

**Review Article**

**ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES OF SCHIFF BASE METAL COMPLEXES – A REVIEW**

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**ABSTRACT**

Schiff bases are aldehyde - or ketone - like compounds in which the carbonyl group is replaced by an imine or azomethine group. They are widely used for industrial purposes and also exhibit a broad range of biological activities. The reaction is acid catalysed, however only aldehydes and ketones which do not aldolize easily in acidic media, can be condensed with amines in presence of strong acid catalyst (e.g. BF<sub>3</sub>-etherate, anhydrous ZnCl<sub>2</sub> or POCl<sub>3</sub>). Aromatic aldehydes and aliphatic or aromatic ketone gives stable azomethines. The basic mechanism is a two step addition elimination mechanism. In the first step, the nitrogen base adds to the carbonyl compound to give a carbinolamine intermediate, followed by elimination of water to form the carbon-nitrogen double bond. Rate of condensation passes through a maximum with changing acidity, falling off on either side of an optimum pH. Generally the optimum pH range is 3-5. Schiff bases are biologically active compounds and have been reported to possess various important pharmacological properties like antifungal, anticancer, anticonvulsant and diuretic activities. Schiff bases are derived from heterocycles has been reported to possess cytotoxic properties. This short review compiles examples of the most promising, analgesic anti-inflammatory Schiff bases. An overview of synthetic methodologies used for the preparation of Schiff bases is also described.

**Key Words:** *Schiff bases, Analgesic activity, Anti-inflammatory activity, Azomethine group*

**INTRODUCTION**

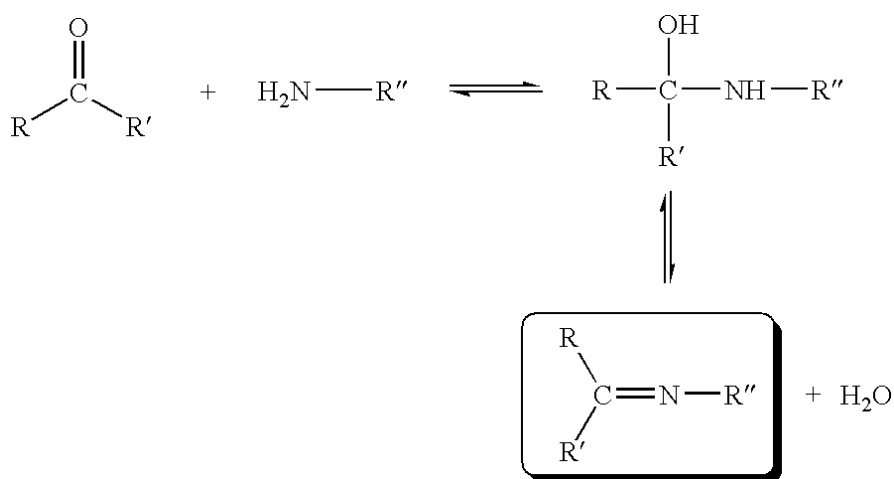
Schiff bases, named after Hugo Schiff, (Da Silva *et al.*, 2011) are formed when any primary amine reacts with an aldehyde or a ketone under specific conditions. Structurally, a Schiff base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group (>C=O) has been replaced by an imine or azomethine group. Schiff bases are some of the most widely used organic compounds. They are used as pigments and dyes, catalysts, intermediates in organic synthesis, and as polymer stabilizers. Schiff bases have also been shown to exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties. Imine or azomethine groups are present in various natural, natural-derived, and non-natural compounds. The imine group present in such compounds has been shown to be critical to their biological activities. In this review we present the general approaches to the synthesis of Schiff bases. Several Schiff bases possess anti-inflammatory, allergic inhibitors reducing activity radical scavenging, analgesic and anti-oxidative action. Thiazole-derived Schiff bases show analgesic and anti-inflammatory activity. Schiff base of chitosan and carboxymethyl-chitosan shows an antioxidant activity such as superoxide and hydroxyl scavenging. Furansemicarbazone metal complexes exhibit significant anthelmintic and analgesic activities (Prakash *et al.*, 2011). Schiff bases are very important compounds in pharmaceuticals and medicines (Yusuf *et al.*, 2007). They show a range of biological activities such as herbicidal, antibacterial, antiviral, antifungal, anti-inflammatory and antioxidant activities (Karatepe and Karatas, 2006). We also highlight the most significant examples of compounds belonging to this class, which exhibit analgesic, anti-inflammatory, and non-ulcerogenic activities to have been reported in the literature.

