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REVIEW ON DRUG SYNTHESIS BASED ON SCHIFF BASE

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ABSTRACT

Schiff bases are aldehyde- or ketone-like compounds in which the carbonyl group isreplaced by an imine or azomethine group. These compounds are very important in medicinal and Pharmaceutical fields because of their wide spectrum they are widely used for industrial purposes. This short review compiles examples of the mostpromising antimalarial, antibacterial, antifungal, and anti-inflammatory Schiff bases.

KEYWORDS: Schiff base, antimicrobial activity, anti-inflammatory, organic compounds.

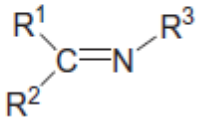
IINTRODUCTION

Compounds with the structure of -C=N- (azomethine group) are known as Schiff bases, which are usually synthesized from the condensation of primary amines and carbonyl groups. Schiff bases are important class of compounds in medicinal field.

The study of Schiff base has been fast developing because they possess excellent characteristics such as structural similarities with natural biological substances, relatively simple preparation procedures and synthetic flexibility that enables the design of suitable structural properties Schiff bases also serve as back bone for synthesis of various heterocyclic compounds. The biological activities reported in the literature on Schiff bases are antibacterial, antifungal, antioxidant, anticonvulsant, CNS depressant, anti-HIV, anti-inflammatory, antitumor, Angiotensin-II receptor antagonist, antioxidant, insecticidal, antimalarial, ant proliferative, antipyretic. Schiff's base have the potentials to be used in

different areas such as color photography, catalysis, metallic deactivators, separation processes and environmental chemistry and they are becomingly important in pharmaceutical, dye, plastic industries.

In this review we present the general approaches to the synthesis of Schiff bases. We also highlight the most significant examples of compounds belonging to this class, which exhibit antimalarial, antibacterial, antifungal, and/or anti-inflammatory activities to have been reported in the literature.



R1 R3

R1, R2, and/or R3 = alkyl or aryl

METHODS

1. The synthesis of Schiff base was done by the condensation of sulfamerazine (0.7mmol) and 5- bromo-2-hydroxy benzaldehyde(0.7mmol) in equimolarquantity by using the solvent ethanol. The solution was refluxed for 3 hours. The precipitates formed was cooled and collected by suction filtration. It was then washed thoroughly with ethanol.[11]
2. 2-amino-4-(o-chloroanilino)-1, 3-thiazoleand various substituted aromatic aldehydes were refluxed for four hours in presence of sodium methoxide. Then the reaction mixture was neutralized with dilute HCl. The resulting precipitate was filtered and recrystallized from ethanol.[20]
3. 4-Aminobenzenesulfamide and carbonyl ligand were prepared by reacting equimolarsolutions dissolve in anhydrous ethanol, into a chromic acid scrubbed, cleaned and dried crucibles. The reaction mixtures were stir vigorously to get uniform mixing before the mixtures were transferred to a Continent MW800G microwave oven. These mixtures were subjected to MW irradiation for 1 minute at 385 watt power. After that the mixture was cooled, the formed crystals were filtered off, washed with several portions of anhydrous ethanol.[21]
4. A mixture of 2-amino-4-phenyl thaizole (0.52 g, 3mmol) and aldehydes (3 mmol) in ethanol (15 mL) was stirred at room temperature. The progress of reaction was monitored

by TLC, after the completion of reaction solvent was removed by evaporation (rotary evaporator), the resulting product was crystallized by appropriate alcohol.[17]

Biological activities of schiff bases

Anti-inflammatory activity

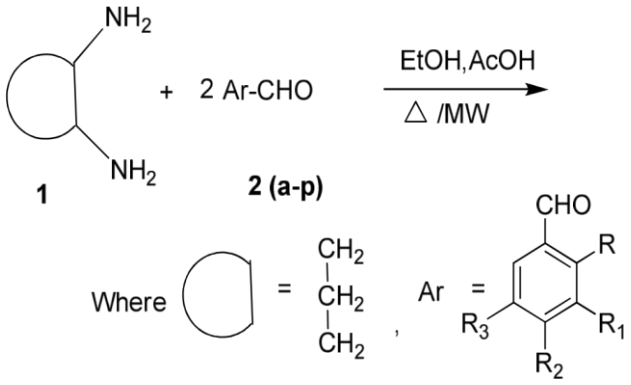
The Schiff base displayed good activity against the Gram-positive bacteria Staphylococcus aureus, the Gram-negative bacteria *Escherichia coli* and the fungi *Aspergillus Niger* & *Candida albicans*.

