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Research Article

SYNTHESES AND CHARACTERIZATION OF SOME NOVEL OXADIAZOLES FOR *IN-VITRO* ANTI-INFLAMMATORY ACTIVITY

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ABSTRACT

Oxadiazole derivatives are an important class of heterocyclic compounds, specifically 2-amino substituted oxadiazoles reported to possess a wide spectrum of biological activities such as antibacterial, antifungal, analgesic, anti-inflammatory, antioxidant, antitumor, anticancer activities and so on. Moreover, oxadiazole nucleus occupies a very important place in the field of anti-inflammatory agents. In view of the above observations we have synthesized new Oxadiazoles with various substitution. The starting material 2-amino-5-(3'-acetamidophenyl)-1,3,4-oxadiazole (SBM-4) was synthesized by refluxing a mixture of 3-aminophenol and aceticanhydride in glacial acetic acid. This was followed by refluxing with ethyl chloroacetate and anhydrous K_2CO_3 in dry acetone, followed by refluxing with hydrazine hydrate in ethanol and the hydrazide was finally treated with CNBr in methanol. The parent compound was then converted to the desired title compounds by reacting with various substituted aromatic aldehydes. The *In-vitro* anti-inflammatory activity of synthesized compounds (SBM 4a-n) was evaluated using inhibition of bovine serum albumin denaturation method. Compound SBM-4d, SBM-4f, SBM-4h and SBM-4i have shown significant *in-vitro* anti-inflammatory activity. The findings of the present study clearly demonstrate that 3",4"-dimethoxy, 4"-hydroxy-3"-methoxy, 4"-methyl and 2"-hydroxy functional group possess inhibition of bovine serum albumin denaturation capacity and has *in-vitro* anti-inflammatory activity. The remaining compounds exhibited mild to moderate activities compared to the standard Ibuprofen.

Keywords: Synthesis, Oxadiazole, *in-vitro* anti-inflammatory activity.

INTRODUCTION

Generally many drugs are obtained from plants and animals, but most drugs used in modern medicine are products of advances in synthetic organic chemistry and biotechnology. Oxadiazoles are five membered heterocyclic compounds with two nitrogen atoms and one oxygen atom. 1,3,4-Oxadiazoles are a class of heterocycles which have attracted significant interest in medicinal chemistry and they have a

wide range of pharmaceutical and biological activities. Molecules containing a 1,3,4-oxadiazole core have been shown to have a broad range of important biological activities including antimicrobial (1-3), pesticidal, anti-mycobacterial, antitumor (4-5) , anti-inflammatory (6-8), anti-convulsant, insecticidal, anti-cancer, and anti-hypertensive properties. Among the 1,3,4-oxadiazoles, 2,5-unsymmetrical disubstituted derivatives have attracted considerable attention because of their biological and electrochemical properties. Numerous studies have been performed with the aim of exploring the anti-inflammatory properties of 1,3,4-oxadiazole analogues. These studies found that 1,3,4-oxadiazole analogues are equipotent with phenylbutazone, naproxen and other NSAIDs. Oxatamine can be used as an anti-inflammatory agent in case of respiratory tract infection, it contains the oxadiazole heterocycle. Methazole and Pleconaril also contain oxadiazole heterocycle that are having herbicide and anti-viral activity respectively. With the aim of finding a COX/LOs dual inhibitor, which may have improved efficacy and fewer side effects compared with existing NSAIDs, we considered it of interest to synthesize novel 1,3,4-oxadiazole analogues to investigate their anti-inflammatory activity.

MATERIALS AND METHODS

Step-1

Synthesis of 3-Acetamido phenol (SBM-1)

A mixture of 3-Amino phenol (21.8 g, 0.2 mole), acetic anhydride (24ml, 0.3 mole) and glacial acetic acid (60ml) were refluxed for 4 hrs. Excess solvent was removed by distillation and the residual mixture was poured over crushed ice. The resultant product was recrystallized from water to yield pure 3-Acetamido phenol (SBM-1). **%** Yield: 71%, M.P.: 152^{0}C, IR (KBr) (cm^{-1}): 3594.21(O-H), 3461.47 (NH stretch of amide), 3098.06 (Ar. C-H), 2961.17 (Ali. C-H), 1684.73 (C=O of amide), 1578.96 (NH bend), 1605.49 & 1468.42 (Ar. C=C), 898.92 (Ar. C-H bend).

