Available online through www.sciensage.info

Journal of Advanced Scientific Research

J.Adv.Sci.Res, 2011; 2(2): 35-44
Review Article

ISSN: 0976-9595

SYNTHETIC AND BIOLOGICAL MULTIPLICITY OF ISATIN: A REVIEW

Manju Pal*
Neeraj K. Sharma
Priyanka
K.K.Jha
College of Pharmacy, Teerthankar Mahaveer University, Moradabad

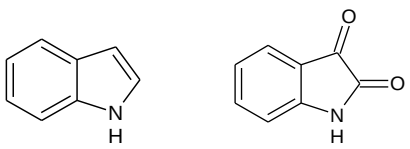
***Corresponding Author:**
manju.pal87@gmail.com

ABSTRACT

Isatin (2,3-dioxindole) is an endogenous compound identified in humans, and its effect has been studied in a variety of systems. Isatin nucleus having both the keto and lactam moiety has aroused tremendous curiosity due to its diverse biological and pharmacological studies. From literature survey it is well known that isatin heterocycles exhibit manifold importance in the field of medicinal chemistry as a potent chemotherapeutic agent. Biological properties of isatin include a range of actions in the brain and offer protection against certain types of infections. This review represents some synthesized isatin derivatives and their pharmacological profiles which may contribute in future to synthesize various analogs and to develop new pharmacologically less toxic medicines.

Keywords: Isatin, Antimicrobial, Anticonvulsant, anti-HIV

INTRODUCTION



Indole Isatin

Fig: 1

Isatin or 1H-indole-2,3-dione is an indole derivative. The compound was first obtained by Erdman[1] and Laurent[2] in 1841 as a product from the oxidation of indigo dye by nitric acid and chromic acids. The compound is found in many plants. In recent years, indole derivatives have acquired conspicuous significance due to their wide spectrum of biological activities[3].

The synthetic versatility of isatin has led to the extensive use of this compound in organic synthesis. In nature, isatin is found in plants of the genus *Isatis*, in *Calanthe* discolor LINDL. Isatin is the biologically active chemical produced by an *Altermones* sp. strain inhibiting the surface of embryos of the cardiean shrimp *Palaemon macrodectylus*, which protect them from the pathogenic fungus *Lagenidium callinectes*[4].

Isatin ring system consists of pyrrole ring fused with benzene ring. Pyrrole ring is a five-member ring containing one nitrogen in the ring system.

Isatin moeity shows biological activites like antimicrobial, CNS depressant, anti-HIV, cytotoxicity, anti-inflammatory, anlagesic, antianixety and many other activities. A brief account is given below:

1. ANTIMICROBIAL ACTIVITY

Antimicrobial drugs are effective in the treatment of infection because of their selective toxicity; that is, they have the ability to injure or kill an invading microorganism without harming the host[5]. It is evident from literature that isatin derivatives are known to be associated with broad spectrum of biological activities like antibacterial, antifungal. Bis-shiff bases, N-mannich bases, phthalimidoxy substituted and spiro-thiazolidinone derivatives of isatin & spiroindoles and imidazolines derivatives possess antimicrobial activity and it act against variety of gram +ve and gram -ve bacterias, some fungi and viruses.

2-Amino-11-hydronaphtho[2,1:5,6]pyrano[4,3-*d*]thiazole on treatment with isatin, chlroacetyl chloride and mercaptoacetic acid affords corresponding N [naphtha [1,2b] pyrano3,4d]thiazol-8-yl]spiro-[3H-indole-(1H,2H)3,4-(2H)-3chloroazetidine-2,2-diones and N[naphtha [1, 2b]pyrano[3,4-d]thiazol-8-yl]spirol-[3H- indole-(1H, 2 H)-3,2-(4H)-thiazolidine]-2,4-dione (fig.2). All the synthesized compounds were screened for their antibacterial activity against *S.aureus, S.pyogene, S.albus and E.coli* according to the standard procedure. The minimum inhibitory concentration (MIC) was determined using tube dilution method according to standard procedure. DMF was used as a solvent and blank. Ciprofloxcin (MIC: 5ug/ml) was used as the antibacterial standard. The obervation reveals that the compound found to possess considerable antibacterial activity[6].

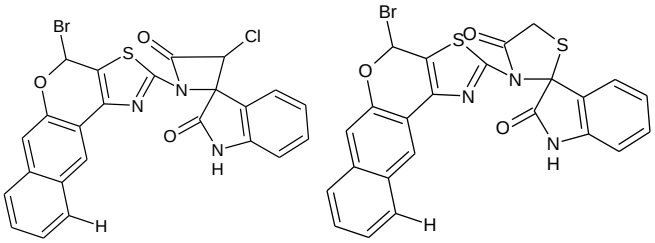


Fig:2. Cyclization of isatin

G L Talesara[7] et al had been synthesized 3'-[(4-acetate phenyl-1N-ethoxyphthalimido-6'-pyridin-2-yl]-3,3a'-dihydro-6'H-spiro [indole-3,5'-[1,3]-thiazole[4,5-c]isoxazol]-2(1H)-ones (fig. 3) by reacting 3-(4-acetate phenyl)-6-pyridin-2-yl-3,3a-dihydro-6H-spiro[indole-3,5[1,3]thiazolo[4,5-c]isoxazol]-2(1H) -ones with bromoethoxypthalimide which shows good antimicrobial activity.