***Analgesic, Anti-Inflammatory Activity***

For the discovery of new analgesic drugs, cyclic imides like 1, 8-naphthalimide and 1, 4, 5, 8-naphthalene diimide were prepared and their analgesic properties were evaluated by using the writhing test in mice (Andricopulo *et al.*, 2000). Rana *et al.*, (2012); Okunrobo *et al.*, (2006) and Gaikwad *et al.*, (2010)

### Review Article

evaluated schiff bases of imides for their anti-inflammatory and analgesic potential. Tail immersion and hot plate methods were carried out to evaluate the analgesic potential of Schiff bases of imides. Results of the study indicate the significant decrease in the reaction time of tail withdrawal by ethanolic solution of Schiff bases of imides. It shows that ethanolic solution of Schiff bases of imides possesses analgesic property. This analgesic activity may be due to its free radical scavenging activity as these free radicals are involved during pain stimulation and antioxidants show reduction in such pain (Kim *et al.*, 2004). The synthesized compound was further evaluated for its *in vivo* anti-inflammatory potential. Carrageenan induced rat paw edema test has frequently been used to assess the anti-edematous effect of the synthesized compound. Carrageenan is used to cause inflammation and it helps in releasing various inflammatory mediators like prostaglandins, leukotrienes, histamine, bradykinin etc. (Crunkhorn and Meacock, 1971). Decrease of edema in rat paw indicated that the ethanolic solution of Schiff bases of imides possess anti-inflammatory activity.



Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of pain and inflammation, particularly for different types of arthritis (Zhou *et al.*, 2010). Among the most popular NSAIDs worth mentioning is diclofenac sodium, which is approved in more than 120 countries across the globe since its introduction, 28 years ago, and is ranked 30th among the top 200 drugs with respect to new prescriptions. The pharmacological activity of NSAIDs is related to the suppression of prostaglandin biosynthesis from arachidonic acid by inhibiting the enzyme prostaglandin endoperoxidase, popularly known as cyclo-oxygenase (COX). It was discovered that COX exists in two isoforms, COX-1 and COX-2, which are regulated and expressed differently. COX-1 provides cytoprotection in the gastrointestinal tract (GIT), whereas inducible COX-2 selectively mediates inflammatory signals. Since most of the currently available NSAIDs in the market show greater selectivity for COX-1 than COX-2, chronic use of NSAIDs, including diclofenac, may elicit appreciable GI irritation, bleeding and ulceration. The incidences of clinically significant GI side effects due to long term use of NSAIDs are very high (30%) and cause some patients to abandon NSAID therapy. GI damage from NSAID is generally attributed to two factors. Local irritation by the direct contact of carboxylic acid (-COOH) moiety of NSAID with GI mucosal cells (topical effect) and decreased tissue prostaglandin production in tissues which undermines the physiological role of cytoprotective prostaglandins in maintaining GI health and homeostasis. Synthetic approaches based upon chemical modification of NSAIDs have been taken with the aim of improving safety profile and in turn therapeutic window of this NSAID. Several studies have described the derivatization of the carboxylate function of representative NSAID with less acidic azoles, viz. 1,3,4-oxadiazole, Triazole, etc. which resulted in an increased anti-inflammatory activity with reduced ulcerogenicity. Furthermore, it has been reported in the literature that certain compounds bearing 1, 3, 4-

### **Review Article**

oxadiazole nucleus possess significant anti-inflammatory activity. In our attempt to discover new, safer and potent agents for treatment of inflammatory diseases, we have replaced the carboxylic acid group of diclofenac acid with less acidic heterocycle, 1,3,4- oxadiazole, in order to accentuate potency and reduce GI toxicities associated with the parent diclofenac due to its free  $-\text{COOH}$  group. The compounds designed so were found to possess much significant analgesic-anti-inflammatory profile with significant reduction in potential for ulcerogenic toxicities (Cardile *et al.*, 2002).