Step-2

Synthesis of Ethyl-(3-acetamidophenoxy)-acetate (SBM-2)

A mixture of 3-Acetamido phenol (15.1 gm, 0.1 mole), Ethylchloroacetate (10.5 ml, 0.1mole) and anhydrous K_2CO_3 (20.7 gm, 0.15 mole) in dry acetone (150 ml) was refluxed on a water bath for 24 hrs. The reaction mixture was cooled and filtered and from filtrate excess acetone was removed by distillation. Then the reaction mixture was poured into ice cold water and stirred well. The resultant product was recrystallized with ethanol (95%) to yield pure Ethyl-(3-acetamidophenoxy)-acetate (SBM-2). **%** Yield: 62%, M.P.: 70^{0}C, IR (KBr) (cm^{-1}): 1752.87 (C=O of ester), 3460.76 (NH stretch of amide), 3109.83 (Ar. C-H), 2990.38 (Ali. C-H), 1684.85 (C=O of amide), 1560.24 (NH bend), 1218.35 (Ar-O-C), 1170.71 (O-C_2H_5), 1600.76 & 1469.74 (Ar. C=C), 830.86 (Ar. C-H bend)

Step-3

Synthesis of 2-(3'-Acetamidophenoxy)-acetohydrazide (SBM-3)

A mixture of Ethyl-(3-acetamidophenoxy)-acetate (11.85 gm, 0.05 mole) and hydrazine hydrate 99% (10 ml, 0.2 mole) in ethanol (50 ml) was refluxed for 8 hrs. Excess of ethanol was removed by distillation. On cooling 2-(3'-acetamidophenoxy)-acetohydrazide initiated to separate. It was collected by filtration and recrystallized with ethanol (95%) to yield pure 2-(3'-Acetamidophenoxy)-acetohydrazide (SBM-3). **%** Yield: 80%, M.P.: 175^{0}C, IR (KBr) (cm^{-1}) : 3344.84(NH_2 strech), 3470.46 (NH stretch of amide), 3078.79 (Ar. C-H), 2919.37 (Ali. C-H), 1680.65 (C=O of amide), 1556.75 (NH_2 bend), 1520.40 (NH bend), 1230.14 (Ar-O-C), 1605.17 & 1463.92 (Ar. C=C), 840.51 (Ar. C-H bend).

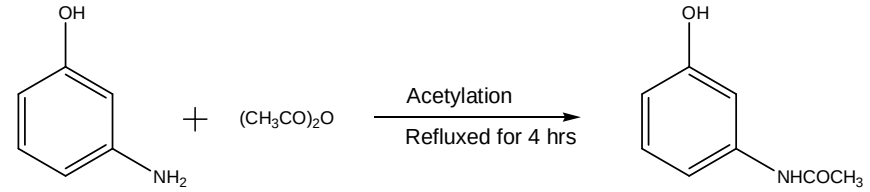
Step-4

Synthesis of 2-Amino-5- (3'-acetamidophenoxymethyl)-1,3,4-oxadiazole (SBM-4)

2-(3'-Acetamidophenoxy)-acetohydrazide (4.46 gm, 0.02 mole) was added to a solution of Cyanogen bromide (2.12 gm, 0.02 mole) in 50 ml of methanol in such a way that the temp. should not rise above 40^{0}C. The solution was then stirred for 1.5 hrs at 40^{0}C and then it was refluxed at 70^{0}C for 1.5 hrs, filtered hot and allowed to cool at room temp. Then the solution was neutralized with dil. ammonia. The resultant product was collected and recrystallized with methanol to yield pure 2-Amino-5-(3'-acetamidophenoxymethyl)-1,3,4-oxadiazole (SBM-4). **%** Yield: 54% , M.P.: 198^{0}C, IR (KBr) (cm^{-1}) : 3394.45 (NH_2 strech), 3473.17 (NH stretch of amide), 3116.70 (Ar. C-H), 2901.86 (Ali. C-H), 1674.46 (C=O of amide), 1090.48 (C-O of Oxadiazole), 1640.71 (C=N), 1561.23 (NH bend), 1230.6 (Ar-O-C), 1460.24 (Ar. C=C), 830.8 (Ar. C-H bend)

