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N Saritha Devi
Department of Pharmaceutical Chemistry, University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Divya Sreepada
Department of Pharmaceutical Chemistry, University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Sarangapani Manda
Department of Pharmaceutical Chemistry, University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Correspondence
N Saritha Devi
Department of Pharmaceutical Chemistry, University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India

Synthesis and screening of 3-(4-Oxo-2-phenyl-1,3-thiazol-5(4*h*)-ylidene)-1,3-dihydro-2*h*-indol-2-one - *N*-methylaniline for *In vitro* antiinflammatory activity

N Saritha Devi, Divya Sreepada and Sarangapani Manda

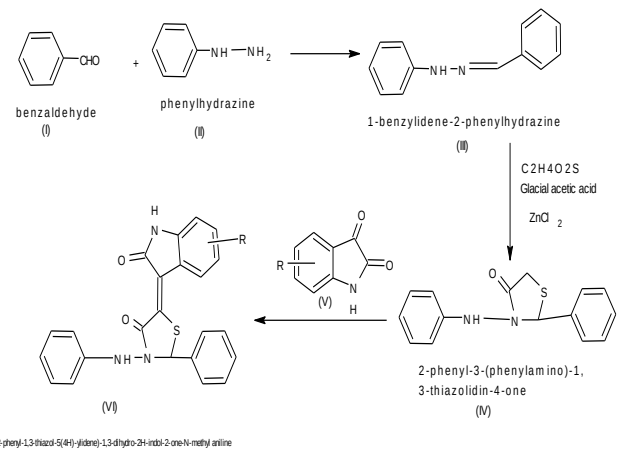
Abstract
A novel synthesis of 3-(4-oxo-2-phenyl-1, 3-thiazol-5(4*H*)-ylidene)-1, 3-dihydro-2*H*-indol-2-one - *N*-methylaniline derivatives is synthesized by cyclization of isatins with thiazolidinones.The synthesized compounds were characterized by spectral data (IR, ^{1}HNMR, MASS) and evaluated for *In vitro* antiinflammatory activity. The compounds VIi(R=5, 6-dichloro) VIf(R=5-F), VIb(R=5=Cl) and VIh(R=5-Br) are considered to possess more potent antiinflammatory activity when compared to standard drug indomethacin.

Keywords: cyclooxygenase, inflammation, isatin, thiazolidinones

1. Introduction
Inflammation is the response of living tissue injury. Inflammation involves fluid and cellular changes within living tissue. The inflammatory process is redundant and complex.In this inflammatory proceess various mediators are involved. Some of the inflammatory mediatorsare having same functions and some of the inflammatory mediatorsare having multiple functions. The same mediator may have different effects on different tissues. The process is continuous over a period of time. Pera
cute, acute, subacute,and chronic are terms used to describe different stages of inflammation. Inflammation is caused by a stimulus and removal of the stimulus should result in abatement of inflammation. It doesn't get fixed in the acute period,it becomes chronic. Blood is the primary delivery system for inflammatory components. Inflammation is a continuum with the healing process.
It is evident from previous studies the isatin derivatives are known to be associated with broad spectrum of biological activities like antibacterial [1], anti-inflammatory [2], analgesic [3], anti-viral [4], anti-fungal [5], anti-tubercular [6], anti-depressant [7]. Isatin hydrazones have been reported to possess anticonvulsant [7] activity also. Thiazolidinones are one ofthe derivatives of thiazolidine whichbelongsto a group of heterocyclic compounds containing sulfur and nitrogen in a five memberedring.
Various Researchers was done researchonthiazolidinones. The nucleus is also known as wonder nucleus because it gives different derivatives with different biological activities.
In view of above facts we were usedisatinsand thiazolidinones in our research. Thecontinuation of our work in the laboratory, prompted us to synthesize some new3-(4-Oxo-2-Phenyl-1,3-Thiazol-5(4*H*)-ylidene)-1,3-Dihydro-2*H*-indol-2-one-*N*-Methylanilines. All the synthesized compounds were screened for their*In vitro* antiinflammatory activity.