In vitro evaluated thiazolyl and benzothiazolyl Schiff bases for screening anti-degenerative activity on nasal pig cartilage and cultures treated with interleukin 1beta, (IL-1beta). The results suggested that thiazolyl and benzothiazolyl Schiff bases in general, and particularly the Schiff base with bromine and methoxyl group in position three would protect cartilage matrix from degenerative factors induced by IL-1beta. These studied exhibited that these compounds have anti-inflammatory activities. Many human diseases are associated with the overproduction of oxygen free radicals that inflict cell damage. A manganese (II) complex with bis (cyclohexylpyridine)- substituted macrocyclic ligand has designed as a functional mimic of the superoxide dismutase (SOD) enzymes that normally remove these radicals (Li *et al.*, 2002)

Alagarsamy *et al.*, (2003) reported the synthesis of series of novel Schiff bases of 2-benzylamino-3-substituted quinazolin-4(3H)-ones having analgesic and anti-inflammatory activities. C-2 and N- 3 disubstituted quinazolines exhibit analgesic and anti-inflammatory activities. (Geronikaki *et al.*, 2003) reported the synthesis of series of novel LO. Few Compounds exerts significant anti-inflammatory and not a high LO inhibitor activity. Thiazolyl/thiazolinyl/benzothiazolyl Schiff bases having anti-inflammatory activity against asthma, rheumatoid arthritis and psoriasis. Thiazolyl and benzothiazolyl groups are of importance in biological systems as antiinflammatory, analgesic agents and inhibitors on lipoxygenase activities. vanilloids, possess high anti-inflammatory activity. Among transition metals complexes of Cu and Fe are capable of catalyzing dismutation of the superoxide anion. In addition, Mn complexes dose not bind to NO and react slowly with  $\text{H}_2\text{O}_2$ , demonstrating specificity towards superoxide anion. Interaction of SOD mimics with NO and  $\text{H}_2\text{O}_2$  levels, both of which can cause high blood pressure and weaken the immune system. NO are an excellent ligand for transition metal ions and these metal nitrosyls having therapeutic values. Sodium nitropruside is used clinically to treat cardiovascular diseases by releasing NO but CN- toxicity limited its application, however, discovery of new ruthenium nitrosyl complexes offer promising biological applications (Cameron *et al.*, 2003). Over production of NO contributes to various diseases like sepsis, arthritis, diabetes and epilepsy. Ruthinium polyaminocarboxylate complexes are efficient NO scavengers (Mosi *et al.*, 2002; Spasojevic *et al.*, 2003 and Clark *et al.*, 2003).

There are some side effects of anti-arthritis therapy using Au (I), mostly when it is oxidized to Au (III) by some of the potentially strong oxidants such as  $\text{H}_2\text{O}_2$  available in inflammatory situations. Excessive use of gold complexes for the treatment of juvenile rheumatoid arthritis and osteoarthritis causes pain and fever. Among cutaneous symptoms intolerance was measured at low frequency, wider use of gold salts like gold salicylates and gold pyrazolone derivatives cause urticaria and angioedema (Rethy *et al.*, 2004) (Iana *et al.*, 2004) prepared two small sets of aromatic Schiff bases and 2,3-diaryl-1,3-thiazolidin-4-one derivatives. These compounds were tested for their anti-inflammatory and antinociceptive activities. The thiazolidinone derivatives have been obtained from the azomethines through the addition of  $\alpha$ -mercaptoacetic acid. Both types of compounds displayed good level of activity against carrageenan induced edema in rat hind paw, while only moderate activity was observed in the writhing test in mice. (Vazzana *et al.*, 2004) reported the synthesis of series of novel Schiff base derivatives of 2, 3-diaryl-1, 3-thiazolidin-4-one having anti-inflammatory activity against the rat hind paw edema induced by carrageenan. The N-(2/3/4-pyridinylmethylene)-3- trifluoromethylbenzenamines shows the potent anti-inflammatory activity. The Schiff bases and the thiazolidinone derivatives were screened for Antiinflammatory activity. Gold has been used in the treatment of peripheral psoriatic arthropathy (Nash and Clegg, 2005). As a product of oxygen metabolism, superoxide anion can trigger oxidative injury to

### **Review Article**

tissues. This activity has been suggested to be associated with riper fusion and inflammatory diseases as well as neurological disorders such as Parkinson's disease and Alzheimer's disease.

