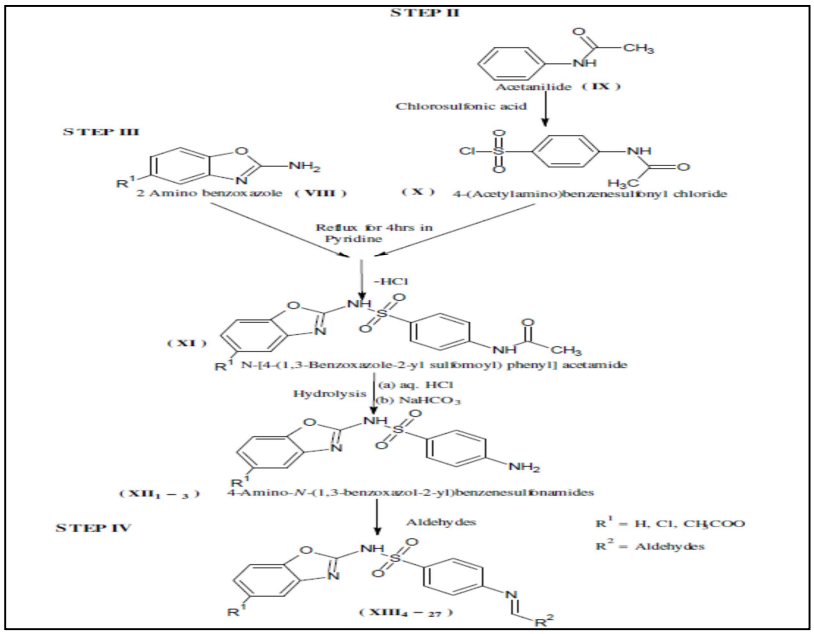

Figure 1: Synthetic scheme (contd)

Spectral characterization:

The structures of the title compounds were established by IR, ^{1}H-NMR (DMSO-d_6), Mass spectrum. The author provides the complete spectral data for the selected titled compounds such as XII and XII_{17} in this present investigation. The spectral characteristics of 4-Amino-*N*-(1,3-benzoxazol-2-yl)benzene sulfonamide(XII) were as follows: IR (KBr, cm^{-1}): 3494.15, 3395.35(N-H str),3093.59 (aromatic C-H str), 2078.68(C-S str),1639.68(C=N str), 1593.39(aromatic C=Cstr), 1356.61(C-N str), 1325.78(C-O str.),1155.04 (S=O str):^{1}H-NMR (DMSO-d_6, 400MHz) δ=11.76(s,1H, NH),7.162-6.866(m,4H,Ar-H),6.772 (d, 2H, Ar-H), 6.672(d, 2H, Ar-H), 4.068 (s, 2H, NH_2).Mass (ESI): molecular ion (M^+) peak was observed at 290 m/z (100%). The spectral data of derivative of titled compound namely *N*-(5-Chloro-1, 3-benzoxazol-2-yl)-4-{[phenyl methylidene] amino} benzene sulfonamide was as follows($XIII_{17}$): IR(KBr, cm^{-1}): 3110.87 (aromatic C-H str),3025.89 (alkene C-H str),2063.17(C-S str),1629.68 (C=N str),1575.94(aromaticC=C str),1327.18(C-O str.),1156.07(S=O str), 778 (C-Cl str):^{1}H-NMR (DMSO-d_6, 400MHz) δ=11.45(s, 1 H, NH),8.45(s,1H,C=H),7.482(d,2H, Ar-H), 7.38 (d, 2H, Ar-H), 7.30-7.23 (m, 3H, Ar-H), 7.15-6.91 (m, 5H, Ar-H):Mass (ESI): molecular ion (M^+) peak was observed at 412 m/z (100%).The details of physical properties of 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamide and derivatives were incorporated in **Table-1**.