2. Material and Methods
All the chemicals were used of analytical grade and obtained from Himedia and SD Fine. Melting points were determined by open capillary tubes using VEEGO VMP-D Digital melting point. FTIR spectra of the powdered compounds were recorded using KBr on a JASCO FTIR 4100 series and are reported in cm^{-1} and 1H NMR spectra were recorded on a Varian Mercury YH300 (300 MHz FT NMR) spectrophotometer using TMS as an internal reference (Chemical shift represented in ppm). Elemental analyses were carried out on Elemental Vario EL (Germany) apparatus. Purity of the compounds was checked by using pre coated TLC plates (silica gel G as a stationary phase) and iodine vapors as the visualizing agent.

3. Chemistry



Scheme 1

3.1 Preparation of 1-Benzylidene-2-phenyl hydrazine (III)

Benzaldehyde (I, 0.01mol) was taken in a beaker and to it phenyl hydrazine hydrate (II, 0.01mol) was added drop by drop, precipitate was formed during addition of phenyl hydrazine. It is kept a side for some time. Then to it add crushed ice and filtered to get the product. The product obtained was washed with ice cold water and dried. The dried compound were recrystalised from suitable solvent.

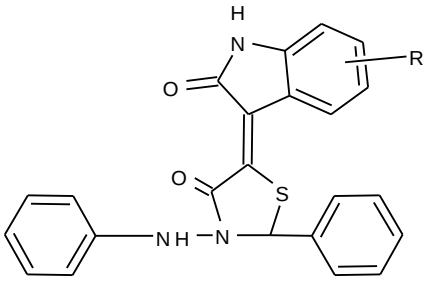
3.2 Preparation of 2-phenyl-3-(phenylamino)-1, 3-thiazolidin-4-one (IV)

To the above product (III) (0.01mol) thioglycollic acid (0.01mol), pinch of ZnCl2 and 10 ml of glacial acetic acid were added and refluxed for 6 hrs. Then the reaction mixture waspoured into crushed ice.

Then to it 10% sodium carbonate solution was added to neutralize the acid. After neutralization the reaction mixture was filtered and the product obtained was washed thoroughly with cold water and allow to dry. The dried compound were recrystalised from suitable solvent.

3.3 Preparation of3-[4-oxo-2-phenyl-3-(phenylamino)-1, 3-thiazolidin-5-ylidene]-1, 3-dihydro-2*H*-indol-2-one (VI)

To the compound (IV) (0.01mol), different isatin derivatives (V) (00.01mol) were added separately to it add 10ml of methanol and 2-3 drops of glacial acetic acid and reflux for 10-12hrs.Cool the reaction mixture and poured into crushed ice precipitate is formed filter the precipitate and dry. Then the dried compound were recrystalised from suitable solvent.



Scheme 1

Table 1: Physical data of the newly synthesized compounds (VIIa–l)

S. No	Compound	R	M.F	M.Wt.	M.P	%Yield
1	VIa	H	$C_{23}H_{17}N_3O_2S$	413	290-292	53
2	VIb	5-Cl	$C_{23}H_{16}ClN_3O_2S$	433	310-312	78.93
3	VIc	7-Cl	$C_{23}H_{16}ClN_3O_2S$	433	295-297	67
4	VId	5-CH_3	$C_{24}H_{20}N_3O_2S$	429	322-324	62.85
5	VIe	7-CH_3	$C_{24}H_{20}N_3O_2S$	429	348-350	63
6	VIf	5-F	$C_{23}H_{16}FN_3O_2S$	417	288-290	78
7	VIg	7-F	$C_{23}H_{16}FN_3O_2S$	417	330-332	67.32
8	VIh	5-Br	$C_{23}H_{16}BrN_3O_2S$	478	326-328	69.18
9	Vii	5,6-Dichloro	$C_{23}H_{15}Cl_2N_3O_2S$	484	340-342	63
10	VIj	5-NO_2	$C_{23}H_{16}N_4O_4S$	444	300-302	76
11	VIk	7-NO_2	$C_{23}H_{16}N_4O_4S$	444	356-358	76
12	VIl	5-OH	$C_{23}H_{17}N_3O_3S$	415	289-291	62.31

Spectral Data of the Synthesized Compounds

VI(a) 3-(4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline

IR(KBr) cm−1:3443.59(N-H),3103.33(N-H), 1786.69(C=O), 1621.53(C=O);$_1$HNMR(400MHz,CDCl3):δ [ppm], 5.6(s,1H,aliphatic),5.8(s,1H,NNH),6.8(t,1H, aromatic7.0(d,2H,aromatic),7.18(d,1H,aromatic), 7.25(m,6H,aromatic), 7.4(d,2H,aromatic), 7.6(t,1H,ArH), 8.82(d,1H,indoleArH); ^{13}CNMR:29.6,110.2, 113.5, 113.5, 120.8, 122.6, 123.2, 124.2, 128.1, 128.8, 128.8, 129.2, 129.2, 129.5, 129.5, 131.0, 137.2, 140.2, 141.4, 149.4, 150.0, 163.7, 167.2, 170.3 Elemental analysis: $C_{23}H_{17}N_3O_2S$ Calculated Values:C-69.71,H-4.63,N-10.16,S-7.75 observed values:C-69.68,H-4.61,N-10.11,S-7.73.