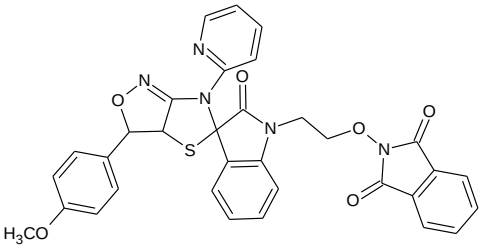


Fig:3. Cyclocondensation of isatin

5-substituted-3-(4-arylimino)-1-[5-mercapto(1,3,4-oxadiazolyl)] -methyl-indol-2-one (fig. 4) have been synthesized by heterocyclization of 5-substituted-3-(4-arylimino)-2-oxo-1-indole acetylhyrazide on treatment with CS_2 in ethanolic KOH. All the compounds were evaluated for their *in-vitro* anti-bacterial activity against *S. aureus NCIM 2079, B subtilis ATCC 6633, E. coli ATCC M 200, P. vulgaris NCIM 2813* and anti-fungal against *C. albicans NCIM 3471, A. niger NCIM 545* standard strains using disc diffusion method. The synthesized compounds showed good antibacterial and antifungal activity[8].

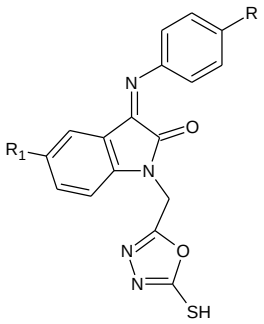


Fig:4. 5-substituted-3-(4-arylimino)-1-[5-mercapto (1,3,4 -oxadiazolyl)]-methyl-indol-2-one analogs

Ali Asghar Jarrahpour[9] et al had been synthesized bis-Schiff bases of isatin by condensation of isatin, benzylisatin and 5-fluoroisatin (fig.5) with primary aromatic amines which posses significant antiviral, antibacterial and antifungal actvity.

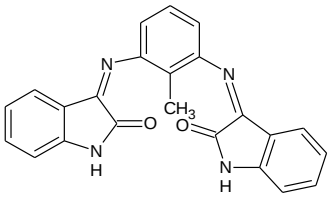


Fig:5. bis-Shiff bases of isatin

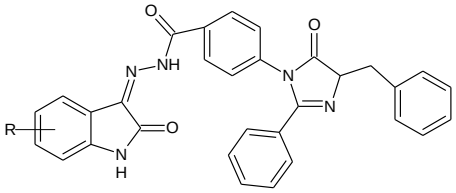


Fig:6. Isatin derivatives

3-[(5-benzylidene-2-phenyl)-3,5-dihydro-4-H-imidazol-4-one -3-(4-bezoylhydrazono)]-indole-2-ones(fig.6)were sythesized by Sanjay Bari[10] and coworkers which is reacted by isatin hydrazones (II, 0.01 mol) and 2-phenyl 5-bezylidene 3N (4-acetyl phenyl)-1,5-dihydroimidazole-4-one which shows promising antimicrobial activity.

R S Verma[11] et al had been synthesized 2-[(3-chloro-2-phenyl)-4-azetidinon-3yl]-1,3,4-thiadiazinol[6,5-b]indole (fig.7) by reacting benzyliden amino-1,3,4-thiadiazione[6,5-b]indole and chloroacetyl chloride. The compounds were evaluated for their antimicrobial susceptibility test *against S.aureus,E.coli, K.pneumoniae, P.vulgaris, A.fumigatus, C.albicans, albicans* ATCC, *C.krusei* G03 respectively. The compounds showed significant antibacterial and antifungal activity.

G L Teralesara[12] et al had been synthesized 3'{4(1acetyl-5(4-flurophenyl)-2pyrazoline-3yl)phenyl} 1-N-ethoxyphthalimido-4'-spiro[indole-3,2'-[1,3]thiazolidene]-2,4'-1H-dione (fig. 8) which is formed by reacting 3{4-(1-acetyl-5-(4-chlorophenyl)-2pyrazoline-3-yl)phenyl}-4'H-spiro[indole-3,2'-[1,3]thiazolidene]-2,4'-1H-dione in DMF and sodium hydride which showed good antibacterial activity.

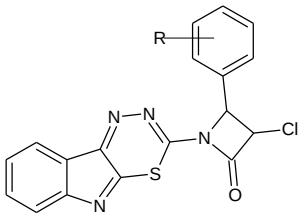


Fig:7. Isatin thiadiazino derivatives

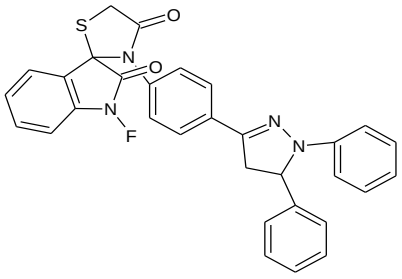


Fig:8. Phthalimidoxy substituted and spiro-thiazolidinone

5-Nitro-1H-indole-2,3dione-3-N-(4H-methylphenyl)thiosemicarbazones (fig.9) were synthesized by Vikash Kumar[13] et al by reacting 3-hydrazono-5-nitro-1,3-dihydro-2H-indole-2-one and p-methyl phenylisothio cyanate. The compounds were screened for antibacterial activity against *E.coli* and *S. aureus* by Cup–plate method.

Isatin and its chloro derivative had been reacted with 5-amino, 8-hydroxy-quinoline to from Shiff and the N-Mannich bases of isatin (fig. 10). Compounds were synthesized by reacting them with formaldehyde and several secondary amines. Investigation of antimicrobial activity of the compounds was made by the agar dilution method. The compounds are significantly active against bacteria and fungi[14].

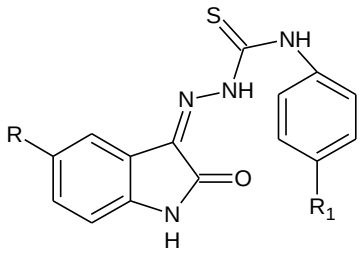


Fig:9. Isatin thiosemicarbazone derivatives

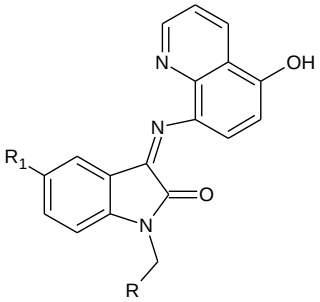


Fig: 10. Hydroxyquinoline Schiff bases

A series of schiff and mannich bases of isatin (fig. 11) had been synthesised by S K Singh[15] et al which is formed by dimethyl amine, diethyl amine, piperidine, morphine, pyrazinamide and formaldehyde and shows significant antimicrobial activity.