Table 1: Physical data of 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamide and derivatives

S.No	Compound	M. Formula	M. Weight	M.P(ºC)	% yield
1	XII_1(R_1=H)	$C_{13}H_{11}N_3O_3S$	289.30	98-105	73
2	XII_2(R_1=Cl)	$C_{13}H_{10}ClN_3O_3S$	323.75	120-123	75
3	XII_3(R_1=CH_3COO)	$C_{15}H_{13}N_3O_3S$	347.34	145-148	70
4	$XIII_4$(R_1 =H and R_2=C_6H_5)	$C_{20}H_{15}N_3O_3S$	377.41	132-134	76
5	$XIII_5$(R_1=Cl and R_2= C_6H_5)	$C_{20}H_{15}ClN_3O_3S$	411.86	160-165	82
6	$XIII_7$(R_1=H and R_2=C_4H_4O)	$C_{18}H_{13}N_3O_4S$	367.37	183-184	75
7	$XIII_8$(R_1=H and R_2=H)	$C_{18}H_{12}ClN_3O_4S$	401.82	201-203	77
8	$XIII_{16}$(R_1 =H and R_2=C_8H_8)	$C_{23}H_{19}N_3O_3S$	417.48	268-269	72
9	$XIII_{17}$(R_1 =Cl and R_2=C_8H_8)	$C_{23}H_{18}ClN_3O_3S$	451.92	275-276	69
10	$XIII_{26}$(R_1=Cl and R_2=CH_3)	$C_{15}H_{12}ClN_3O_3S$	349.79	152-155	77
11	$XIII_{27}$(R_1= CH_3COO and R_2= CH_3)	$C_{17}H_{15}N_3O_3S$	373.38	213-215	84

Pharmacological evaluation:

Evaluation of in vivo anti-inflammatory activity of synthesized compounds by carragenan induced rat paw edema method: Plethysmograph, Carrageenan, Celecoxib, and test compounds, Normal saline, water, 1ml reusable glass

syringe, needles for intraperitonial (IP) injection, marker pens, cotton, 0.1% Sodium CMC suspension were used for the anti-inflammatory activity of the synthesized compounds.

All the experiments were carried out using male, Sprague-Dawley rats (300-350 g) were obtained from animal house. On arrival the animals were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at a temperature of $24^oC \pm 2^oC$ and relative humidity of 30-70 %. A 12:12 light: day cycle was followed. All animals were allowed to free access to water and fed with standard commercial rat chew pellets. Carrageenan suspension was prepared as 1% w/v Suspension of carrageenan by adding 100mg of carrageenan powder to 10ml of saline (0.9% NaCl) solution and set aside to soak for 1 hour. A homogenous suspension was then obtained by thorough mixing with a magnetic stirrer.

The experimental procedure for the anti inflammatory activity of titled compounds was in which Sprague-Dawley strain Albino rats of either sex, weighing between 250-300g, fasted overnight before the test and allowed water *ad libitum*, were divided into 12 groups of six animals each. The volume of the right hind paw was measured using a plethismograph. This constituted the initial reading. The test compounds were tested at a dose of 30mg/kg body weight. Celecoxib 5mg (0.014mmoles)/kg body weight was used as standard. All these were administered as suspensions using sodium CMC (0.1% w/v) as suspending agent. Control group of animals received a suspension of sodium CMC only. All these were administered intraperitonially 1h before the injection of carrageenan. 0.1 ml of 1% w/v carrageenan suspension in normal saline was injected in to the plantar region of the right hind paw.

The swelling produced after injection of the carrageenan was measured at 1hour intervals for 4 hours. Details of Mean paw edema volume (n=6) of 4-Amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamide and derivatives (30mg/kg bw) compared to standard drug Celecoxib (5mg/kg bw) was presented in the **Table-2**. Percentage inhibition of edema was calculated for the titled compound derivatives were mentioned in the **Table-3**.

Table 2: Mean paw edema volume (n=6) of 4-Amino-N-[1, 3-benzoxazole-2-yl] Benzene sulphonamide and derivatives (30mg/kg bw) compared to standard drug Celecoxib

