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SYNTHESIS OF SOME SUBSTITUTED BENZOTHIAZOLE DERIVATIES AND ITS BIOLOGICAL ACTIVITIES

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Abstract: The title compounds were synthesized by facile synthetic procedure with starting from p-substituted aniline and potassium thiocyanate to give 6- substituted 2-amino benzothiazole subsequently added substituted benzaldehyde, thioglycolic acid in anhydrous zinc chloride and again substituted benzaldehyde in sodium ethoxide to give the title compounds. All the prepared compound were characterized for structural confirmation by IR, ^{1}HNMR and Mass spectroscopy .The prepared compounds are screened for their Anti-inflammatory activity Carrageenan paw edema induced method and antitumor activities by MTT assay against M-14, HLB-100 and SW-620 Cancer cell lines. All the title compounds have shown significant activities.

Introduction

4-Thiazolidinones exhibit pharmacological activities such as anti inflammatory[1], antitubercular[2], antitumor[3], antibacterial[4,5] and antifungal[6] activities. Moreover, benzothiazole derivatives are associated with anti inflammatory[7], anticonvulsant[8], antibacterial[9] and anti-HIV[10] activities. In the light of these findings synthesis of some new 4-thiazolidinones derivatives having benzothiazole nucleus has been undertaken in order to assess their pharmacological profile. Therefore, we have prepared 5-(4-Substituted benzylidene)-3-(6-Substituted benzo[d]thiazol-2-yl)-2-(4-Substituted phenyl) thiazolidin-4-one from substituted aniline.

Experimental

1. Chemistry

Melting points were determined in open capillary tubes with LAB-INDIA MS-VIS Visual melting point apparatus and uncorrected. T.L.C was run on silica gel G plates using toluene: ethyl acetate: formic acid (5:4:1) as developing solvent for the purity of the compounds. IR spectra were obtained on FT-IR 8300 (shimadzu) spectrometer by pressed-pellet technique. ^{1}HNMR spectra were determined on AVANCE 300 MHz instrument. Chemical shifts are given in δ values down field from TMS as internal standard. Mass spectra were recorded on SHIMADZU QP2010 PLUS. All compounds showed appropriate IR, ^{1}HNMR and Mass spectra. Elemental analyses were carried out with a VARIO EL III, CHNS Elimentar analyzer and results were within ± 0.6% of theoretical values.

Synthesis of 6-Substituted-1, 3-benzothiazol-2-amine (I)

A mixture of aniline (0.01 *M*) and potassium thiocyanate (0.01 *M*) in glacial acetic acid (20 mL) was cooled and stirred. To this solution bromine (0.01 *M*) was added from dropping funnel at such a rate that the temperature does not rise beyond 0^{o}C. After all the bromine has been added, the solution was stirred for an additional 2h at 0^{o}C. It was allowed to stand for overnight during which period an orange precipitate settled at the bottom, water (6 mL) was added quickly slurry was heated at 85^{o}C on steam bath and filtered hot. The orange residue was placed in a reaction flask and treated with 10 mL of glacial acetic acid, heated again to 85^{o}C and filtered in hot. The combined filtrate was cooled and neutralized with concentrated ammonia solution to pH 6 when dark yellow precipitate was appeared and recrystallized from benzene to obtain the 6- substituted-1, 3-benzothiazol-2-amine[11].