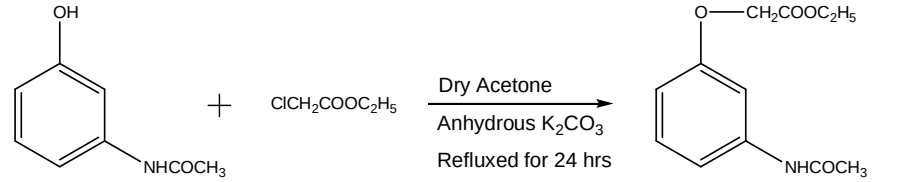
SCHEME

Step-1



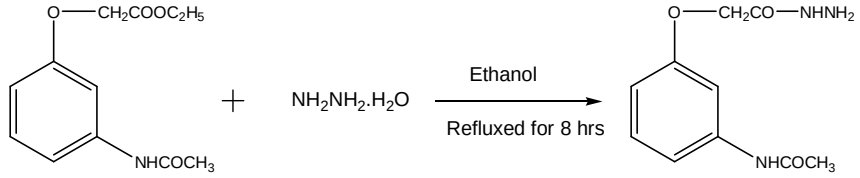
3-Amino phenol — Acetic anhydride — 3-Acetamido Phenol (SBM-1)

Step-2



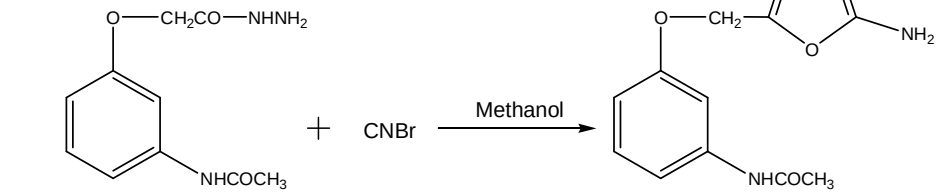
3-Acetamido phenol (SBM-1) — Ethylchloroacetate — Ethyl-(3-acetamidophenoxy)-acetate (SBM-2)

Step-3



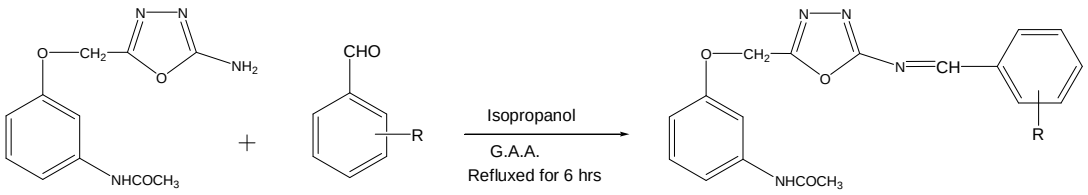
Ethyl-(3-acetamidophenoxy)-acetate (SBM-2) — Hydrazine hydrate — 2-(3'-Acetamidophenoxy)-acetohydrazide (SBM-3)

Step-4



2-(3'-Acetamidophenoxy)-acetohydrazide (SBM-3) — Cyanogen bromide — 2-Amino-5-(3'-acetamidophenoxy methyl)-1,3,4-oxadiazole (SBM-4)

Step-5



2-Amino-5-(3'-acetamidophenoxy methyl)-1,3,4-oxadiazole (SBM-4) — Various aromatic aldehydes (a-n) — 2-[(substituted benzylidene) imino]-5-(3'-acetamidophenoxy methyl) -1,3,4-oxadiazoles (Schiff bases) SBM-4(a-n)

R	Sample code	R	Sample code
4-chloro	SBM - 4a	4-methyl	SBM – 4h
4-dimethylamino	SBM – 4b	2-hydroxy	SBM – 4i
2-nitro	SBM – 4c	4-methoxy	SBM – 4j
3, 4-dimethoxy	SBM – 4d	3-nitro	SBM – 4k
4-hydroxy	SBM – 4e	3,4,5-trimethoxy	SBM – 4l
4-hydroxy-3-methoxy	SBM – 4f	H	SBM – 4m
2-chloro	SBM – 4g	4-nitro	SBM – 4n