MS:m/z:413.12(100.0%),414.12(27.9%),415.12(5.4%),415.13(3.3%),416.12(1.2%).

VI(b) 3-(5-Chloro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1, 3-dihydro-2*H*-indol-2-one - *N*-methylaniline

IR(KBr) cm−1:3442.49(N-H),3101.31(N-H), 1787.29(C=O), 1620.33(C=O);$_1$HNMR(400MHz,CDCl3):δ [ppm], 5.61(s,1H,aliphatic),5.82(s,1H,NNH), 6.81(t,1H, aromatic 7.1(d,2H,aromatic),7.2(d,1H,aromatic),7.3(m,5H,aromatic),7.45(d,2H,aromatic),7.65(t,1H,ArH),8.83(d,1H,indoleArH);^{13}CNMR:29.6,113.5,113.5,120.8,124.0,125.0,126.6,128.2,128.8, 128.8,129.2,129.2,129.5,129.5,129.8,131.0,137.2,139.5,140.2, 149.4,150.0,163.7,167.2,170.3Elementalanalysis: $C_{23}H_{16}ClN_3O_2S$ Calculated Values:C-64.35,H-4.05,N-9.38,S-7.16observedvalues:C-64.33,H-4.01,N-9.36,S-7.13.

MS:m/z:447.08(100.0%),449.08(37.0%),448.08(27.9%),450.08(9.9%),449.09(3.7%),451.08(1.5%),451.07(1.4%).

VI(c) 3-(7-Chloro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3444.69(N-H),3105.13(N-H),1785.29(C=O),1622.33(C=O);$_1$HNMR(400MHz,CDCl3): *δ*[ppm],5.59(s,1H,aliphatic),5.81(s,1H,NNH),6.82(t,1H,aromatic7.15(d,2H,aromatic),7.22(d,1H,aromatic),7.35(m,5H,aromatic),7.35(d,2H,aromatic),7.55(t,1H,ArH),8.84(d,1H,indoleArH);^{13}CNMR:29.6,113.5,113.5,120.8,121.3,124.0,125.6,128.8,128.8,129.2,129.2,129.3,129.5,129.5,130.4,131.0,136.3,137.2,140.2,149.4,150.0,163.7,167.2,170.3Elemental analysis: $C_{23}H_{16}ClN_3O_2S$ Calculated Values:C-64.35,H-4.05,N-9.38,S-7.16 Observed values:C-64.31,H-4.03,N-9.37,S-7.14.MS:m/z:447.08(100.0%),449.08(37.0%),448.08(27.9%),450.08(9.9%),449.09(3.7%),451.08(1.5%),451.07(1.4%).

VI(d) 3-(5-Methyl-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3441.49(N-H),3100.23(N-H),1784.29(C=O),1623.43(C=O);$_1$HNMR (400MHz,CDCl3): *δ*[ppm],5.58(s,1H,aliphatic),5.8(s,1H,NNH),6.8(t,1H,aromatic 7.2(d,2H,aromatic), 7.25 (d,1H,aromatic),7.37(m,5H,aromatic),7.4(d,2H,aromatic),7.62 (t,1H,ArH),8.85(d,1H,indoleArH);^{13}CNMR:21.7,29.6,113.5,113.5,120.8,121.4,122.5,126.8,128.4,128.8,128.8,129.2,129.2,129.5,129.5,131.0,133.9,137.2,138.4,140.2,149.4,150.0,163.7,167.2,170.3 Elemental analysis: $C_{24}H_{20}N_3O_2S$ Calculated Values:C-70.24,H-4.95,N-9.83,S-7.50 Observed values:C-70.21,H-4.92,N-9.81,S-7.47.MS: m/z: 427.14(100.0%), 428.14(27.4%),429.13 (4.5%),429.14(4.5%), 428.13(1.9%), 430.13(1.3%).