R. Nirmalet, al. they were synthesized a series of novel 3-(4-(benzylideneamino) phenylimino) 4-fluoroindolin-2-one derivatives and characterized by spectral (I.R, 1H NMR, mass) and elemental analysis. The title compounds (N1-N10) were evaluated for analgesic, anti-inflammatory, and ulcerogenic index activities. Results displayed that compound N3 exhibited significant analgesic activity. Among the title compounds studied, N2, N3, and N8 exhibited significant anti- inflammatory activity comparable to reference standard diclofenacsodium. Interestingly, the test compounds showed only mild ulcerogenic side effect when compared to aspirin.[1]

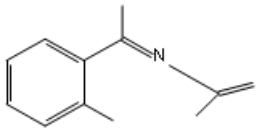
Antimicrobial activity

A. Shinde et, al. they were synthesized Propane-1,3-diamineon condensation with different halogeno substituted benzaldehydesundermicrowave irradiation affords novel series of bis-schiff bases. Structures of the newly synthesized bis-Schiff bases established on the basis of spectroscopic data. Further, all compounds screened for antimicrobial activity against *Staphylococusaureus*, *Escherchia coli*, *Aspergillusniger*and *Aspergillusflavus*. Most of thecompounds show potent activity. P.Mangaiyarkkarasi et, al. synthesized a series of novel metal complexes of general formula [ML2]Cl2 and [CrL2Cl2]Cl where M is Cu(II), Co(II) and L is a Schiff base formed by condensation of dihydropyrimidone derivative of vanillin (Biginelli Product) and 4-aminoantipyrine have been prepared and characterized by analytical, spectral, magnetic and conductance measurements. Magnetic measurements and electronic spectral studies suggest an octahedral structure for the Cr(III) complex and square planar geometry for Cu(II) and Co(II) complexes. The data show that the complexes have composition of the ML2 type. The antimicrobial screening of the ligand and its complexes have been extensively studied on bacterias like *E.coli, Vibrio spp., Staphylococcus aureus, Pseudomonas aeroginosa, Bacillus spp., Vibrioparahaemolytics, Salmonella spp., Aeromonas spp., Klebsiella spp., Proteus spp.* and fungi such as *Candida albicans,*

Aspergillusflavus, Pencillium spp., Aspergillusniger, Trichophyton. The results also indicate that the metal complexes are better antimicrobial agents as compared to the Parent Schiff base ligand and Biginelliproduct.[5]