Sondhi *et al.*, (2006) reported the synthesis of N-(acridin-9-yl)-4 (benzo[d]imidazol/oxazol-2-yl) benzamides Schiff bases which exhibit analgesic and anti-inflammatory activity. Compounds showed good anti-inflammatory activity and good analgesic activity.

Sondhi *et al.*, (2009) reported the synthesis of series of novel bis Schiff bases of hydrazone and guanidine derivatives are heterocyclic molecules possess analgesic and anti-inflammatory activity.

Pontiki *et al.*, (2008) evaluated anti-inflammatory and antioxidant activities of copper (II) Schiff mono-base and copper (II) Schiff base coordination compounds of dien with heterocyclic aldehydes and 2-amino-5-methyl-thiazole. These compounds have been tested for anti-inflammatory and antioxidant activity. The tested compounds inhibit the carrageenin-induced rat paw edema (52.0-82.6%) and present important scavenging activity. (Bhandari *et al.*, 2008) reported the synthesis of series of novel Schiff bases having potential analgesic, anti-inflammatory activity without GI toxicities, toxicity associated with all traditional NSAIDs having new chemical entities. In this series compounds exhibited very significant anti-inflammatory activity compared to standard drug diclofenac.

Transition metals have also been used as anti-inflammatory and anti-arthritic agents (Arayne *et al.*, 2009). Several injectable transition gold complexes like sodium aurothiomalate, aurothioglucose and sodium aurothiopropanol are used clinically in the treatment of severe cases of rheumatoid arthritis. Gold and silver nanoparticles conjugated with heparin derivative possess antiangiogenesis properties (Kemp *et al.*, 2009). Silver nanoparticles are used in the development of an antimicrobial gel formulation for topical use (Jain *et al.*, 2009). In living systems, a natural defense system against superoxide mediated oxidative damages involves SODs, enzymes that catalysis the conversion of superoxide into oxygen and hydrogen peroxide. Metallic gold treatment reduces proliferation of inflammatory cells in brain injury (Pedersen *et al.*, 2009). Tolfenamic acid and its metal complexes has been studied as anti-inflammatory, anti proliferative, and radical-scavenging agents by Kovala *et al.*, (2009). Manganese complexes have also been used to treat cell and tissue oxidative injuries by acting as superoxide anion scavenger (Failli *et al.*, 2009). Magnesium is used for the treatment of asthma in children (Bichara and Goldman, 2009). Some Cu complexes are also active against inflammation but their use is limited (Angelusiu *et al.*, 2009). Cu (II) complexes tend to dissociate and bind to natural ligands such as albumins (Halova *et al.*, 2006 and Ward *et al.*, 2005). Zinc has been proved to be involved in the inhibition of pro inflammatory cytokines (Haddad, 2009).

Fluorine has become an essential tool in drug discovery, including fluorine atom in potential medicines can have a variety of dramatic effects on the molecular properties perhaps making them more selective, increasing efficacy. Hence the 6-fluoro-7-chloroaniline was selected as starting molecule to synthesize novel fluorobenzothiazole schiff's bases in hope of getting molecule with biodynamic potentials. fluorobenzothiazoles are known to exhibit anti-inflammatory activities. (Gelas, 1998; Williams, 2008 and Sancak, 2005). Almost all the non steroidal anti-inflammatory agents which are under clinical use are associated with sever gastrointestinal toxicity. Patil *et al.*, (2009) synthesized eight new 4-Substitutedaryl-6-methyl-2-pyrimidinone-5 - (N-p-tosyl) Carbohydrazides in three step reaction. These compounds were tested for antihypertensive activity by non-invasive tail-cuff, and evaluated by carotid artery cannulation method for determining the diastolic blood pressure. Hypertension was induced by DOCA-salt. Anti-inflammatory activity was carried out by carrageenan induced rat-paw oedema method. Test compounds exerted comparative anti-hypertensive activity at 10 mg/kg dose level compared to nifedipine. Some Compounds showed excellent results on evaluation by direct method and other compounds exerted moderate to comparative anti-inflammatory activity at the 100 mg/kg dose level compared to indomethacin. Panneerselvam *et al.*, (2009) reported the synthesis of novel Schiff bases of 4-(2-Aminophenyl)-Morpholines.N-benzylidene-2- morpholino benzenamine and N-(3-nitro benzylidene)-2-morpholino benzenamine exhibited significant analgesic and anti-inflammatory activities. Substitution of 4-phenyl morpholine to quinazoline moiety results in potent analgesic and anti-inflammatory activities.