Scheme

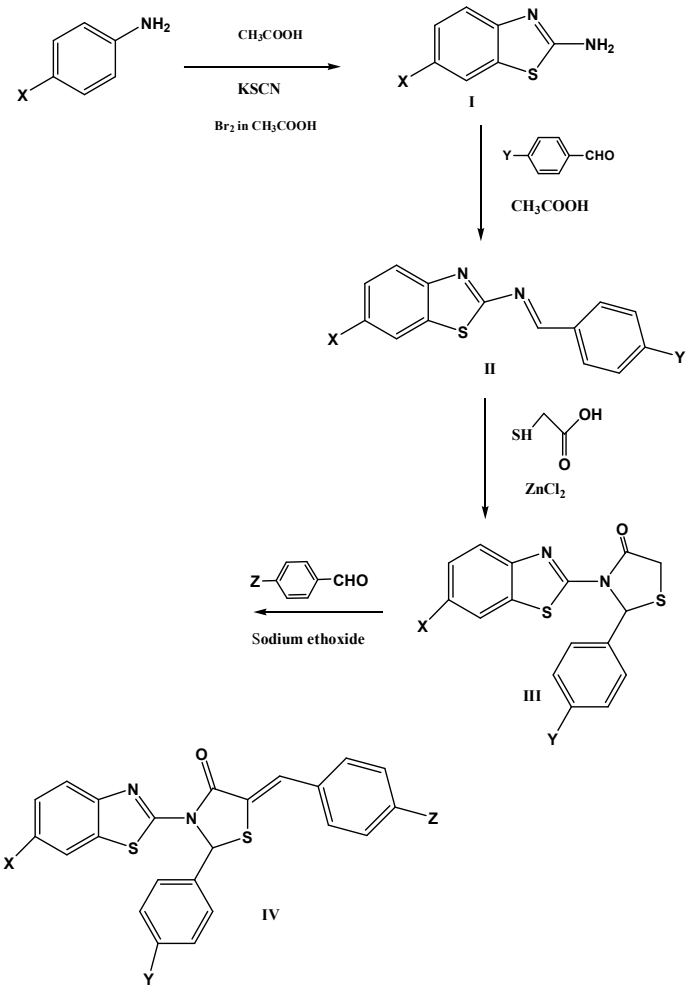

Table 1: Physico chemical properties of DS1-DS12

Compound ID	X	Y	Z	Melting point (^{o}C)	Yield (%)
DS1	Cl	Cl	Cl	195	72
DS2	Cl	Cl	OCH_3	221	65
DS3	Cl	OCH_3	OCH_3	172	81
DS4	F	Cl	Cl	188	49
DS5	F	Cl	OCH_3	170	53
DS6	F	OCH_3	OCH_3	216	52
DS7	NO_2	Cl	Cl	160	72
DS8	NO_2	Cl	OCH_3	196	74
DS9	NO_2	OCH_3	OCH_3	215	61
DS10	OCH_3	Cl	Cl	224	53
DS11	OCH_3	Cl	OCH_3	210	59
DS12	OCH_3	OCH_3	OCH_3	188	67

6-Chloro-2-aminobenzothiazole: yield 75%; m.p. 210-215°C; IR (KBR) 3430, 3010, 1350, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10 (s,1H, Ar), 7.56 (s,1H, Ar), 4.00(s,2H,NH_2) ; MS m/z 183(M^+),184(M^{+1}),185(M^{+2}) 74(base).

6-Floro-2-aminobenzothiazole: yield 31%; m.p. 192-196°C; IR (KBR) 3430, 3010, 1350, 1215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (s, 1H, Ar), 8.12 (s, 1H, Ar), 6.68(s, 2H, NH_2); MS m/z 168(M^+), 169(M^{+1}), 170(M^{+2}) 100(base).

6-Nitro-aminobenzothiazole: yield 74%; m.p. 162-165°C; IR (KBR) 3430, 3010, 1558, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.48 (s, 1H, Ar), 9.05(s, 1H, Ar), 5.14(s, 2H, NH_2); MS m/z 195(M^+), 197(M^{+2}) 74(base).

6-Methoxy-aminobenzothiazole: yield 69.4%;m.p. 262-265°C; IR (KBR) 3360, 3300, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.90 (s, 3H, Ar), 7.16 (s, 1H, Ar), 5.32(s, 2H, NH_2); MS m/z 180(M^+), 182(M^{+2}) 45(base).

Synthesis of 4-substituted benzylidene)-6-substituted benzo[d]thiazol-2-amine (II)

A mixture of compound (I) (0.01*M*) and substituted benzaldehyde (0.02 *M*) and 2-3 drops of glacial acetic acid in methanol (20 mL) was refluxed on a water bath for about 5 h. The solid was separated and recrystallized from ethanol[12].

4-Chlorobenzylidene)-6-chlorobenzo[d]thiazol-2-amine: yield 45%; m.p.216-218°C; IR(KBR) 1555,707 cm^{-1}; ^1H NMR (DMSO) δ 7.56 (s,1H, Ar), 7.6 (s,1H, Ar), 7.75(s,1H,N=CH); MS m/z 305(M^+), 306(M^{+1}).

4-Methoxybenzylidene)-6-chlorobenzo[d]thiazol-2-amine: yield 45%; m.p. 264-268°C; IR (KBR) 1575, 1029, 760 cm^{-1}; ^1H NMR ((DMSO) δ 7.13 (s, 1H, Ar), 8.17 (s,1H, Ar), 3.73 (s, 3H, Ar), 7.73(s,1H,N=CH); MS m/z 302(M^+), 303(M^{+1}),304(M^{+2}).