1-(3-phenyl-spiro[3H-indole-3,2-thiazolidine]-2,4(1H)-dione-1-ylacetamido)-2-phenyl-4-phenyl-idene-5-oxoimidazolines (fig. 12) were formed by the mixture of 3-phenyl-spiro[3H-indole-3,2-thiazolidine]-2,4(1H)-dione-1-ylacetyl hydrazine and 2-phenyl-4-phenylidene-5-oxazolone in the presence of glacial acetic acid by U.C.Mashelkar[16] and coworkers. The synthesized compound shows good antibacterial activity.

N-Mannich bases of isatin (fig. 13) were formed by U.K.Singh[17] and coworkers by reacting Schiff's bases of Isatin with formaldehyde and secondary amine. The compounds show promising antimicrobial activity.

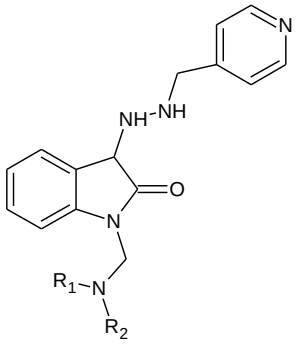


Fig:11. N-Mannich bases of isatin

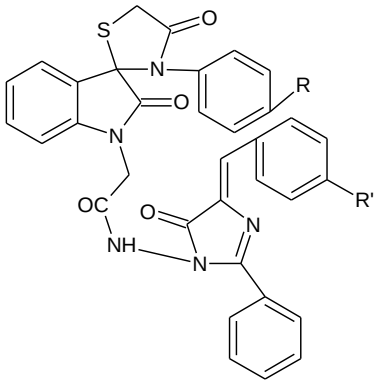


Fig:12. Spiroindoles and imidazolines derivaties

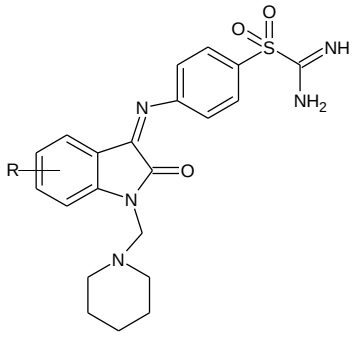


Fig:13. N-Mannich bases of isatin

2. CNS DEPRESSANT ACTIVITY

Depression is defined as disorders of mood rather than disturbances of thought or cognition. Depression accompanied by hallucination and delusion[18]. Some of isatin derivatives show CNS depressant activity. Semicarbazones, thiosemicarbazole, heterocyclic derivatives of isatin and Isatin-based spiroazetidinones shows anticonvulsant activity.

S N Pandey[19] et al had been synthesized Isatin-3-hydrazone (fig. 14) by istain, parabromo and phenoxy acetyl hydrazide with glaceial acetic acid which shows anticonvulsant activity.

Krishan Nand Singh[20] et al had been synthesized (3*Z*)-5-bromo-1-methyl-3-[(4-nitrophenyl)imino]-1,3-dihydro-2*H*-indol-2-one (fig. 15) by reacting 5-substituted *N*-methyl/*N*-acetyl isatin and aromatic amine with glacial acetic acid and was shown to possess good anticonvulsant activity.

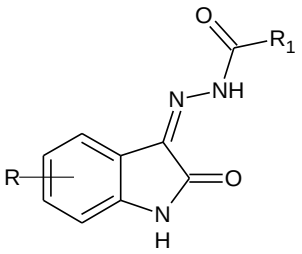


Fig:14. Semicarbazone isatin derivatives

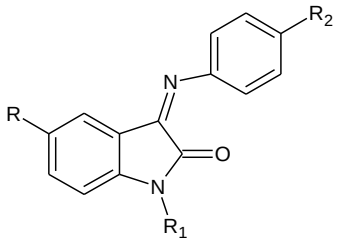


Fig:15. Shiff bases of isatin derivatives

N-methyl/acetyl-5-(un)-substituted isatin-3-semicarbazones (fig. 16) were formed by Sivakumar Smith[21] and coworkers by reacting N-methyl/acetyl isatin, 5-bromo/nitro-N-acetyl isatin and p-substituted phenyl semicarbazides. The compounds possess anticonvulsant and sedative activity.

Ashok Kumar[22] et al had been synthesized 3-Spiro[1', 3', 4'-oxa/thiadiazolyl-2'-{5"-(substitutedphenyl-3"-amino)-4'-{5"-(substituted phenylisoxazolinyl)}]-5'-indol-2-ones (fig. 17) by the reaction of 3-Spiro-[1', 3', 4'-oxadiazolyl-2'-{1"-acetyl-5"-(2-hydroxyphenyl-3"-amino)-4'-{1"-acetyl-5"- (2-hydroxyphenyl) pyrazolinyl}]-5'-indol-2-ones with methanol, hydroxyl amine and NaOH solution which shows anticovulsant and antipsycotic activity.