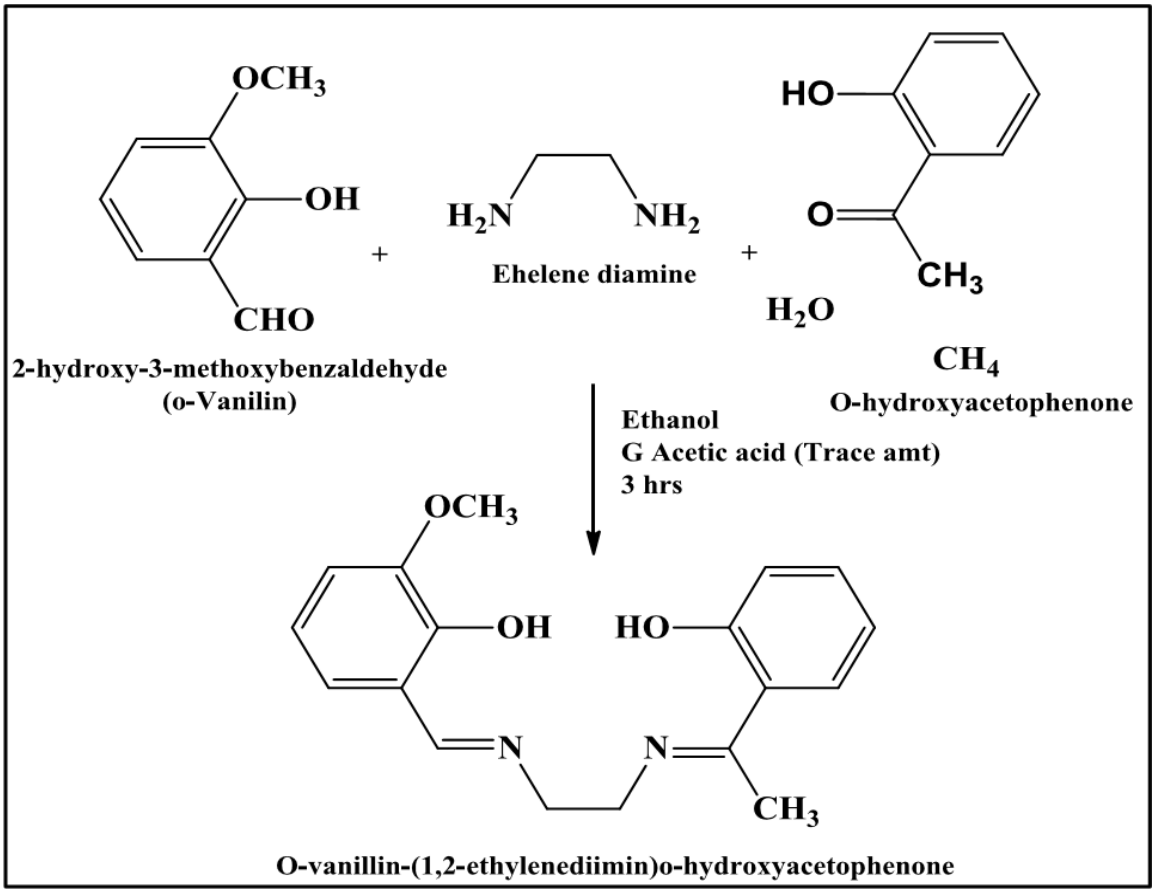


S.H. Baui et, al. they were synthesizedsome new chelates of Mn(II), Co(II), Cu(II) and Cr(III) ions with Schiff base derived from salicylaldehyde and thiourea have and investigated by elemental analysis, molar conductance measurements, infrared and electronic spectra. The elemental analysis data exhibited the formation of 1:1 [M:L] ratio. The obtained molar conductance values revealed that all the chelates are non-electrolytic in nature. The infrared spectral data showed the chelateationbehaviour, which is through to the nitrogen and oxygen atoms of the ligand. The electronic absorption spectral data displayed the existence of π-π*, n-π* (HC=N) transitions and the expected geometrical structures. By testing the effects of these Schiff base ligands on five species of bacteria (*S. aureus, K. pneumoniae, E. coli, P. aeruginosa*and *P. mirabilis*) *in vitro*, it hasbeen found that Mn(II) chelate was very effective, Co(II) chelatehad moderate effect and no effect of Cu(II) chelate was found on these bacteria. The effects of Mn(II) and Co(II) chelates increased with higher concentrations.[7]



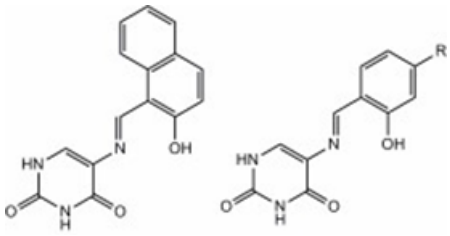
sThe Schiff base, o-vanillin-(1,2ethylenediimine)ohydroxyacetophenone(VEH), and its six metal complexes were synthesized, characterised and tested for their cytotoxic activities. The copper complex was found to have high IC50 value, around 48 µ/ml. Daltons Lymphoma Ascites cell (DLA cell) induced solid and Ehrliche`s Ascites Carcinoma cell (EAC cell) induced ascites tumour models were used for antitumor studies of the compounds. Copper complex administrated at different concentrations in mice inhibited the solid tumour

development and increased the mean survival rate and the life span of Ascites tumour enduring mice in a concentration dependent manner. The ligand and its metal complexes were screened against *C. albicans*, *C. Tropicalis*and *A. Flavus*fungi and *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus cereus* bacteria to assess their potential antimicrobial activities. The results are quite promising. It is clear from the antifungal screening data that the metal complexes are more fungitoxic than the chelating agent itself. The bacterial screening results revealed that the free ligand has more sensitivity for gram-positive than gram-negative bacteria.[12]