4-Chlorobenzylidene)-6-florobenzo[d]thiazol-2-amine: yield 38%; m.p. 254-256°C; IR (KBR) 1576, 1215, 770 cm^{-1}; ^1H NMR ((DMSO) δ 7.19(s,1H, Ar), 7.31 (s,1H, Ar),7.75(s,1H,N=CH); MS m/z 290(M^+).

4-Methoxybenzylidene)-6-florobenzo[d]thiazol-2-amine: yield 49%; m.p.221-224°C; IR(KBR) 1640, 1252, 1030, 760 cm^{-1}; ^1H NMR ((DMSO) δ 7.18 (s, 1H, Ar), 7.74 (s,1H, Ar), 3.42(s, 3H, Ar),7.76 (s,1H,N=CH); MS m/z 286(M^+), 287(M^{+1}),288(M^{+2}).

4-Chlorobenzylidene)-6-nitrobenzo[d]thiazol-2-amine: yield 51%; m.p. 196-198°C; IR (KBR) 1571, 1560, 780 cm^{-1}; ^1H NMR ((DMSO) δ 7.19(s,1H, Ar), 7.31 (s,1H, Ar),7.75(s,1H,N=CH); MS m/z 317(M^+),318(M^{+1}).

4-Methoxybenzylidene)-6-nitrobenzo[d]thiazol-2-amine: yield62%; m.p.221-224°C; IR(KBR) 1576, 1558, 1027, 760 cm^{-1}; ^1H NMR ((DMSO) δ 7.18 (s, 1H, Ar), 7.76 (s,1H, Ar), 3.45(s, 3H, Ar),7.72 (s,1H,N=CH); MS m/z 313(M^+),315(M^{+2}).

4-Chlorobenzylidene)-6-methoxybenzo[d]thiazol-2-amine: yield 55%; m.p. 201-205°C; IR (KBR) 1575, 1029, 780 cm^{-1}; ^1H NMR ((DMSO) δ 7.3(s,1H, Ar), 7.6(s,1H, Ar), 3.73(s, 3H, Ar),7.75(s,1H,N=CH); MS m/z 302(M^+),303(M^{+1}).

4-Methoxybenzylidene)-6-methoxybenzo[d]thiazol-2-amine: yield 62%; m.p. 221-224°C; IR (KBR) 1576, 1558, 1027, 760 cm^{-1}; ^1H NMR ((DMSO) δ 7.18 (s, 1H, Ar), 7.76 (s,1H, Ar), 3.45(s, 3H, Ar),7.72 (s,1H,N=CH); MS m/z 298(M^+),300(M^{+2}).

Synthesis of 3-(6-substituted benzo[d]thiazol-2-yl)-2-(4-substituted phenyl) thiazolidin-4-one (III)

A mixture of compound (0.01*M*) (II) in ethanol (50 mL) and mercaptoacetic acid (0.01 *M*) with pinch of $ZnCl_2$ was refluxed on a water bath for 8 h. The solid was recrystallized from methanol & chloroform (1:1) mixture to give compound[12].

3-(6-Chlorobenzo[d]thiazol-2-yl)-2-(4-chloro phenyl) thiazolidin-4-one: yield 59%; m.p. 169-172°C; IR (KBR) 2815, 1649, 1555, 1531, 707 cm^{-1}; ^1H NMR (DMSO) δ 7.56 (s,1H, Ar), 7.6 (s,1H, Ar), 5.21(s,1H,HC-Ar),3.91(s,2H,SCH_2); MS m/z 381(M^+), 382(M^{+1}).

3-(6-Chlorobenzo[d]thiazol-2-yl)-2-(4-methoxyphenyl) thiazolidin-4-one: yield 62%; m.p. 212-214°C; IR (KBR) 2837, 1732, 1531, 1029, 699 cm^{-1}; ^1H NMR (DMSO) δ 7.14 (s,1H, Ar), 7.77 (s,1H, Ar), 5.21(s,1H,HC-Ar); 3.91(s,2H,SCH_2), 3.73 (s, 3H, Ar); MS m/z 376(M^+), 377(M^{+1}).

2-(4-Chlorophenyl)-3-(6-fluorobenzo[d]thiazol-2-yl) thiazolidin-4-one: yield 32%; m.p. 195-197 °C; IR (KBR) 2814, 1716, 1262,770 cm^{-1}; ^1H NMR (DMSO) δ 7.14 (s,1H, Ar), 7.65 (s,1H, Ar), 5.16(s,1H,HC-Ar); 3.89(s,2H,SCH_2), 3.73 (s, 3H, Ar); MS m/z 363(M^+), 364(M^{+1}).