### Review Article

Zhou *et al.*, (2010) reported the synthesis of novel Schiff's bases, N, N'-(Z-allylidene-1, 3-diyl) bisamino acid methyl esters which exhibit moderate analgesic activity against tail-flick mouse model. Thus the present Schiff's bases are able to treat chronic pain from inflammation. Chinnasamy *et al.*, (2010) reported the synthesis of series of novel Schiff bases of Isatin. These compounds were screened for the analgesic activity by tail-immersion method. 3-(4-(4-Hydroxy-3-methoxybenzylideneamino)phenylimino) indoline-2-one exhibited better analgesic activity when compared to standard pentazocine. In this compounds containing electron-donating groups exhibit better analgesic activity than the electron-withdrawing groups. Nirmal *et al.*, (2010) reported the synthesis of novel Schiff bases analogues of 3-(4-amino) Phenylimino) 5-fluoroindolin-2-one. Among the Schiff bases compound N-3 exhibited significant analgesic activity. Among the title compounds studied some exhibited significant anti-inflammatory activity comparable to reference standard diclofenac sodium. The test compounds showed only mild ulcerogenic side effect when compared to aspirin. Panneerselvam (2010) synthesized novel Schiff base by condensation of 5-substituted imesatin with different substituted aromatic aldehydes. These synthesized compounds were investigated for analgesic (Tail-immersion method), anti-inflammatory (carrageenan-induced paw oedema method) and anti-bacterial activities by paper disc diffusion technique. The minimum inhibitory concentrations (MIC) of the compounds were also determined by Agar streak dilution method. Most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities. Compounds 5-Chloro- 3-(4-(4-nitrobenzylideneamino)-phenylimino) indolin-2-one, 5-Fluoro -3-(4-(4-nitrobenzylideneamino)-phenylimino) indolin-2-one, and 5-Fluoro -3-(4-(4-methoxybenzylideneamino)-phenylimino) indolin-2-one, were found to possess equipotent analgesic and anti-inflammatory activity when compared with standard drugs (Pentazocin, 10 mg/kg, i.p and Indomethacin 20mg/kg respectively). Among synthesized compounds 5-fluoro substituted title compound 5-Fluoro -3-(4-(4-methoxybenzylideneamino)-phenylimino) indolin-2-one showed promising analgesic and anti-inflammatory activity, this may be due to high lipophilicity imparted by the versatile pharmacophore. Compounds 5-Chloro- 3-(4-(4-chlorobenzylideneamino)-phenylimino) indolin-2-one, 5-Chloro-3-(4-(4-methoxybenzylideneamino)-phenylimino) indolin-2-one, 5-Chloro-3-(4-(2-hydroxybenzylideneamino)-phenylimino) indolin-2-one and 5-Fluoro -3-(4-(4-chlorobenzylideneamino)-phenylimino) indolin-2-one were found to exhibit moderate analgesic activity. Above results concluded that compounds substituted with electron withdrawing groups were found to possess promising analgesic activity, whereas 5-Methoxy- 3-(4-(4-chlorobenzylideneamino)-phenylimino) indolin-2-one exhibited lowest analgesic and anti-inflammatory activity.