VI(e) 3-(7-Methyl-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3440.29(N-H),3105.13(N-H),1782.29(C=O),1624.23(C=O);$_1$HNMR(400MHz,CDCl3): *δ*
[ppm],5.57(s,1H,aliphatic),5.82(s,1H,NNH),6.81(t,1H,aromatic7.25(d,2H,aromatic),7.27(d,1H,aromatic),7.4(m,5H,aromatic),7.45(d,2H,aromatic),7.63(t,1H,ArH),8.82(d,1H,indoleArH);^{13}CNMR:9.1(s,1H,amide)^{13}CNMR:17.7,29.6,113.5,113.5,120.2,120.8,122.5,124.1,127.0,128.8,128.8,129.2,129.2,129.5,129.5,129.9,131.0,137.2,140.2,141.9,149.4,150.0,163.7,167.2,170.3 Elemental Analysis: $C_{24}H_{20}N_3O_2S$ Calculated Values:C70.24-,H-4.95,N-9.83,S-7.50 Observed values:C-70.21,H-4.92,N-9.80,S-7.48.MS:m/z:
427.14(100.0%),428.14(27.4%),429.13(4.5%),429.14(4.5%),428.13(1.9%),430.13(1.3%).

VI(f) 3-(5-Fluoro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3441.20(N-H),3105.22(N-H),1784.23(C=O),1623.43(C=O);$_1$HNMR(400MHz,CDCl3): *δ* [ppm],5.55(s,1H,aliphatic), 5.8(s,1H,NNH), 6.82(t,1H,aromatic)
7.24(d,2H,aromatic),7.26(d,1H,aromatic),7.45(m,5H,aromatic),7.5(d,2H,aromatic),7.64(t,1H,ArH),8.84(d,1H,indoleArH);^{13}CNMR:29.6,111.4,112.5,113.5,113.5,114.9,120.8,124.2,128.8,128.8,129.2,129.2,129.5,129.5,131.0,137.0,137.2,140.2,149.4,150.0,158.4,163.7,167.2,170.3 Elemental analysis: $C_{23}H_{16}FN_3O_2S$ Calculated Values:C-66.81,H-4.20,N-9.74,S7.43Observedvalues:
C66.79,H4.17,N9.71,S7.42;MS:m/z:431.11(100.0%),432.11(27.9%),433.11(5.4%),433.12(3.3%),434.11(1.2%)

VI(g) 3-(7-Fluoro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3443.59(N-H),3103.33(N-H),1786.69(C=O),1621.53(C=O);$_1$HNMR(400MHz,CDCl3): *δ* [ppm],5.56(s,1H,aliphatic), 5.82(s,1H,NNH),6.84(t,1H,aromatic)7.25(d,2H,aromatic),7.28(d,1H,aromatic),7.5(m,5H,aromatic),7.55(d,2H,aromatic),7.65(t,1H,ArH),8.81(d,1H,indoleArH);^{13}CNMR:29.6,113.5,113.5,114.9,118.8,120.8,122.9,124.2,125.8,128.8,128.8,129.2,129.2,129.5,129.5,131.0,137.2,140.2,149.4,150.0,162.7,163.7,167.2,170.3 Elemental analysis: $C_{23}H_{16}FN_3O_2S$ Calculated Values:C-66.81,H-4.20,N-9.74,S-7.43 Observed values:C-66.78,H-4.18,N-9.72,S-7.41 MS: m/z: 431.11(100.0%),432.11(27.9%),433.11(5.4%),433.12(3.3%),434.11(1.2%).

VI(h) 3-(5-Bromo-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr)cm−1:3441.59(N-H),3100.33(NH), 1784.69 (C=O),1624.53(C=O);$_1$HNMR(400MHz,CDCl3): *δ* [ppm],5.5(s,1H,aliphatic),5.81(s,1H,NNH),6.85(t,1H,aromatic)7.3(d,2H,aromatic),7.35(d,1H,aromatic),7.55(m,5H,aromatic),7.6(d,2H,aromatic),7.7(t,1H,ArH),8.82(d,1H,indoleArH);^{13}CNMR:29.6,113.5,113.5,117.8,118.6,120.8,124.8,128.8,128.8,129.2,129.2,129.5,129.5,130.1,131.0,133.8,137.2,140.2,140.4,149.4,150.0,163.7,167.2,170.3 Elemental analysis: $C_{23}H_{16}BrN_3O_2S$ Calculated Values:C-58.54,H-3.68,N-8.53,S-6.51 Observed values:C-58.52,H-3.67,N-8.52,S-6.49 MS:m/z:493.03(100.0%),491.03 (97.4%),494.03 (27.9%),492.03(27.2%),495.02 (4.3%),495.03 (4.1%),493.04(3.2%),496.03(1.2%).