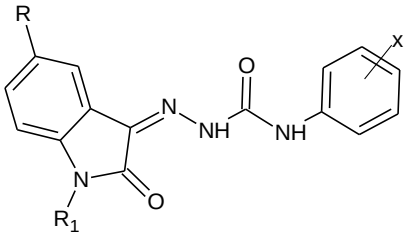


Fig:16. Thiosemicarbazole isatin derivatives

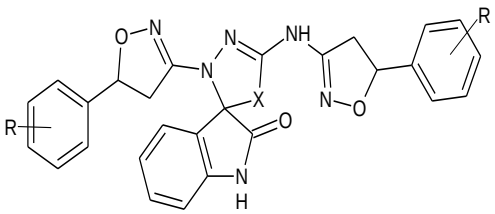


Fig:17. Pyrazolinyl/isoxazolinyl indol-2-ones derivatives

Heterocyclic derivatives of isatin (fig. 18) were formed by reacting a heterocyclic system like isatin/5-fluoroisatin with ethyl cyano acetate and substituted ketones which shows anticonvulsant activity[23].

3-aryloxyl, arylthioxy acetyl hydrazono-2-indolinones (fig. 19) had been synthesized by Gursoy and Karali[24] et al.

Singh[25] et al had been synthesized a series of isatin-based spiroazetidinones (fig. 20) and screened them for their anticonvulsant activity.

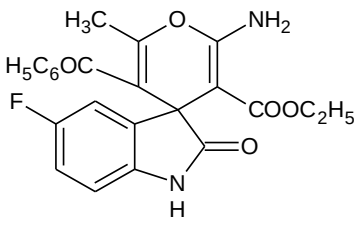


Fig:18. Heterocyclic derivatives of isatin

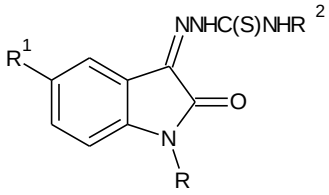


Fig:19. Hydrazono-2-indolinones

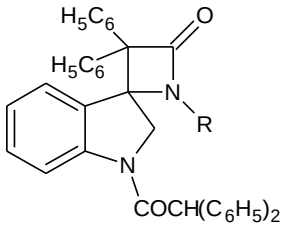


Fig:20. Isatin-based spiroazetidinones

3-(-4-(4-hydroxy-3-methoxylbenzylideneamino) phenyl imino) indoline-2-one (fig. 21) was synthesized by the isatin and p-phenylenediamine by dissolving in sufficient quantity of methanol (30 mL) in the presence of acetic acid. Various aromatic aldehydes were allowed to react to obtain final compounds[26]. The compounds showed excellent anticovulsant activity.
Isatin schiff's bases (fig. 22) were formed by the 6-(un)substituted 1,3 benzothiazol-2-amine and indole 2, 3-dione by dissolving 20 ml of absolute alcohol and were refluxed in presence of few drops of glacial acetic acid[27].

Isatin-5-Sulphonamide derivatives (fig. 23) were formed by the M. Sarangapani[28] and the compounds were evaluated for anticonvulsant ability using Phenytion as standard. All the synthesized compounds showed excellent anticonvulsant activity against electric shock induced and Pentylenetetrazole induced seizures.

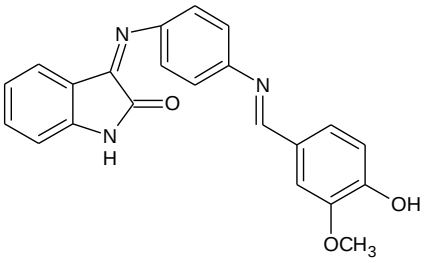


Fig:21.Phenylimino Shiff bases of isatin

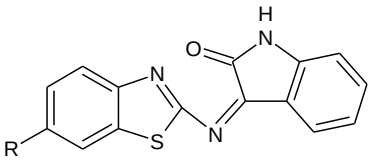


Fig:22. Isatin schiff bases

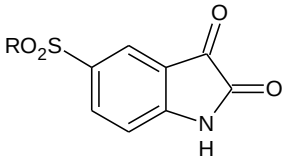


Fig:23. Isatin-5-Sulphonamide derivatives

3. CYTOTOXICITY

Cancer is a disease characterised by uncontrolled multipication and spread of abnormal forms of the body's own cells[18]. From literature survey it is well known that isatin heterocycles exhibit manifold importance in the field of medicinal chemistry as a potent chemotherapeutic agent. Bis-diisatin derivatives, Bis-Isatin Thiocarbohydrazone Metal Complexes, 3-*o*-Nitrophenyl hydrazones of isatin possess cytotoxicity activity.

Co(II), Ni(II), Cu(II), and Zn(II) complexes of thiocarbohydrazone ligand (fig. 24) were formed by reacting with ethanolic solution of metal chloride or aqueous ethanolic solution of metal acetates with specific amount of the ligand. Compound shows antitumour activity[29].

Md. Arifuzzaman[30] et al had been synthesized Bis-diisatin [3,3´] furan (fig. 25) on treatment with furan in presence of diethylamine under intensive stirring. The compounds were evaluated for cytotoxicity study on the brine shrimp as a test organism.