3-(6-Fluorobenzo[d]thiazol-2-yl)-2-(4-methoxyphenyl) thiazolidin-4-one: yield 49%; m.p. 175-179 °C; IR (KBR) 2817, 1649, 1262, 1026 cm^{-1}; ^1H NMR (DMSO) δ 7.14 (s,1H, Ar), 7.77 (s,1H, Ar), 5.21(s,1H,HC-Ar); 3.91(s,2H,SCH_2), 3.73 (s, 3H, Ar); MS m/z 360(M^+).

2-(4-Chlorophenyl)-3-(6-nitrobenzo[d]thiazol-2-yl) thiazolidin-4-one: yield 61%; m.p. 246-249 °C; IR (KBR) 3090, 1724, 1558,1535, 780 cm^{-1}; ^1H NMR (DMSO) δ 8.14 (s,1H, Ar), 9.05 (s,1H, Ar), 5.92(s,1H,HC-Ar); 3.38(s,2H,SCH_2), 3.28 (s, 3H, Ar); MS m/z 390(M^+).

2-(4-Methoxyphenyl)-3-(6-nitrobenzo[d]thiazol-2-yl) thiazolidin-4-one: yield 70%; m.p. 156-158 °C; IR (KBR) 3026, 1743, 1565, 1027 cm^{-1}; ^1H NMR (DMSO) δ 8.48 (s,1H, Ar), 9.05 (s,1H, Ar), 5.76(s,1H,HC-Ar); 3.38(s,2H,SCH_2), 3.73 (s, 3H, Ar); MS m/z 387(M^+) 389(M^{+2}).

2-(4-Chlorophenyl)-3-(6-methoxybenzo[d]thiazol-2-yl) thiazolidin-4-one: yield 62%; m.p. 269-271 °C; IR (KBR) 2837,1732,1531,1029,699 cm^{-1}; ^1H NMR (DMSO) δ 7.14 (s,1H, Ar), 7.77 (s,1H, Ar), 5.21(s,1H,HC-Ar); 3.91(s,2H,SCH_2), 3.73 (s, 3H, Ar); MS m/z 376(M^+), 377(M^{+1}).

3-(6-Methoxybenzo[d]thiazol-2-yl)-2-(4-methoxyphenyl) thiazolidin-4-one: yield 58%; m.p. 269-271 °C; IR (KBR) 2830,1742,1525,1024,641 cm^{-1}; ^1H NMR (DMSO) δ 7.14 (s,1H, Ar), 7.77 (s,1H, Ar), 5.21(s,1H,HC-Ar); 3.91(s,2H,SCH_2), 3.73 (s, 3H, Ar); MS m/z 372(M^+).

Synthesis of 5 - (4-Substituted benzylidene) – 3 - (6-substituted benzo[d]thiazol–2–yl) 2 - (4-substituted phenyl) thiazolidin-4-one (IV)

Equimolar solution of (III) (0.02 *M*) and substituted benzaldehyde (0.02 *M*) in 1,4-dioxan (30 mL) in the presence of sodium ethoxide was refluxed for about 5h on water bath and solvent was removed in vacuo.The resulting solid was recrystallized from methanol[12].

DS1: IR (KBR) 3542, 2815, 1649, 1555,707 cm^{-1}; ^1H NMR (DMSO) 3.18(s, 1H, N-CH), 5.17(s, 1H, C=C-Ar), 7.56 (s, 1H, Ar), 8.13(s, 1H, Ar); MS m/z 503(M^+), 501.

DS2: IR (KBR) 3545, 2837, 1732, 1575, 1029, 760 cm^{-1}; ^1H NMR (DMSO) 3.18(s, 1H, N-CH), 3.73 (s, 3H, Ar), 5.17(s,1H,C=C-Ar), 7.56 (s,1H, Ar), 8.13(s,1H, Ar); MS m/z 498(M^+),500(M^{+2}).

DS3: IR (KBR) 3537, 2672, 1730, 1571, 1024,751 cm^{-1}; ^1H NMR (DMSO) 3.18(s, 1H, N-CH), 3.73 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.56 (s, 1H, Ar), 8.13(s, 1H, Ar); MS m/z 495(M^+), 496(M^{+1}).

DS4: IR (KBR) 3586, 2814, 1576, 1265, 770 cm^{-1}; ^1H NMR (DMSO) 3.18(s, 1H, N-CH), 5.17(s, 1H, C=C-Ar), 7.26 (s, 1H, Ar), 7.83(s, 1H, Ar); MS m/z 485(M^+), 487(M^{+2}).