VI(i) 3-(5,6-Dichloro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3442.21(N-H),3105.23(N-H),1784.69(C=O),1624.23(C=O);$_1$HNMR(400MHz,CDCl3): *δ*
[ppm],5.55(s,1H,aliphatic),5.83(s,1H,NNH),6.88(t,1H,aromatic)7.4(d,2H,aromatic),7.45(d,1H,aromatic),7.6(m,4H,aromatic),7.65(d,2H,aromatic),7.75(t,1H,ArH),8.83(d,1H,indoleArH);^{13}CNMR:
29.6,113.5,113.5,120.8,122.1,123.3,128.0,128.8,128.8,128.9,129.2,129.2,129.5,129.5,130.4,131.0,137.2,140.2,143.5,149.4,150.0,163.7,167.2,170.3 Elemental analysis: $C_{23}H_{15}Cl_2N_3O_2S$ Calculated Values:C-59.76,H-3.55,N-8.71,S-6.65 observed values:C-59.74,H-3.53,N-8.69,S-6.63
MS:m/z:481.04(100.0%),483.04
(69.0%),482.05(26.2%),484.04(19.1%),485.04(11.0%),483.05(3.7%),486.04(3.6%),485.03(2.9%),485.05(2.1%),482.04(1.9%)

VI(j) 3-(5-Nitro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline
IR(KBr) cm−1:3440.67(N-H),3101.45(N-H),1782.45(C=O),1625.32(C=O);$_1$HNMR(400MHz,CDCl3): *δ* [ppm],5.57(s,1H,aliphatic), 5.84(s,1H,NNH),6.9(t,1H,aromatic)7.45(d,2H,aromatic),7.5(d,1H,aromatic),7.65(m,5H,aromatic),7.7(d,2H,aromatic),7.8(t,1H,ArH),8.84(d,1H,indoleArH);^{13}CNMR:
29.6,113.5,113.5,120.2, 120.8,122.4, 123.3,123.5,128.8,128.8,129.2,
129.2,129.5,129.5,131.0,137.2,140.2,143.4,147.5,149.4,150.0,163.7,167.2,170.3 Elemental analysis: $C_{23}H_{16}N_4O_4S$ Calculated Values:C-62.87,H-3.96,N-12.22,S-6.99 observed

values:C-62.85,H-3.94,N-12.20,S-6.98 MS:m/z:458.10 (100.0%),459.11(26.3%), 460.11(4.7%), 460.10(4.5%), 459.10(2.3%),461.10(1.3%).

VI(k) 3-(7-Nitro-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline

IR(KBr) cm−1:3441.24(N-H),3105.12(N-H),1782.24(C=O),1624.21(C=O);$_1$HNMR(400MHz,CDCl3): δ [ppm],5.5(s,1H,aliphatic), 5.7(s,1H,NNH),6.85(t,1H,aromatic)7.5(d,2H,aromatic),7.55(d ,1H,aromatic),7.7(m,5H,aromatic),7.75(d,2H,aromatic),7.85(t, 1H,ArH),8.85(d,1H,indoleArH);^{13}CNMR:29.6,113.5,113.5, 120.8, 123.5,124.5, 125.1,128.8,128.8,129.2, 129.2,129.3,129.5,129.5,131.0,131.0,137.2,140.2,142.3,149.4, 150.0,163.7,167.2,170.3 Elemental analysis: $C_{23}H_{16}N_4O_4S$ Calculated Values:C-62.87,H-3.96,N-12.22,S-6.99 Observed values:C-62.85,H-3.94,N-12.20,S-6.98 MS:m/z:458.10(100.0%),459.11(26.3%),460.11(4.7%),460.10 (4.5%),459.10(2.3%), 461.10(1.3%).