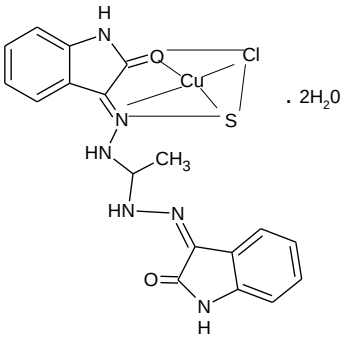


Fig:24. Bis-Isatin Thiocarbohydrazone Metal Complexes

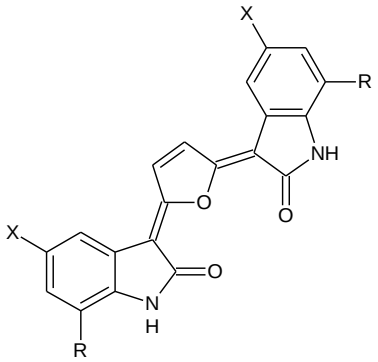


Fig:25. Bis-diisatin derivatives

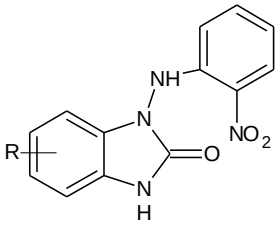


Fig:26. 3-o-Nitrophenyl hydrazones of isatin

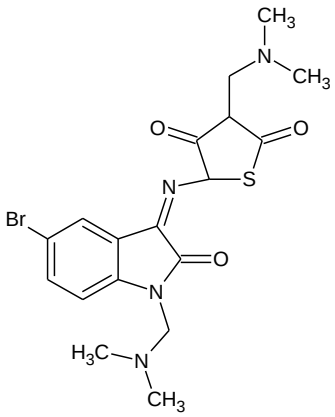


Fig:27. 5-(2-Oxo-3-indolinylidine) thiazolidine-2,4-dione

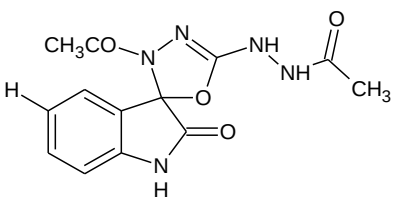


Fig:28. Isatin derivatives

F.D.Popp[31] et al had been synthesized 3-*o*-nitrophenyl hydrazones (fig. 26) of isatin by the condensation of isatin with *o*-nitrophenyl hydrazine which shows anticancer activity.

N.H Eshba[32] et al had been synthesized 5-(2-oxo-3-indolinyl) thiazolidine-2,4-dione (fig. 27) having positions 1 and 3 of the isatin and thiazolidine rings, respectively, substituted by various Mannich bases and had been shown anticancer activity.

5-spiro (isatin) 2(N-acetyl hydra-zino)-4-(N-acetyl)-Δ^{2}-1,3,4-oxadiazoline (fig.28) was formed by the oxidative cyclization of isatin 3-carbohydrazone with freshly distilled acetic anhydride[33].

4. ANALGESIC AND ANTI-INFLAMMATORY

Inflammation is a normal, protective response to tissue injury caused by physical trauma, noxious chemicals, or microbial agents[5]. It inhibits Prostaglandin synthesis at the site of injury[34]. Analgesic drug is used to control the pain. Prostaglandin E_2 (PGE_2) is thought to sensitize nerve ending to the action of bradykinin, histamine and other chemical mediators released locally by the inflammation process[5]. thiosemicarbazino isatin, Isatin-3-p-chlorophenylimine, Azetidinone derivatives of isatin possess analgesic and anti-inflammatory activity. The anti-inflammatory activity was studied by Carrageenan induced paw oedema method and anaglesic activity studied by tail flick and hot plate method.

1-(phenylaminomethyl)3-thiosemicarbazino isatin (fig. 29) was formed by 3-thiosemicarbazino isatin and appropriate aromatic amine reacted with formeldehyde. The compound possess analgesic activity[35].

3'-(p-chlorophenyl) 6'-Furyl-cis- 5'a, 6'- dihydro spiro [3H-indole 3, 4'-thiazolo(5', 1'-c) isoxazolo-2(1H)-one] (fig. 30) was synthesized by the reaction of 3'-p-chlorophenyl 5'-phenyl spiro [3H-indole 3, 2'-thiazolidine]-2- (1H), 4'-(5'H)-dione with hydroxylamine hydrochloride. It possess analgesic and anti-inflammatory activity[36].

S.K.Srivastav[37] et al had been synthesized a series of compounds from carbazole (fig. 31) by condensation with chloroacetyl chloride in the presence of triethylamine afforded azetidinones. The compounds exhibited promising anti-inflammatory activity.

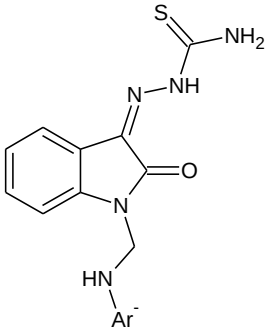


Fig:29. Thiosemicarbazino isatin

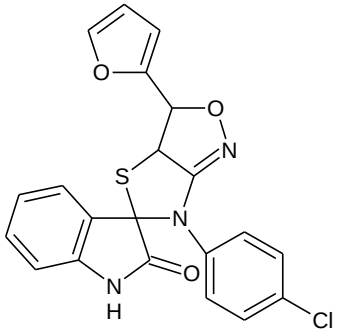


Fig:30. Isatin-3-p-chlorophenylimine

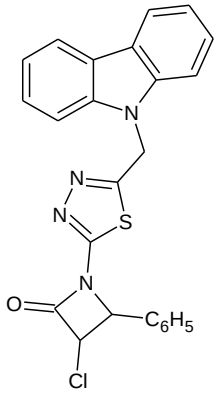


Fig:31. Azetidinone derivatives of isatin

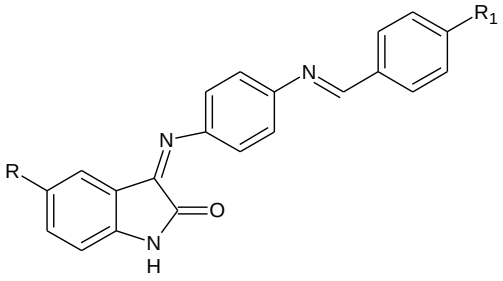


Fig:32. 5-Substituted Isatin derivatives

Perumal Panneerselvam[38] et al had been synthesized Novel series of Schiff bases of 5-subsituted Isatin and N-acetyl isatin (fig. 32) using different substituted aromatic aldehydes. These synthesized compounds were investigated for analgesic activity by tail immersion method and anti-inflammatory activity by carrageenan-induced paw oedema method. All the synthesized compounds were active against all the tested micro-organisms like *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Micrococcus luteus*, *Bacillus cereus*, *Escherichia coli*, *Pseudomonas aeruginos*, *Klebsiella pneumoni*, *Aspergillus niger* and *Aspergillus fumigates*.