DS5: IR (KBR) 3439, 2721, 1541, 1248,1026,770 cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 5.17(s,1H,C=C-Ar), 7.15 (s,1H, Ar), 7.83(s,1H, Ar); MS m/z 482(M^+),484(M^{+2}).

DS6: IR (KBR) 3539, 2921, 1541, 1248, 1026 cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 3.73 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.15 (s, 1H, Ar), 7.83(s, 1H, Ar); MS m/z 478(M^+),479(M^{+1}).

DS7: IR (KBR) 3586, 2920, 1560,770 cm^{-1}; ^1H NMR (DMSO) ; ^1H NMR (DMSO) 3.18(s, 1H, N-CH), 5.17(s,1H,C=C-Ar), 7.26 (s,1H, Ar), 7.83(s,1H, Ar); MS m/z 512(M^+),514(M^{+2}).

DS8: IR (KBR) 3577, 2721, 1602, 1027,680 cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.15 (s, 1H, Ar), 7.83(s, 1H, Ar); MS m/z 509(M^+), 511(M^{+2}).

DS9: IR (KBR) 3539, 2921, 1565, 1026 cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 3.73 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.15 (s, 1H, Ar), 7.3(s, 1H, Ar); MS m/z 505(M^+),506(M^{+1}).

DS10: IR (KBR) 3573, 2921, 1576, 1026,743cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 3.73 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.12 (s, 1H, Ar), 7.53(s, 1H, Ar); MS m/z 498(M^+),500(M^{+2}).

DS11: IR (KBR) 3573, 2921, 1576, 1026,761 cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 3.73 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.15 (s, 1H, Ar), 7.83(s, 1H, Ar); MS m/z 494(M^+),496(M^{+2}).

DS12: IR (KBR) 3573, 2921, 1576, 1026 cm^{-1}; ^1H NMR (DMSO) 3.12(s, 1H, N-CH), 3.61 (s, 3H, Ar), 3.73 (s, 3H, Ar), 5.17(s, 1H, C=C-Ar), 7.06 (s, 1H, Ar), 7.63(s, 1H, Ar); MS m/z 474(M^+),475(M^{+1}).

2. Pharmacology

Antitumor MTT assay

Cell viability was determined by measuring the metabolism of a tetrazolium substrate, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT)[13]. Briefly, the cells (1×10^4 cell per well) were incubated in 96 well plates in which each cell contained 200µl of the growth medium at 37°C. Following overnight incubation, the growth medium was removed from cultures and replaced with 200µL of the test solution. The MTT test was conducted using six concentrations, 31.25µg/mL, 62.5µg/mL, 125µg/mL, 250µg/mL, 500µg/mL, 1000µg/mL, in three cell lines. Tests article solution were incubated with target cells for 72h at 37°C with 5% CO_2.Following exposure, the test solutions were removed and replaced with 500µg/mL MTT solution. The optical density of the mixture in each plate was then measured at 570 nm with a ELISA reader. The tumor cell inhibitory concentration (IC) of each test compound was calculated using the following formula.

$$\%\ Growth\ Inhibition = 100 - \left(\frac{Mean\ OD\ of\ individual\ test\ group}{Mean\ OD\ of\ control\ group} \right) X\ 100$$

The IC_{50} value, the drug concentration lethal to 50% of the tumor cells, was calculated from appropriate dose response curves.

Anti-inflammatory activity

Anti inflammatory activity of prepared compounds was evaluated using Carrageenan induced rat hind paw method[14]. The animals were divided into control, standard and test groups each consisting of six animals. The first group was treated with Tween-80(1%) suspension which served as a control, second group was administered with a dose of 20mg/kg suspension of diclofenac sodium intrapertioneally which served as a standard and other groups were treated with 30 mg/kg of suspension of test compounds in Tween-80 after 30 min, the rats were injected with 0.1mL of Carrageenan (1% w/v) to the sub plantar region of left paw of the rats. The volume of paw was measured using potassium permanganate solution displacement technique with the help of plethysmograph both in control and animals treated with standard and test compounds at 0, 1, 2 and 3 h after injection of Carrageenan. The percentage inhibition of oedema was calculated by using formula,

Percent inhibition = (1-Vt/Vc) ×100

Where Vt is the mean paw volume of the test drug, Vc is the mean paw volume of control.