Pandey *et al.*, (2011) synthesized 2-amino-5-aryl-1, 3, 4-thiadiazole derivatives with different aromatic aldehyde. All the compounds were evaluated for their analgesic activity against swiss albino mice, anti-inflammatory activity against Wister albino rats. (Hussein *et al.*, 2011) synthesized and evaluated some new anti-inflammatory pyrazolo[3, 4-d]pyrimidine derivatives. A number of new Schiff's bases  $C_{29}H_{21}N_5O_3$ ,  $C_{29}H_{21}N_5O_2$ ,  $C_{30}H_{23}N_5O_3$ ,  $C_{31}H_{26}N_6O_2$ ,  $C_{31}H_{26}N_6O_2$ ,  $C_{29}H_{20}N_5O_2$  were prepared via reaction of N-amino 5a, b with aromatic aldehydes. The synthesized compounds were characterized by elemental analysis, IR, <sup>1</sup>H-NMR and mass spectral data. Some of the newly synthesized compounds  $C_{29}H_{21}N_5O_3$ ,  $C_{29}H_{21}N_5O_2$ ,  $C_{30}H_{23}N_5O_3$ ,  $C_{31}H_{26}N_6O_2$ , and  $C_{29}H_{20}N_5O_2$  showed good anti-inflammatory activities. (Sathe *et al.*, 2011) reported the synthesis of series of novel fluorobenzothiazole Schiff bases with fluorine at 6th position. Ibuprofen was used as standard reference anti-inflammatory drug. Fluorobenzothiazole Schiff base derivatives have potent anti-inflammatory activity with good therapeutic values and minimum toxic levels. Ali *et al.*, (2011) reported the synthesis of series of novel macrocyclic Schiff bases containing amino acid and pyridine moiety having good anti-inflammatory and analgesic activities. Macrocyclic bisimides and macrocyclic bis-hydrazone showed good analgesic and anti-inflammatory activity comparable to diclofenac potassium and valdecoxib as reference drugs. Ghadage *et al.*, (2011) reported the synthesis of series of novel Schiff bases of quinoxaline-2(1H)-one as potent anti-inflammatory agents. Among all compounds some showed maximum anti-inflammatory activity, while few compound showed slight anti-inflammatory activity at both dose when compared with standard drug. Jayakumarswamy *et*

### Review Article

*al.*, (2011) synthesized novel complexes of Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) with a new schiff base 3,3'-[1,2- phynylenebis[nitrilo(E)methylidene]}diquinolin-2-ol. All the synthesized Ligand and its complexes showed good anti-inflammatory activity. The anti-inflammatory activity data shows that the metal chelates showed significant anti-inflammatory activity than the free ligand when compared with that of standard diclofenac. The literature shows that the compounds having methoxy, nitro, hydroxyl groups possess significant anti inflammatory activity, when compared to other groups .The synthesized ligand possess OH group in its structure. So the anti inflammatory activity is due to the presence of the respective functional groups. Moreover, the antimicrobial activity and anti-inflammatory activity data revealed that the complexes were superior to the free ligand. It is proposed that concentration plays a vital role in increasing the degree of inhibition the activity increased with increasing concentration of the complexes.