VI(l) 3-(7-Hydroxy-4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylaniline

IR(KBr) cm−1:3443.59(N-H),3103.33(N-H),1786.69(C=O),1621.53(C=O);$_1$HNMR(400MHz,CDCl3): δ [ppm],5.55(s,1H,aliphatic), 5.72(s,1H,NNH),6.8(t,1H,aromatic)7.55(d,2H,aromatic),7.65(d,1H,aromatic),7.75(m,5H,aromatic),7.8(d,2H,aromatic),7.85(t,1H,ArH),8.82(d,1H,indoleArH);^{13}CNMR: 29.6,112.3,113.5,113.5, 115.3, 120.8,122.9,124.0,128.8,128.8, 129.2,129.2,129.5,129.5,131.0,134.0,137.2,140.2,149.4,150.0, 154.0,163.7,167.2,170.3Elemental analysis: $C_{23}H_{17}N_3O_3S$ Calculated Values:C-67.12,H-4.46,N-9.78,S-7.47 observed values:C-67.10,H-4.45,N-9.77,S-7.45 MS:m/z:429.11 (100.0%),430.12(26.3%),431.11(4.5%),431.12(4.4%),430.11(1.9%),432.11(1.2%).

4. Biological Activity

The newly synthesized compounds were screened for *In vitro* antiinflammatory activity. The assay was performed using colorimetric COX(ovine) inhibitor screening assay kit (Cyaman Chemical, MI, USA).The colorimetric COX(ovine) inhibitor screening assay utilizes the peroxidase activity of ovine cyclooxygenase to oxidize the colorimetric substrate N,N,N′,N′-tetramethyl-p-phenylenediamine (TMPD) [8]. Enzyme assays were run in 220µl volumes. The mixture in background wells,100%initial activity well and inhibitor wells were prepared according to instructions provided in the kit and pre incubated for five minutes at 25^0C .The reaction was initiated by addition of 20µl of TMPD solution followed by 10µl of arachidonic acid in all the wells. The assay mixture was shaked and incubated at 25^0C for 5 min. The enzyme activity was measured as an increase in absorbance at 590nm. The results were presented in Table 2.

Table 2: *In vitro* antiinflammatory activity data of 3-(4-oxo-2-phenyl-1, 3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylanilines. (VI(a-l))

S. No.	Compound	R	% of COX-2 Inhibition
1	VIa	H	46.23±0.14
2	VIb	5-Cl	66.35±0.54
3	VIc	7-Cl	61.590±0.11
4	VId	5-CH_3	50.65±0.32
5	VIe	7-CH_3	48.34±0.45
6	VIf	5-F	69.64±0.56
7	VIg	7-F	57.21±0.33
8	VIh	5-Br	64.71±0.67
9	VIi	5,6-Dichloro	71.56±0.40
10	VIj	5-NO_2	55.63±0.23
11	VIk	7-NO_2	53.18±0.46
12	VIl	5-OH	59.42±0.19
13	Indomethacin		73.32±0.32

5. Results and Discussion

In this research we have synthesized some of the new isatin derivatives were obtained by cyclization of isatins with 2-phenyl-3-(phenylamino)-1,3-thiazolidin-4-one in presence of methanol with glacial acetic acid depicted in scheme 1. Physical data of all the synthesized compounds are shown in Table1.

5.1. *In Vitro* Antiinflammatory Activity: From scheme-1, the compounds were evaluated for *in vitro* antiinflammatory activityby using colorimetric COX(ovine) inhibitor screening assay kit (Cyaman chemical, MI, USA). The colorimetric COX(ovine) inhibitor screening assay utilizes the peroxidase activity of ovine cyclooxygenase to oxidize the colorimetric substrate,N,N,N',N'-tetramethyl-p-phenylenediamine (TMPD), From the above data it is cleared that all the tested compounds showing significant activity. The results were presented in Table2. Among the tested compounds VIi(R=5,6-dichloro),VIf(R=5-F),VIb(R=5=Cl) and VIh(R=5-Br) are considered to possess potent anti-inflammatory activity when compared to standard drug indomethacin. From the obtained results it is clear that di halo substituted derivative(VIi(R=5,6-dichloro)) is found to be more potent compared to other synthesized compounds.

6. Conclusion

The present study involves synthesis and evaluation of 3-(4-Oxo-2-phenyl-1,3-thiazol-5(4*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-one - *N*-methylanilines for *In vitro* antiinflammatory activity. The title compounds have shown potent antiinflammatory activity.

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