S.No	Compound	Mean paw edema volume (ml±SD)			
		1h	2h	3h	4h
1	$XII_1(R_1=H)$	0.82± 0.00	0.80± 0.07	0.80± 0.04	0.78± 0.05
2	$XII_2(R_1=Cl)$	0.83± 0.05	0.78± 0.05	0.74± 0.07	0.74± 0.02
3	$XII_3(R_1=CH_3COO)$	0.80± 0.06	0.75± 0.06	0.72± 0.05	0.68± 0.06
4	$XIII_4(R_1$ =Hand $R_2=C_6H_5)$	0.75± 0.06	0.69± 0.08	0.63± 0.07	0.59± 0.06
5	$XIII_5(R_1$=Cl and $R_2= C_6H_5)$	0.61± 0.04	0.60± 0.01	0.51± 0.04	0.46± 0.04
6	$XIII_7(R_1$=H and $R_2=C_4H_4O)$	0.68± 0.08	0.62± 0.04	0.56± 0.07	0.53± 0.08
7	$XIII_8(R_1$=H and R_2=H)	0.70± 0.08	0.64± 0.05	0.58± 0.08	0.54± 0.03
8	$XIII_{16}(R_1$ =Hand $R_2=C_8H_8)$	0.78± 0.06	0.73± 0.06	0.68± 0.04	0.67± 0.06
9	$XIII_{17}(R_1$ =Cland $R_2=C_8H_8)$	0.82± 0.05	0.82± 0.04	0.78± 0.05	0.74± 0.06
10	$XIII_{26}(R_1$=Cl and $R_2=CH_3)$	0.78± 0.04	0.73± 0.03	0.68± 0.06	0.63± 0.04
11	$XIII_{27}(R_1= CH_3COO$ and $R_2= CH_3)$	0.74± 0.05	0.68± 0.08	0.58± 0.08	0.57± 0.07
12	Celecoxib	0.63± 0.04	0.53± 0.08	0.63± 0.05	0.54± 0.05
13	Control	0.85± 0.10	0.95± 0.11	1.45± 0.12	1.85± 0.10

Celecoxib: 5mg/Kg; Contro: 0.1% sodium CMC; Test compounds: 30mg/kg

Table 3: % inhibition of paw edema of 4-Amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamide and derivatives (30mg/kg bw) compared to standard drug Celecoxib (5mg/kg bw).

S.No	Compound	% inhibition of paw edema				PLP score
		1h	2h	3h	4h	
1	$XII_1(R_1=H)$	13.61	25.25	42.86	59.69	-63.02
2	$XII_2(R_1=Cl)$	15.21	27.18	46.45	60.84	-68.29
3	$XII_3(R_1=CH_3COO)$	15.76	30.15	49.26	64.21	-72.67
4	$XIII_4(R_1$ =H and $R_2=C_6H_5)$	20.12	35.89	54.82	70.23	-83.43
5	$XIII_5(R_1$=Cl and $R_2= C_6H_5)$	29.43	46.05	62.98	75.34	-91.37
6	$XIII_7(R_1$=H and $R_2=C_4H_4O)$	27.33	44.14	60.84	71.85	-88.71
7	$XIII_8(R_1$=H and R_2=H)	25.30	40.19	60.27	72.07	-88.42
8	$XIII_{16}(R_1$ =H and $R_2=C_8H_8)$	18.78	35.80	51.06	66.00	-73.88
9	$XIII_{17}(R_1$ =Cl and $R_2=C_8H_8)$	14.52	23.42	45.22	61.98	-67.10
10	$XIII_{26}(R_1$=Cl and $R_2=CH_3)$	19.95	35.78	50.87	69.36	-74.66
11	$XIII_{27}(R_1= CH_3COO$ and $R_2= CH_3)$	24.16	37.15	59.12	71.52	-84.22
12	Standard Celecoxib (5mg/kg.bw)	28.59	48.45	65.73	77.75	-92.77

in vitro antioxidant activity:
The following materials were employed for the study of antioxidant activity of titled compounds such as Ascorbic acid (Analytical grade, Merck India), Methanol (HPLC grade, Merck India), DPPH (α,α-diphenyl,β-picrylhydrazyl) (Sigma Aldrich),Test compounds, Double distilled water.

Required amount of Ascorbic acid was accurately weighed and dissolved in distilled water to prepare 1mM stock solution. Solutions of different concentrations (10nM, 30nM, 100nM, 300nM, 1µM, 3µM, 100µM, 300µM, and 1mM) of Ascorbic acid were prepared from stock solution. 0.2mM solution of DPPH was prepared by dissolving required amount of DPPH in 100ml of methanol. The solution was protected from sunlight to prevent the oxidation of DPPH. Required amount of test compounds was dissolved in methanol and 1mM stock solution was prepared. Solutions of concentration ranging from 10mM to 1mM were prepared.

The procedure for the antioxidant activity was carried as follows. To 0.1 ml of test sample/ascorbic acid, 2.5ml of methanol and 0.5ml of DPPH solution were added, mixed thoroughly and absorbance was measured at 517nm against blank, prepared in an identical way but without the test compound. The reduction in absorbance in calculated. The details of the results were incorporated in **Table-4**.

Table 4: Antioxidant activity of 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides compared to standard Ascorbic acid.