Step-5

General method for the syntheses of 2-[(substituted benzylidene) imino]-5-(3'-acetamidophenoxy methyl)-1,3,4-oxadiazoles (SBM 4a-n) (Schiff bases)

A mixture of 2-Amino-5-(3'-acetamidophenoxy methyl)-1,3,4-oxadiazole (SBM-4) (0.001 mol), the required aryl aldehydes (0.001 mol) in isopropanol (15 ml) and catalytic amount of glacial acetic acid (0.5 ml) was subjected to reflux for 6 hrs. The reaction mixture was cooled to room temperature. The solid separated was filtered, washed with isopropanol and recrystallized with DMF : Water mixture (5:2). The new titled compounds formed were confirmed by MP, TLC, IR and representative compounds by NMR and Mass spectra.

***In-vitro* Anti-inflammatory activity**

The synthesized compounds were screened for *in-vitro* anti-inflammatory activity by inhibition of bovine serum albumin denaturation method according to M.N.A. Rao et al (9).

Experimental design

The test compounds were dissolved in minimum amount of dimethyl formamide (DMF) and diluted with phosphate buffer (0.2M, pH 7.4). Final concentration of DMF in all solution was less than 2.5%. Test solution (1 ml) containing different concentrations of drug was mixed with 1 ml of 1mM albumin solution in phosphate buffer and incubated at 27^0 $\pm 1^0$ C for 15 min. Denaturation was induced by keeping the reaction mixture at $60^0 \pm 1^0$ C in a water bath for 10 min. After cooling the turbidity was measured at 660 nm. (Shimadzu Spectrometer). Percentage inhibition of denaturation was calculated from control where no drug was added. Each experiment was done in triplicate and the average was taken. The percentage of inhibition is calculated from the following formula.

The standard solution was also prepared as similar to that of the test solution. Ibuprofen was used as a standard.

% Inhibition = 100(1 - Vt/Vc)

Where,

Vt = Drug absorbance of triplicate average

Vc = Control absorbance of triplicate average

RESULTS

Physical data

Melting points were determined in open capillaries and are uncorrected. Purity of the compounds was checked by TLC on silica gel plates. The solvent system used to carry out the TLC is Toluene : Acetonitrile (2:8). The physical data are reported in Table 1.

Spectral data

IR spectra (cm^{-2}) were recorded in KBr on a Shimadzu FTIR-8700 spectrometer.^{1}H NMR (ppm) in DMSO using TMS as reference on Bruker 400 AMX. Mass spectra of the compound coded SBM-4 was carried out.

IR (KBr) cm^{-2}

Compound SBM -4a

3462.89 (NH stretch of amide), 3156.49 (Ar. C-H), 2986.47 (Ali. C-H), 1676.81 (C=O of amide), 1097.60 (C-O of Oxadiazole), 771.70 (C-Cl), 1648.53 (C=N), 1598.65 (N=CH), 1561.35 (NH bend), 1224.18 (Ar-O-C), 1489.91 (Ar. C=C), 920.08 (Ar. C-H bend).

Compound SBM-4b

3465.42 (NH stretch of amide), 3045.05 (Ar. C-H), 2924.27 (Ali. C-H), 1684.57 (C=O of amide), 1098.83 (C-O of Oxadiazole), 1656.41 (C=N), 1583.52 (N=CH), 1530.63 (NH bend), 1228.45 (Ar-O-C), 1412.44 (Ar. C=C), 831.21 (Ar. C-H bend).

Compound SBM-4c

1550.93 & 1378.21 (N=O), 3470.46 (NH stretch of amide), 3155.76 (Ar. C-H), 2980.67 (Ali. C-H), 1685.17 (C=O of amide), 1093.82 (C-O of Oxadiazole), 1640.05 (C=N), 1605.81 (N=CH), 1596.06 (NH bend), 1245.46 (Ar-O-C), 1417.65 (Ar. C=C), 837.31 (Ar. C-H bend).