Gummadi Sridhar Babu[39] et al had been synthesized a series of isatin derivatives (fig. 33) by condensation of N-(1H-benzimidazol-2-yl)-hydrazine carboxamide with various isatin derivatives and evaluated *in vivo* (rat paw edema) for their anti-inflammatory activity using carrageenan induced rat paw oedema model.

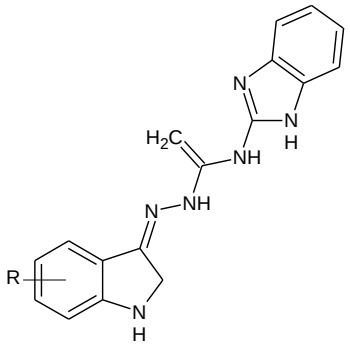


Fig:33. 2-aminobenzimidazole derivatives

5. ANTI-HIV ACTIVITY

HIV is an RNA retrovirus. Two forms are known HIV-1 is an organism responsible for human AIDS. The HIV-2 organism is similar to the HIV-1 virus in that it also causes immune suppression, but it is less virutent. HIV-1 is distributed around the world, whereas the HIV-2 virus is confined to parts of Africa[18]. In view of the broad spectrum activity of isatin derivatives, discussed here some novel thiosemicarbazides of isatin, Schiff bases of isatin derivatives with sulfodoxine and N-(4,6-dimethyl-2pyrimidiny)benzene sulphonamide and its derivatives which shows anti-HIV activity.

S.N.Pandey[40] et al had been synthesized 1-[N,N-dimethylaminomethyl]isatin-3-[1'(6"-chloro benzothiazol-2"-yl)] (fig. 34) by reacting 3-[-1-(-6-chloro benzothiazol-2 yl)thiosemicarbazone] and formalin with dimethylamine. The synthesized compounds were screened for anti-HIV activity at HIV-1(III B) in MT-4 cells.

S.N.Pandey[41] et al had been synthesized Schiff bases of isatin derivatives with sulfodoxine (fig.35). All the compounds

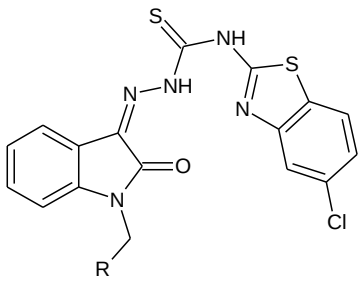


Fig:34. Thiosemicarbazide of isatin

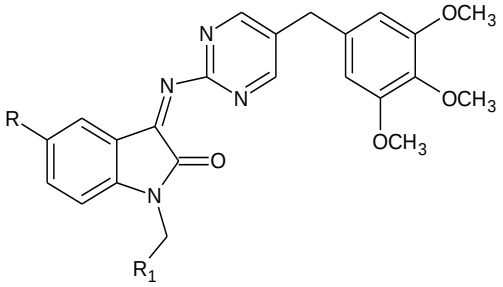


Fig:35. Schiff bases of isatin with sulfodoxine

showed notable activity when compared to sulphadoxine. The piperidino methyl compounds were found to be the most active ones in the series. Six compounds were active against *Candida albicans*, *Candida neoformis*, *Histoplasma capsulatum*, *Microsporum audounii* and *Trichophyton mentagrophytes* at a concentration of 100 gml^{-1}. The compound containing piperidino methyl group showed appreciable activity (10%) against the HIV-2 (ROD) strain.

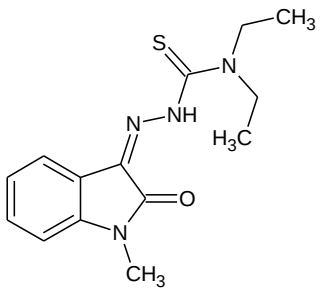


Fig:36. Isatin thiosemicarbazone derivatives

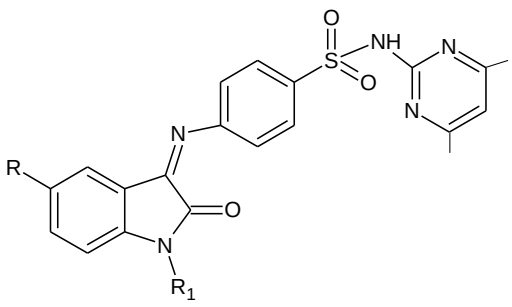


Fig:37. N-(4,6-dimethyl-2pyrimidiny)benzene sulphonamides

Y.Teiltz[42] et al had been synthesized *N*-methyl isatin-β-4',4'-diethylthiosemicarbazone (fig. 36) and shown inhibition of HIV by their action on reverse transcriptase and viral structural proteins

P.Selvam[43] et al had been synthesized 4-[(1,2-dihydro-2-oxo-3H-indole-3-ylidene)amino]N-(4,6-dimethyl-2pyrimidiny)benzene sulphonamide (fig. 37) and its derivatives by condensing the isatin and its 5-chloro, 5-bromo, 5-floro, 5-methyl, N-acetyl derivatives with sulphadimidine in the presence of glacial acid. The compounds showed antiviral activity against SARS-COV in *in -vitro* E6 cell.

6. ANTIANXIETY ACTIVTIES:

Anxiety is an unpleasant of tension, apprehension, or uneasiness a fear that seems to arise from a sometimes unknown source. The physological symptoms of severe anxiety are similar to those of fear and involve sympathetic activation[5]. It enhances the response to GABA by facilitating the opening of GABA-activated chloride channel[18]. Isatin derivative like Schiff bases of *N*-methyl and *N*-acetyl isatin, Spirobenzodiazepines, 5-Hydroxy isatin and isatinic acid act as antianxiety agents.