Alam, 2012 synthesized 4-Aminoantipyrine (4-amino-1,5-dimethyl-2-phenylpyrazole-3-one) and its analogues have been found to be compounds of interest for their anti-inflammatory, analgesic, antiviral, antipyretic, antirheumatic and antimicrobial activities. In the present study, Schiff base analogues of 4-aminoantipyrine were synthesized by the condensation reaction with substituted benzaldehydes and then evaluated for their antioxidant and anti-inflammatory activities. Among the synthesized compounds some exhibited the highest antioxidant activity. The IC (50) values for two compounds were found to be 0.44 and 0.93  $\mu$ M, respectively, comparable to that of ascorbic acid (IC (50) 0.41  $\mu$ M), a standard antioxidant agent. From the comparisons between the hydroxylated and methoxylated compounds, the rank order of antioxidant activity for the products resulting from benzylidene phenyl ring substitution was 2,4,6-OH>3,4-OH>3-OMe-4-OH>3,5-OMe-4-OH>2,4-OH>3-Me-4-OMe>3,4-OMe>4-OMe>4-OH. The structure activity relationship study revealed that the position and nature of the substituted group on the benzylidene phenyl ring of the Schiff base analogues of 4-aminoantipyrine play an important role in their antioxidant activity. The anti-inflammatory activity of a compound which also exhibited excellent antioxidant activity was evaluated in terms of its inhibition of NO production, an inflammatory modulator, in LPS pretreated RAW 264.7 cells using the Griess method. . It was observed that compound significantly reduced NO production and inhibited LPS-stimulated iNOS and COX-2 mRNA levels in a dose-dependent manner. Overall, that compound showed promising antioxidant and anti-inflammatory activities and may be used as the lead compound in a future study.(Bhosale 2012) synthesized a series of new 4-(4- substituted phenyl) - N - ( 4- substituted - benzylidene )- thiazol - 2 - amine derivatives and evaluated for their anti-inflammatory and analgesic activities at a dose of 50 mg /kg p.o. The most active compounds 4-(4- chloro phenyl)- N - ( 4- methoxy - benzylidene )- thiazol - 2 - amine. 4-(4- bromo benzylidene )- 4 - ( 4- chlorophenyl ) - thiazol - 2 - amine have been subjected to acute ulcerogenesis study at a dose of 150 mg/kg. (Arora 2012) synthesized 5 aminosalicic acids or mesalamine with molecular formula C<sub>7</sub>H<sub>7</sub>NO<sub>3</sub>.It is proved to a useful drug in an effective treatment of inflammatory bowel disease. It possess both anti-inflammatory and analgesic activity by targeting COX, prostaglandins and lipoxigenase enzyme. The positive control, 5- aminosalicic acid and test compounds (3a-3c) significantly inhibited the Paw edema response in comparison to control group. 5 aminosalicic acids showed an inhibition of 54.1% after 3 hours. Compound 3b showed almost comparable activity with standard with an inhibition of 50.45% and compound 3a showed minimum activity with an inhibition of 41.7 % after 3 hours.(Bassyouni *et al.*, 2012) synthesized series of 1 H-perimidine-2-thiol derivatives and (2-substituted-1 H-perimidin-1-yl)ethane-1,2-dione derivatives and their ligands (CHNSO) HL and (CHNSO) HL with transition metal ions, e.g., Copper (II), Silver (I), Cobalt (II) and Ruthenium (III) and evaluated for their antimicrobial, analgesic and anti-inflammatory activities. All results revealed that some compounds exhibited high inhibitory effects against some bacterial strains by the disc diffusion method and some compounds displayed potent anti-inflammatory activity.

Sharma *et al.*, (2013) synthesized Schiff bases of the imide 4-(1,3-dioxoisindolin-2-yl)benzaldehyde and demonstrated that synthesized Schiff bases of imides possess various significant pharmacological activities like analgesic and anti-inflammatory properties at high dose level which was comparable to that

### **Review Article**

of standard drug. Therefore, these compounds can be used in the treatment of various pains and inflammation. Noureen *et al.*, (2013) reported the synthesis of Schiff base esters, by two synthetic routes using variably substituted hydroxy benzaldehydes with para amino phenol in appreciable yields. All the synthesized were subjected to potatodisc antitumor assay, free radical induced oxidative DNA damage analysis and carrageenan induced edema test in rat hind paw. All the synthesized compounds showed significant tumor inhibitory activities. Compound 9 [N-4'-methoxybenzylidene-4-(3''-phenyl) butyroyloxyaniline] and 7 showed best tumor inhibition activity (IC<sub>50</sub> value 0.15 and 8.03 µg/ml respectively) in potatodisc antitumor assay. All the synthesized compounds (Schiff base esters) exhibited antioxidant effect on plasmid DNA at all the concentrations tested in free radical induced DNA damage analysis. Compound 5 [N-4'-methoxy benzylidene -4-[2''-{4'''-(2'''-methylpropyl)phenyl} propanoyloxyaniline] was found to be most active compound in the early phase of inflammation (88.86% inhibition) and compound 7 [N-benzylidene-4-naphthoyloxyaniline] was found to have the highest activity in the late phase of inflammation, i.e. 90.35%.

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