Compound SBM-4d

3465.57 (NH stretch of amide), 3158.65 (Ar. C-H), 2980.43 (Ali. C-H), 1684.01 (C=O of amide), 1098.47 (C-O of Oxadiazole), 1650.21 (C=N), 1596.84 (N=CH), 1550.90 (NH bend),

1223.93 (Ar-O-C), 1247.59 (C-O-CH_3), 1456.23 (Ar. C=C), 835.73 (Ar. C-H bend).

Compound SBM-4e
3580.36 (O-H), 3463.58 (NH stretch of amide), 3151.47 (Ar. C-H), 2975.71 (Ali. C-H), 1694.05 (C=O of amide), 1089.26 (C-O of Oxadiazole), 1630.35 (C=N), 1590.92 (N=CH), 1546.92 (NH bend), 1220.53 (Ar-O-C), 1450.74 (Ar. C=C), 828.04 (Ar. C-H bend).

Compound SBM-4f
3510.99(O-H), 3466.14 (NH stretch of amide), 3197.67 (Ar. C-H), 3074.19 (Ali. C-H), 1688.28 (C=O of amide), 1093.15 (C-O of Oxadiazole), 1648.23 (C=N), 1579.89 (N=CH), 1550.75 (NH bend), 1226.83 (Ar-O-C), 1259.54 (C-O-CH_3), 1483.78 (Ar. C=C), 901.45 (Ar. C-H bend).

Compound SBM-4g
3465.83 (NH stretch of amide), 3120.37 (Ar. C-H), 2980.41 (Ali. C-H), 1658.79 (C=O of amide), 1090.67 (C-O of Oxadiazole), 760.59 (C-Cl), 1620.54 (C=N), 1574.43 (N=CH), 1563.07 (NH bend), 1228.74 (Ar-O-C), 1484.91 (Ar. C=C), 901.73 (Ar. C-H bend)

Compound SBM-4h
3460.65 (NH stretch of amide), 3116.53 (Ar. C-H), 2912.30 (Ali. C-H), 1679.15 (C=O of amide), 1091.75 (C-O of Oxadiazole), 1621.71 (C=N), 1602.50 (N=CH), 1568.07 (NH bend), 1224.18 (Ar-O-C), 1489.97 (Ar. C=C), 824.76 (Ar. C-H bend).

Compound SBM-4i
3598.46 (O-H), 3455.12 (NH stretch of amide), 3150.73 (Ar. C-H), 2998.06 (Ali. C-H), 1684.22 (C=O of amide), 1095.82 (C-O of Oxadiazole), 1622.60 (C=N), 1592.31 (N=CH), 1559.30 (NH bend), 1223.96 (Ar-O-C), 1447.29 (Ar. C=C), 826.04 (Ar. C-H bend).

Compound SBM-4j
3467.55 (NH stretch of amide), 3060.75 (Ar. C-H), 2975.83 (Ali. C-H), 1687.92 (C=O of amide), 1084.96 (C-O of Oxadiazole), 1652.85 (C=N), 1570.36 (N=CH), 1553.90 (NH bend), 1211.43 (Ar-O-C), 1240.52 (C-O-CH_3), 1430.82 (Ar. C=C), 830.73 (Ar. C-H bend).

Compound SBM-4k
1546.63 & 1363.14 (N=O), 3460.41 (NH stretch of amide), 3106.73 (Ar. C-H), 2981.38 (Ali. C-H), 1681.78 (C=O of amide), 1090.31 (C-O of Oxadiazole), 1650.19 (C=N), 1603.58 (N=CH), 1568.49 (NH bend), 1223.07 (Ar-O-C), 1430.46 (Ar. C=C), 823.63 (Ar. C-H bend).

Compound SBM-4l
3450.71 (NH stretch of amide), 3126.15 (Ar. C-H), 2976.89 (Ali. C-H), 1681.40 (C=O of amide), 1089.18 (C-O of Oxadiazole), 1654.34 (C=N), 1583.73 (N=CH), 1569.35 (NH bend), 1234.88 (Ar-O-C), 1251.54 (C-O-CH_3), 1454.16 (Ar. C=C), 831.36 (Ar. C-H bend).