G.S.Palit[44] et al had been synthesized Schiff bases of *N*-methyl and *N*-acetyl isatin derivatives (fig. 38). They studied the behavioral effects of isatin, a putative biological factor in rhesus monkeys. Isatin, one of the constituents of tribulin, a postulated endocoid marker of stress and anxiety, has been shown to induce anxiety in rodents

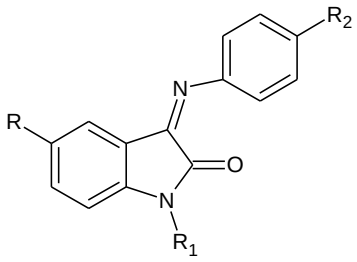


Fig:38. Schiff bases of isatin

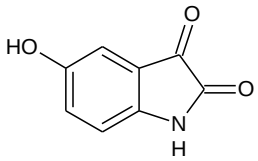


Fig:39. 5-Hydroxy isatin

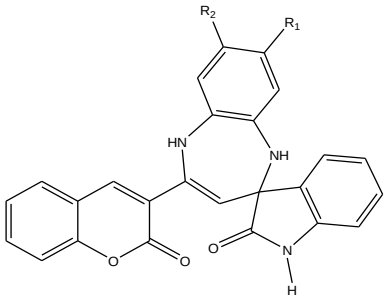


Fig:40. Spirobenzodiazepines derivatives

E. Medvedev[45] et al had been synthesized 5-Hydroxy isatin (fig. 39) by the hydroxylation of the aromatic ring in isatin and showed mild antianxiety effect.

Manohar V Kulkarni[46] et al had been synthesized 3-coumarinyl spiro[indolo-1,5-benzodiazepines] (fig. 40) which is formed by reaction of 3-(3¢-hydroxy-2¢-oxo indolo) acetyl coumarins which on dehydration afforded the corresponding α,β-unsaturated ketones and showed antianxiety effects.

7. MISCELLANEOUS ACTIVITIES:

Isatin and their derivatives shows many activites which is shown above, some more activities are mention below.

3-*p*-(*p*-(alkoxycarbonyl)phenyl)carbamoyl)phenyl)imino-1-aminomethyl-2-indolinones with antitubercular activity had been synthesized by R.S.Verma[47] and coworkers (fig. 41). The compounds are investigated against *M. tuberculosis* H37Rv.

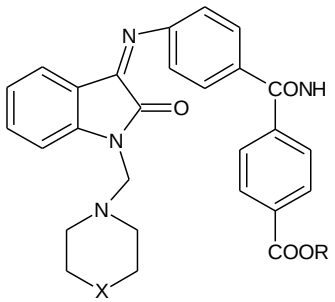


Fig:41. 3-p-(p-(Alkoxycarbonyl)-phenyl)carbamoyl)phenyl) imino-1-aminomethyl-2-indolinones

Nataraj K.S[48] et al had been sythesized 2-{(benzalamino-4-hydroxybenzyl) (1,3,4)-oxadia zino[6,5-b]} Indole derivative (fig. 42) by condensing 2-Amino-4-[(1,3,4)oxadiazino[6,5-b]indole-3-yl]-phenol with various aromatic aldehydes which shows diuretic activity.

M. Sarangapani[49] et al had been sythesized *5*-[2(3)-dialkylamino alkoxy] Indole 2, 3-diones (fig. 43) from 5-hydroxy isatin A mixture of 5-hydroxy isatin, dialkylamino alkylhalide in alcoholic potassium hydroxide was stirred at room temperature for 6 hours to get the *5*-[2(3)-dialkylamino alkoxy] Indole 2,3-diones. All the compounds were evaluated for Antihistaminic activity by Histamine chamber method.

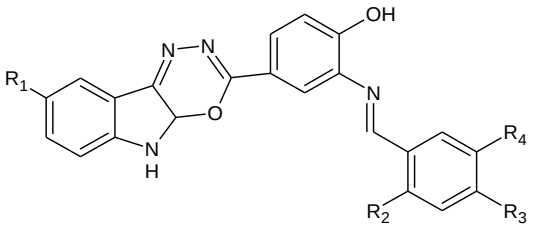


Fig:42. 2-[(benzalamino-4-hydroxybenzyl)(1,3,4)-oxadiazino[6,5-b]] Indole derivatives

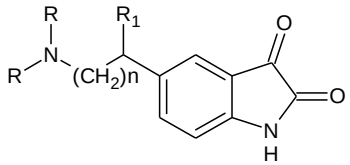


Fig:43. 5-Hydroxyisatin derivatives

DISCUSSION

Isatins (1H-indole-2,3-dione) are synthetically versatile substrates, where they can be used for the synthesis of a large variety of heterocyclic compounds, such as indoles & quinolines, and as raw material for drug synthesis. Isatins have also been found in mammalian tissue and their function as a modulator of biochemical processes has been the subject of several discussions. The advances in the use of isatins for organic synthesis during the last twenty-five years, as well as a survey of its biological and pharmacological properties are reported in this review and in the accompanying supplementary information. The survey of the literature revealed that, Isatin is a versatile lead molecule for designing potential bioactive agents, and its derivatives were reported to possess broad-spectrum antiviral, antimicrobial, cytotoxic, anti-inflamatory, anxiety, analgesic, anhi-histaminic, anti-diuretic activities. Further we can conclude that many other derivatives of isatin can be synthesized which will be expected to show potent pharmacological activities.