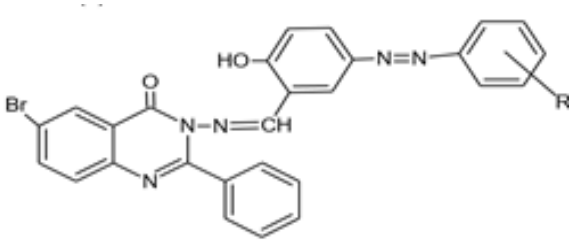
G. Koz et, al.synthesized, spectroscopic and biological activity studies of Ni(II), Cu(II) and Co(II) complexes of Schiff base ligands derived from 5-aminouracil, 2-hydroxy-1-naphtaldehyde,2,4 dihydroxybenzaldehyde and salicylaldehyde are reported. In all cases, the complexes appear to be monomeric. The ligands coordinate in bidentate fashion to Ni(II) and Co(II) but in a tridentate fashion to Cu(II) by coordinating to the carbonyl oxygen atom in the 4th position of uracil ring. The biological activities of the Schiff bases and metal complexes have been tested in vitroagainst a number of bacteria and a fungus. Ni(II) complexes derived

from the saliciylaldehyde Schiff base ligand showed good antimicrobial activity whereas a Co(II) complex derived from the same ligand showed good anticandidalactivity.[15]

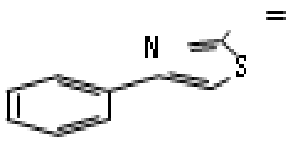


Misra1 P. S. et, al. The novel reaction of 3-(2-methylbenzimidazol-1-yl) propanoic acid hydrazide with CS2/KOH gave Oxadiazole derivative which underwent Mannich reaction to give 3-[(dialkylamino) methyl]-2phenyl-4(3H)-quinazolinone. All compounds were characterized by physical, chemical, analytical and spectral data. All compounds have been screened for their antimicrobial activity and anti-inflammatory activity.[8]

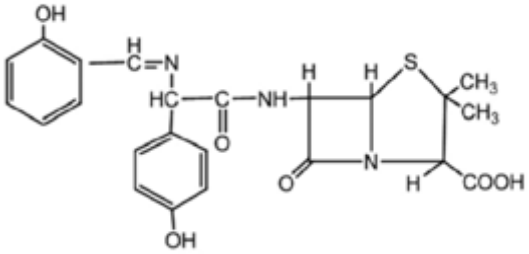
Tiwari S. et, al. They were synthesizedsome new biological active 6-bromo-3-({5[3, 4-substituted) diazenyl]-2-hydroxybenzylidene} amino-2-benzylquinazoline-4(3H)-one by reaction of synthesized quinazoline derivative with substituted azosalicylaldehyde. The structure of the synthesized compounds has been established on the basis of IR, 1HNMR, Mass spectra and elemental analysis. The compounds have been evaluated for their in-vitro antimicrobial activity against different human pathogens using disc diffusion assay.[9]



Khalid M. et, al. synthesized thiazole derivatives by one-pot condensation reaction of a-haloketone, thiourea and thionyl chloride. Starting from 2-amino-4-phenyl-1,3-thiazole (1), Schiff bases of thiazole 2-29 in the search for possible clinically suitable derivatives for antibacterial and antifungal studies. The structure of synthesized compounds were characterized by analytical and spectral (IR, 1H-NMR, and EI-MS) methods. The synthesized compounds were screened for their antibacterial and antifungal activities. Minimum inhibitory concentrations are also calculated.[17]



Sanjivani S. et, al. A new Schiff base ligand derived from sulphonamidesalicylaldehyde and substituted salicylaldehyde have been synthesized. The ligands were characterized by M.P, elemental analysis, TLC and IR spectra. The Schiff base ligands were screened for antifungal activity against Aspergillusniger and antibacterial activity tested against Escherichia coli.[18] Aurora et, al. (2015),[31] were reported metallic compounds of SB obtained from dissimilar antibiotics that are extensively used as organic effective constituents, particularly as sterile mediators. The broad-spectrum formulation proven from tentative data has been [Co L2(H2O)2] and [Ni L2(H2O)2]. This arrangement has been additionally verified by thermal investigation and their thermal stability in nitrogen atmosphere has been studied. Antibacterial investigation revealed that the effectiveness of metallic compounds is greater than the initiated one of free Schiff base ligand.[19]



CONCLUSION

Schiff base compounds have been shown to bepromising leads for the design of more efficient antimicrobial agents and anti-inflammatory drug. Schiff base ligands are considered privileged ligands because they are easily prepared by a simple one pot condensation of an aldehyde and primary amines. In this review, the activities of Schiff base and their complexes are summarized.

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