S.No	Compound	IC_{50}(µM)
1	XII_1(R_1=H)	41.83
2	XII_2(R_1=Cl)	46.21
3	XII_3(R_1=CH_3COO)	55.59
4	$XIII_4$(R_1 =H and R_2=C_6H_5)	74.10
5	$XIII_5$(R_1=Cl and R_2= C_6H_5)	58.95
6	$XIII_7$(R_1=H and R_2=C_4H_4O)	89.06
7	$XIII_8$(R_1=H and R_2=H)	39.56
8	$XIII_{16}$(R_1 =H and R_2=C_8H_8)	35.16
9	$XIII_{17}$(R_1 =Cl and R_2=C_8H_8)	73.88
10	$XIII_{26}$(R_1=Cl and R_2=CH_3)	59.86
11	$XIII_{27}$(R_1= CH_3COO and R_2= CH_3)	66.75
12	Standard Ascorbic acid	8.64

RESULTS AND DISCUSSION

The present research work carried by the author was to synthesize biologically active 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides and their derivatives and was succeeded in preparing titled compounds of interest. The detailed synthetic scheme was incorporated in the **Figure-1** (synthetic scheme). The structures of the title compounds were established by IR, ^{1}H-NMR (DMSO-d_6), Mass spectrum. The preliminary studies on anti-inflammatory activity and antioxidant activity of the new benzoxazole derivatives have generated some interesting data. An attempt has been made to infer the ultimate outcome of the present studies based on this data.

All the synthesized new benzoxazole derivatives were evaluated for their anti inflammatory activity by using the standard Celecoxib for the period of four hours with one hour interval. All the synthesized compounds were tested at the concentration of 0.1mole and the results were compared with standard Celecoxib at concentration of 0.1mole, and were shown in **Table-2.**The investigation of anti-inflammatory activity revealed that the test compounds of 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides showed promising anti inflammatory activity at a dose of 30mg/kg bw. Among the synthesized compounds **$XIII_5$** was more potent with best PLP score followed by **$XIII_7$**, **$XIII_8$**, **$XIII_{27}$**and **$XIII_4$** with best interactions and best percentage inhibition were found to be comparatively potent with %inhibition and PLP scores compared with standard drug Celecoxib. The details were presented in the **Table-3**.

All the eleven new 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides were evaluated for *invitro* antioxidant activity by DPPH method. The results of the evaluation studies have been compared with the standard ascorbic acid and the IC50 values (concentration of test compound require to scavenge the 50% free radical, DPPH) of all compounds were shown in **Table-4**.All these synthetic compounds produced a concentration dependent scavenging of free radical, DPPH. The IC50 values of all synthetic test compounds were found between 35.16µM and 89.06µM.Among these compounds: **$XIII_{16}$, $XIII_8$, XII_1** and **XII_2** were found to be comparatively potent antioxidant activity respectively. **XII_3**, **$XIII_{26}$** and **$XIII_5$** were found to have moderate antioxidant activity respectively. **$XIII_{27}$**, **$XIII_4$**, **XII_{17}**, **$XIII_7$** were found to have weak antioxidant activity.

CONCLUSION

Heterocyclics for the present investigation was synthesis, characterization and physiological activity of 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides derivatives. Synthetic studies could go positive as per the planning and as such in all the reactions carried out. The expected compounds alone could be obtained.

The compounds have been found to be safe even up to a dose of 300mg/kg bodyweight orally in experimental animals. Eleven newly synthesized 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides derivatives were characterized by means of chromatography, IR, ^{1}H-NMR and Mass spectral analysis.4-amino-N-[1,3-benzoxazole-2-yl]benzene sulphon- amides showed activity in varied degrees. The investigation of anti-inflammatory activity revealed that the test compounds of 4-amino-N-[1, 3-benzoxazole-2-yl] benzene sulphonamides showed favorable anti inflammatory activity at a dose of 30mg/kg bw.

Among the above synthesized compounds **$XIII_5$** was more potent with best PLP score followed by **$XIII_7$, $XIII_8$, $XIII_{27}$** and **$XIII_4$** with best interactions and best percentage inhibition were found to be comparatively potent with %inhibition and PLP scores compared with standard drug Celecoxib.

All these synthetic compounds produced a concentration dependent scavenging of free radical, DPPH. The IC50 values of all synthetic test compounds were found between 38.54µM and 80.02µM. Among these compounds **$XIII_{16}$, $XIII_8$, XII_1** and **XII_2** were found to be comparatively potent antioxidant activity respectively.

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