Compound SBM-4m
3457.63 (NH stretch of amide), 3161.48 (Ar. C-H), 2996.84 (Ali. C-H), 1667.72 (C=O of amide), 1087.53 (C-O of Oxadiazole), 1628.57 (C=N), 1591.67 (N=CH), 1560.34 (NH bend), 1218.14 (Ar-O-C), 1441.50 (Ar. C=C), 828.04 (Ar. C-H bend).

Compound SBM-4n
1501.35 & 1354.73 (N=O), 3463.90 (NH stretch of amide), 3110.67 (Ar. C-H), 2991.83 (Ali. C-H), 1674.46 (C=O of amide), 1091.18 (C-O of Oxadiazole), 1650.48 (C=N), 1598.96 (N=CH), 1561.23 (NH bend), 1230.60 (Ar-O-C), 1426.48 (Ar. C=C), 829.38 (Ar. C-H bend).

^{1}H NMR (DMSO) δ (ppm)
Compound SBM-4
2.01 (s, 3H, CH_3 at e); 5.08 (s, 2H, O-CH_2, at f); 6.73 (s, 2H, NH_2 at g); 7.14 (d, 2H, CH, ArH, at a, a'); 7.20 (t, 1H, CH, ArH, at b); 7.31 (d, 1H, CH ArH at c); 9.92 (s, 1H, NH at d).

Compound SBM -4a
2.07 (s,3H, CH_3 at e) ; 5.36 (s,2H, O-CH_2 at f); 7.14 (d, 2H, CH, ArH at a ,a'); 7.18 (d, 4H, CH, ArH at h, h', i , i'); 7.251 (t, 1H, CH, ArH at b); 7.32 (d, 1H, CH, ArH at c); 9.91 (s, 1H, NH at d) ; 10.16 (s,1H, N=CH at g).

Compound SBM-4h
2.08 (s,3H, CH_3 at e) ; 3.38 (s,3H, Ar-CH_3 at j); 5.08 (s,2H, O-CH_2 at f); 6.92 (d, 2H, CH, ArH at a ,a'); 7.18 (d, 4H, CH, ArH at h, h', i , i'); 7.31 (t, 1H, CH, ArH at b); 7.41 (d, 1H, CH, ArH at c); 9.50 (s, 1H, NH at d) ; 10.09 (s,1H, N=CH at g).

***In-vitro* Anti-inflammatory activity data**
Anti-inflammatory activity (10) was carried out using Bovine Serum albumin denaturation method. All the title compounds (SBM-4a-n) were screened for anti-inflammatory activity. The results of the anti-inflammatory activity of the compounds are shown in the table and graphs. SBM-4d, SBM-4f, SBM-4h and SBM-4i having substituents 3",4''-dimethoxy, 4"-hydroxy-3"-methoxy, 4"-methyl and 2"-hydroxy ; respectively showed good activity. Whereas compounds SBM-4a, SBM-4b and SBM-4l having 4"-chloro, 4"-dimethylamino, 3",4",5"-trimethoxy respectively showed mild activity

and remaining compounds showed poor anti-inflammatory activity.

DISCUSSION

The purpose of the present work was to synthesize a series of desired title compounds from 2-amino-5-(3'-acetamido phenoxy methyl)-1,3,4-oxadiazole (SBM-4) by reacting with various substituted aromatic aldehydes. The syntheses were carried out in accordance with the literature as in the scheme.

As discussed earlier, oxadiazoles are a class of heterocyclic compounds that shows an array of biological activities which include anti-inflammatory, anti-oxidant, anti-fungal, anti-bacterial, anti-tubercular, anti-convulsant, anti-cancer, anti-HIV, anti-convulsant, anti-diabetic and so on.

Thus, it was felt worthwhile to take up the present investigation to synthesize a novel class of oxadiazoles using four steps and test their effect on anti-inflammatory activity.

Clinically established anti-inflammatory drugs have shown to inhibit heat coagulation of proteins. These anti-inflammatory drugs have exerted an inhibitory activity on immune haemolysis and also have suppressive effect on vascular reactivity. Denaturation as one of the causes of inflammation is well documented. Anti-inflammatory drugs interact in some way with proteins. To cause the interaction between the drug and the proteins, the stability of proteins against heat coagulation can be measured.