Results and discussion

Chemistry

The target compounds were synthesized by standard protocol. During the synthesis, all intermediates compounds were identified and the completion of reaction was ensured by TLC with suitable solvent system and purified by eluting solvent systems, toluene: Ethylacetate: Formic acid (5: 4: 1). The crystals were collected and then used for characteristic of IR, NMR, and Mass and Melting point determination and pharmacological evaluations.

Pharmacological studies

Antitumor activity

The pharmacological activities of the synthesized compounds were examined by comparing their antitumor activities, using the MTT assay. The effect of benzothiazoles was tested on three tumor cell lines Melanoma cancer cell (M-14), Human Normal epithelial Brest cancer cell (HLB-100), Human Colon cancer cell (SW-620). IC_{50} values of the synthesized compounds given Table-2. All the substituents were able to inhibit tumor cell lines. The most effective one was DS10 with inhibition concentration (IC_{50}) against of Melanoma cancer cell (M-14) is 54.15±0.152 subsequently DS6 of 242.15±0.419 and DS12 of 244.15±0.463 are the top three synthetic analogs. The remaining compounds also their shown the significant activities against M-14 cell lines.

Among the prepared compounds (DS1-DS12) DS12 had shown top most active compounds against Human Normal epithelial Brest cancer cell (HLB-100) cell lines with 126.15±0.44 of inhibitory concentration (IC_{50}), due to electron density group like methoxy at Para, subsequently DS3 possessed 133.35±0.402 due to Cl as Para direction and DS5 possessed 151.60±0.346 with F act as Para direction.

Human Colon cancer cell (SW-620) cell lines, all the prepared compound compounds had shown significant activities. Among the compounds DS3 had shown IC_{50} value of 49.23±0.593, DS2 possess 55.32±0.481 and DS1 possess 75.40±0.384 were the top three substituents which possess Cl at Para as active functional group.

Anti-inflammatory activity

The synthesized compounds have been screened as possible anti-inflammatory activity by Carrageenan induced oedema method in rates. The compounds exhibited significant anti-inflammatory activity. Compounds DS6, DS5 and DS12 shown top three maximum reduction in the paw oedema volume 43.75, 40.41 and 38.30 percentage respectively and the remaining compounds had shown range from 32.08 to 22.08 against standard diclofenac sodium 54 percentage. The maximum activity may be due to the presence of electron donating group F,OCH_3.

Table 2:IC_{50} of synthesized compounds on different cell lines

Compound ID	IC_{50} (µg/ml)*		
	M-14	HLB-100	SW-620
DS1	608.29 ±0.206	211.58±0.522	75.40±0.384
DS2	491.11±0.313	165.1±0.509	55.32±0.481
DS3	378.93 ±0.403	133.35±0.402	49.23±0.593
DS4	294.18±0.521	287.60±0.392	103.25±0.259
DS5	279.67±0.298	151.60±0.346	97.49±0.294
DS6	242.15±0.419	175.61±0.484	90.25±0.529
DS7	340.83±0.321	274.15±0.215	365.4±0.479
DS8	474.30±0.596	248.57±0.387	244.15±0.452
DS9	400.87±0.45	244.15±0.452	395.63±0.436
DS10	54.15±0.152	165.15±0.129	231.35±0.48
DS11	484.15±0.329	184.43±0.612	257.10±0.321
DS12	244.15±0.463	126.15±0.44	254.60±0.364

n=6, Results are expressed in Mean ±S.E.M, P<0.001 (Followed Tukey-Kramer Equation)