REFERENCES

1. Otto LE. *Journal für Praktische Chemie*, 1840; 19(1): 321–362.
2. Laurent A. *Ann Chim Phy*, 1840; 3(3): 393–434.
3. Siddiqui N, Alam M S, Ahsan W. *Acta Pharm*, 2008; 58: 445–454.
4. Jarrahpour A A, Khalili D. *Molbank*, 2005; M437.
5. Richard AH. Lippincott's Pharmcology, 4th edition. Wolter Kluwer Pvt Ltd; 2009, 105, 347,499,502.
6. Pai NR, Suryanvansi JP. *Indian Journal of Chemistry*, 2006; 45B: 1226-1230.
7. Talesara GL,Thadhaney B, Sain D, Pemawat G. *Indian Journal of Chemistry*, 2010; 43B: 368-373.
8. Bari SB, Agrawal AO, Patil UK. *Journal of Sciences*, 2008; 19(3): 217-221.
9. Jarrahpour AA, Khalili D, Clercq ED, Salmi C. *Molecules et al*, 2007; 12: 1720-1730.
10. Bari S, Talele G, Patel J, Sarangapani M et al. *Iranian Journal of Pharmaceutical Research*, 2006; 4: 249-254.
11. Verma RS, Kumar A, Srivastava VK, Panwar H. *Indian Journal of Chemistry*, 2006; 45B: 2099-2104.
12. Talesara GL, Salvi VK, Sharma S, Sharma C. *Indian Journal of Chemistry*, 2006; 48B: 1006-1012.
13. Kumar V, Kukshal A, Rathee P. *Research Journal of Pharmaceutical*, 2010; 1: 98-103.
14. Chhajed SS, Padwal MS. *International Journal of ChemTech Research*, 2010; 2(1): 209-213.
15. Singh SK, Pandey SN, Bhasin PS. *Acta Pharmaceutica Turcica*, 2005; 47: 21-29.
16. Mashelkar UC, Rane DM. *Indian Journal of chemistry*, 2005; 44B: 1937-1939.
17. Singh UK, Pandey SN, Singh A, Srivastava BK. *International journal of Pharmaceutical Sciences and Drug Research*, 2010; 2(2): 151-154.
18. Rang HP, Dale MM, Ritter JM, Flower RJ. Rang and Dale's, Pharmacolgy, 6th edition. Churchil Livingstone Elesevier; 2007, 538, 557, 681.
19. Pandeya SN, Raja AS. *J Pharma Phamaceut Sci*, 2002; 5(3): 266-271.
20. Singh KN, Verma M, Pandaye SN. *Acta Pharm*, 2004; 54: 49-56.
21. Smitha S, Pandeya SN, Stables JP, Ganapathy S. *Sci Pharm*, 2008; 76: 621-636.
22. Kumar A, Kaur H, Kumar S. *International Journal of ChemTech Research*, 2010; 2(2): 1010-1019.
23. Jain R and Bansal. *Pharmazie*, 1995; 50: 224-225.
24. Gursoy A, Karali N. *Farmaco*, 1996; 51: 437-442.
25. Singh GS, Singh T, Lakhan R . *Indian J Chem*, 1997; 36B: 951-954.
26. Prakash C.R, Raja S, Saravanan G. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2010; 2(4): 177-181.
27. Sharma P P, Pandeya SN, Roy RK, Gupta S. *International Journal of ChemTech Research*, 2009; 1(3):758-763.
28. Sarangapani M, Kiran G, Rao JV. *Journal of Pharmacy Research*, 2009; 2(3): 388-390.
29. Sathisha MP, Revankar VK, Pai KSR**.** Metal based drugs, Hindawi Publishing Corporation; 2008, 1-11.
30. Arifuzzaman Md, Kandahary RK, Islam Md R. *Bangladesh J Pharmacol*, 2009; 4: 96-100.
31. Popp FD, Pajouhesh H. *J Pharm. Sci*, 1983; 72: 318-321.

32. Eshbha NH, Salama HM. *Pharmazie*, 1985; 40: 320-322.
33. Islam Md. R, Mohsin M. *Bangladesh J Pharmacol*, 2007; 2: 7-12.
34. Tripathi KD. Essential of Medical Pharmacology, 6th edition. Jaypee Brother Medical Publishers; 2006, 185.
35. Khan SA, Siddiqui N, Imran M, Haque SW. *Journal of Pharmaceutical Research*, 2006; 5(2): 61-64.
36. Mana S, Sharma NK, Pahari N, Priyanka. *The Pharma Research*, 2010; 3: 51-59.
37. Srivastava SK, Srivastava S, Srivastava SD. *Indian J. Chem*, 1999; 38B: 183-187.
38. Panneerselvam P, Kumar NR, Murali K. *Der Pharma Chemica*, 2010; 2(1): 28-37.
39. Babu GS, Ranjani N, Rao V. *Der Pharma Chemica*, 2010; 2(3): 196-204.
40. Pandeya SN, Sriram D, Nath G. *Indian Journal Pharm Science*, 1999; 16(6): 358-361.
41. Pandeya SN, Yogeeswari P, Sriram D, Nath G. *Boll Chim Farm*, 1998; 137: 321-324.
42. Teitz Y, Ronen D, Vansover A, Stematsky T et al. *Antiviral Res*, 1994; 24: 305-314.
43. Selvam.P, Murgesh M, Chandramohan M, Clerco ED. *Indian journal of Pharmaceutical Science*, 2008; 70(1): 90-94
44. Palit G, Kumar R, Patnaik GK, Bhattacharya SK. *Biogenic Amines*, 1997; 13: 131-142.
45. Medvedev AE, Goodwin A, Clow A, Halket J, Glover V, Sandler M et al. *Biochem. Pharmacol*, 1992; 44: 590-592.
46. Kulkarni MV, Kusanur RA, Ghate M. *J Chem.Sci*, 2004; 116(5): 265-270.
47. Varma RS, Pandeya RK. *Indian J Pharm. Sci*, 1982; 46: 132-135.
48. Nataraj KS, Venkateshwara RJ, Jayaveera. *Journal of Pharmacy Research*, 2010; 3(4): 863-865.
49. Sarangapani M, Swathi K , Srinivas A. *J Chem Pharm Res*, 2010; 2(2): 220-225.