The *in-vitro* anti-inflammatory activity; was carried out using inhibition of bovine serum albumin denaturation method according to M.N.A. Rao et al. All the compounds (SBM-4a-n) were screened for *in-vitro* anti-inflammatory activity. The results are shown in the Table 2 and Figure 1.

CONCLUSION

In conclusion, from the *in-vitro* anti-inflammatory activity results, it was observed that both electron donating and electron withdrawing groups on the aldehydic phenyl ring of the compounds influenced the activity. Among all the compounds tested, SBM-4d with 3",4"-dimethoxy, SBM-4f with 4"-hydroxy-3"-methoxy, SBM-4h with 4"-methyl and SBM-4i with 2"-hydroxy substitution at R showed good *in-vitro* anti-inflammatory activity. The remaining compounds exhibited mild to moderate activities compared to the standard Ibuprofen.

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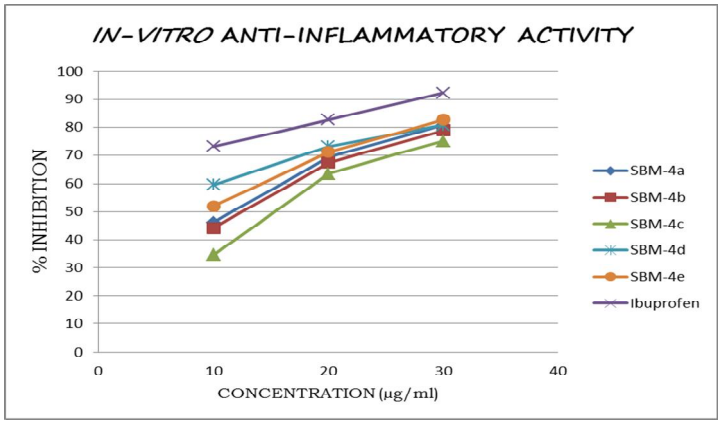
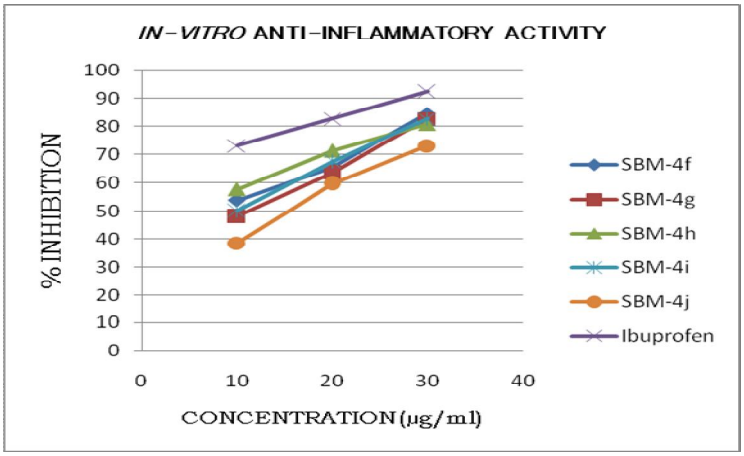
Table 1: Physical data of compounds prepared