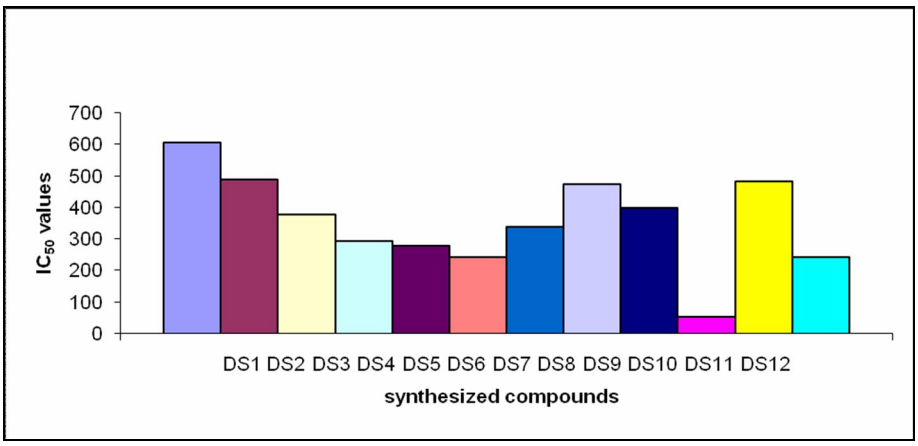

Figure 1: IC_{50} of synthesized compounds on M-14 cancer cell lines

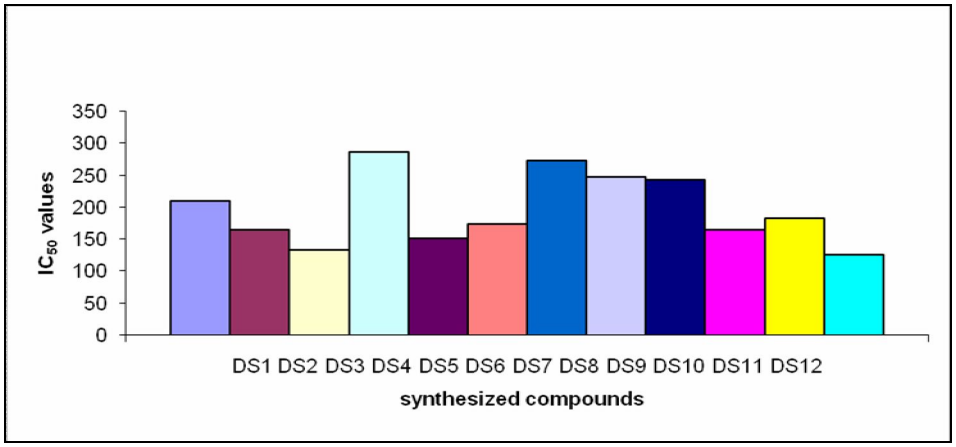

Figure 2: IC_{50} of synthesized compounds on HLB-100 cancer cell lines

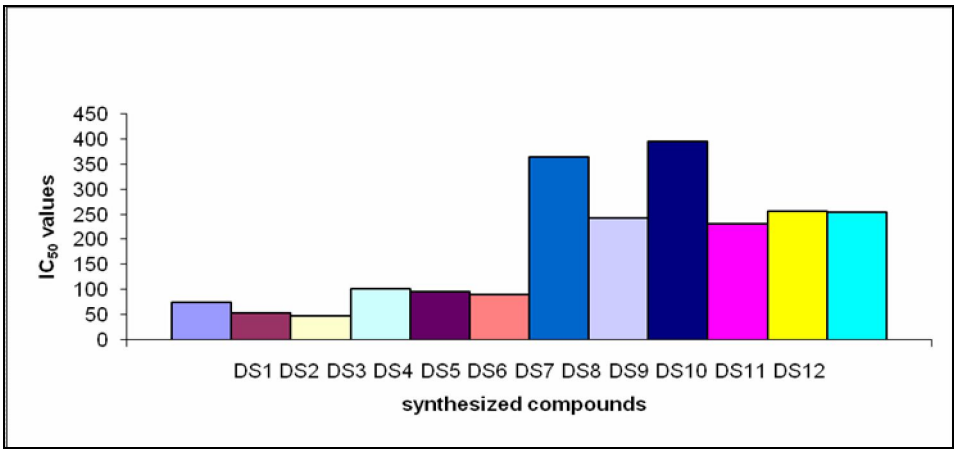

Figure 3: IC_{50} of synthesized compounds on SW-620 cancer cell lines

Table 3: Anti-inflammatory activity of the synthesized compounds

Compound ID	Paw volume ± SEM and Percentage reduction*					
	1h		2h		3h	
	Mean ± SEM	% RPEV	Mean ± SEM	% RPEV	Mean ± SEM	% RPEV
DS1	1.49±0.06	14.60	1.74±0.07	17.14	1.87±0.06	22.08
DS2	1.42±0.02	19.66	1.53±0.05	27.14	1.70±0.04	29.16
DS3	1.39±0.04	21.34	1.45±0.05	30.95	1.63±0.04	32.08
DS4	1.41±0.03	20.22	1.57±0.11	25.23	1.63±0.04	32.08
DS5	1.37±0.05	22.47	1.40±0.06	33.33	1.43±0.05	40.41
DS6	1.31±0.07	25.81	1.35±0.05	35.71	1.35±0.04	43.75
DS7	1.50±0.01	15.73	1.78±0.05	15.23	1.90±0.02	20.83
DS8	1.38±0.05	22.51	1.70±0.05	14.04	1.80±0.05	25.00
DS9	1.48±0.04	22.00	1.65±0.03	21.42	1.75±0.06	27.08
DS10	1.45±0.04	18.50	1.57±0.05	25.23	1.65±0.06	31.25
DS11	1.28±0.03	28.08	1.53±0.05	27.14	1.63±0.06	32.08
DS12	1.32±0.07	25.84	1.42±0.06	32.38	1.48±0.04	38.30
Control	1.78±0.05	-	2.10±0.05	-	2.4±0.03	-
Diclofenac sodium	0.99±0.05	43.24	1.11±0.03	46.60	1.11±0.05	54

REPV is reduction in paw edema volume, *P<0.001 (Followed Tukey-Kramer Equation) when compared to control
% REPV are calculated at 3h

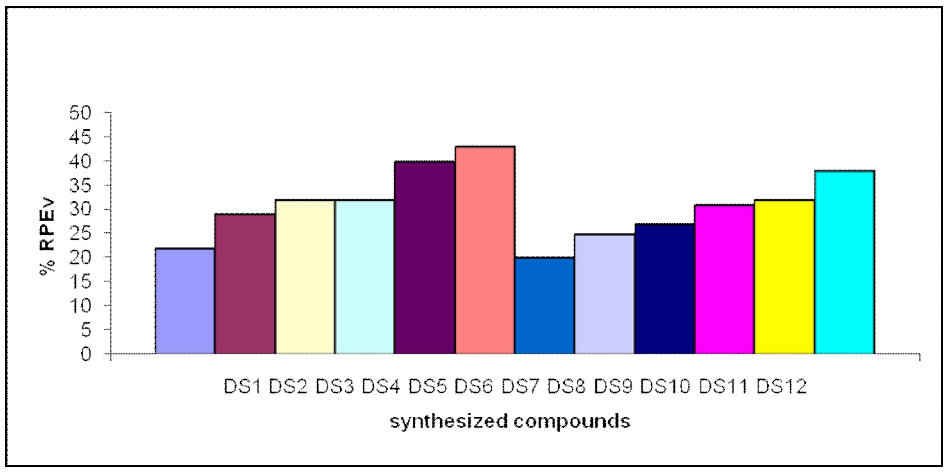

Figure 4: Anti-inflammatory activity of the synthesized compounds

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References

1. Goel. B, Ram. R, Tyagi. E, Bansal. A, Kumar. D, Mukherjee. D, Sinha. J.N, Eur. J. Med Chem., 1999, 34, 265.
2. Joshi. D.G, Oza. H.B, Parekh. H.H, Indian J. Heterocyclic. Chem., 2001, 11, 145.
3. Singh. S.P, Ansari. W.H, Lemiere. G, Jonckers. T, Rogers. D, Eur. J. Med Chem., 2002, 37, 63.
4. Patel. H.D, Misty. B.D, Desai. K.R, Indian J. Heterocyclic. Chem., 2002, 11, 233.
5. Dobaria. A.V, Patel. J.R, Padalia. J.V, Parekh. H.H, Indian J. Heterocyclic. Chem., 2001, 11, 115.
6. Daulatabad. C.D, Bhat. G.G, Indian J. Heterocyclic. Chem., 199, 9, 157.
7. Sharma. P.K, Sawhay. S.N, Gupta. A, Singh. G.B, Bani, Indian J. Chem., 1998, 37B, 376.
8. Yogeeswari. P, Sriram. D, Ramamoorthy. L, Sunil. J.J, Satish. K.S, Stables. J.P, Eur. J. Med Chem., 2002, 37, 231.
9. Bhusari. K.P., Khedekar. P.B., Umathe. S.N., Bahekar. R.H, Rao. R.R.A, Indian J. Heterocyclic. Chem., 2001, 10, 231.
10. Racane. L, Tralic. K.V, Fiser. J.L, Boykin. D.W, Karminski. Z.G, Heterocycles., 2001, 55, 2085.
11. Siddiqui. N, Rana. A, Khan. S.A, Mashooq. A. B, Eur. J. Med Chem., 2008, 43, 1114 – 1122.
12. Singh. S, Smriti singh, Praveen singh, Indian J. Heterocyclic. Chem., 2006, 15, 263-266.
13. Hajduch. M, Mihal. V, Minnarik. V, Faber. E, Safarova. M, Cytotechnology., 1996, 19,243.
14. Kasture. S.B, Veena Kasture. S, Phate. R.P, Pal. S.C, Indian Drugs., 1999, 36, 588-92.

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