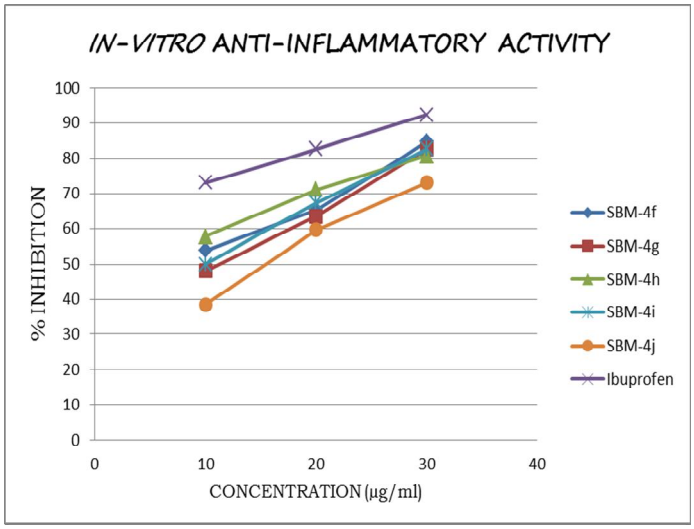
Comp	Molecular formula	M.W. (gm)	M.P. (°C)	R_f Value	Yield (%)
SBM -1	$C_8H_9NO_2$	151	152	0.61	71
SBM -2	$C_{12}H_{15}NO_4$	237	70	0.71	62
SBM -3	$C_{10}H_{13}N_3O_3$	223	175	0.37	80
SBM -4	$C_{11}H_{12}N_4O_3$	248	198	0.67	54
SBM -4a	$C_{18}H_{15}ClN_4O_3$	370	171	0.61	60
SBM -4b	$C_{20}H_{21}N_5O_3$	379	190	0.78	62.1
SBM -4c	$C_{18}H_{15}N_5O_5$	381	192	0.82	58.6
SBM -4d	$C_{20}H_{20}N_4O_5$	396	194	0.73	59.4
SBM -4e	$C_{18}H_{16}N_4O_4$	352	188	0.77	53.6
SBM -4f	$C_{19}H_{18}N_4O_5$	382	191	0.69	51.9
SBM -4g	$C_{18}H_{15}ClN_4O_3$	370	176	0.62	56.7
SBM -4h	$C_{19}H_{18}N_4O_3$	350	186	0.71	64.3
SBM -4i	$C_{18}H_{16}N_4O_4$	352	193	0.76	57.1
SBM -4j	$C_{19}H_{18}N_4O_4$	366	175	0.80	57.6
SBM -4k	$C_{18}H_{15}N_5O_5$	381	185	0.72	55.4
SBM -4l	$C_{21}H_{22}N_4O_6$	426	180	0.64	52.3
SBM -4m	$C_{18}H_{16}N_4O_3$	336	183	0.78	55.6
SBM -4n	$C_{18}H_{15}N_5O_5$	381	181	0.84	58.3

Table 2: In-vitro Anti-inflammatory activity data

Comp Code	% Inhibition				IC_{50}
	10µgm	20µgm	30µgm	Avg	µgm/ml
SBM-4a	46.15	69.23	80.77	65.38	15.30
SBM-4b	44.23	67.31	78.85	63.46	15.75
SBM-4c	34.62	63.46	75	57.70	17.33
SBM-4d	59.61	73.08	80.77	71.15	14.05
SBM-4e	51.92	71.15	82.69	68.59	14.58
SBM-4f	53.85	65.38	84.62	67.95	14.71
SBM-4g	48.08	63.46	82.69	64.74	15.44
SBM-4h	57.69	71.15	80.77	69.87	14.31
SBM-4i	50.00	67.31	82.69	66.67	14.99
SBM-4j	38.46	59.62	73.08	57.05	17.53
SBM-4k	40.38	59.62	78.85	59.62	16.77
SBM-4l	44.23	65.38	78.85	62.82	15.92
SBM-4m	25.00	57.69	69.23	50.64	19.75
SBM-4n	38.46	63.46	73.08	58.34	17.14
Ibuprofen	**73.08**	**82.69**	**92.31**	**82.69**	**12.09**







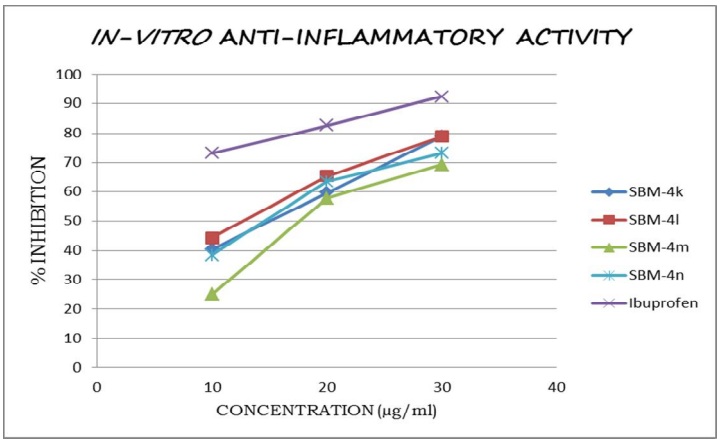


Fig. 1: Graphical representation of in-vitro Anti-inflammatory activity data

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