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Applications for Schiff Bases in a Variety of Biological Domains

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***Abstract* :**Schiff bases are easily synthesized and have a wide range of structural variations. They are commonly produced by simple condensation of an aldehyde or ketone with primary amines. Schiff bases which are imine or azomethine containing compounds with a functional group of (-C=N-), are discovered to be a flexible pharmacophore for the design and development of numerous bioactive lead compounds. Schiff bases are the substances with biological activity that have been found to have a number of significant pharmacological effects, including Antibacterial activity, Antifungal activity, Antimicrobial activity, Antimalerial activity, Analgesic activity, Anti-inflammatory activity, Antidiabetic activity,and Antitumor activity. In this review, a wide variety of schiff bases are discussed that are employed in applications for many types of biological activities.

***Index Terms*- Schiff bases,Pharmacophore,Antifungal, Anticancer, Analgesic, Anti-inflammatoryactivity.**

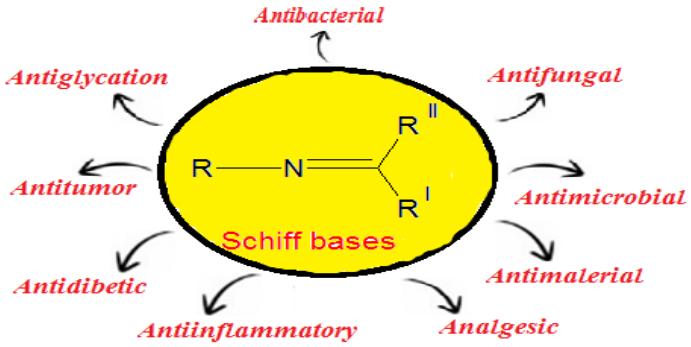


Figure 2.Graphical abstract

I. Introduction

Hugo Schiff, a German scientist who won the Nobel Prize, was the first to recognize Schiff bases as condensation byproducts of primary amines and carbonyl compounds in 1864[1].Hugo Schiff gave Schiff bases its name. The imine group is present in Schiff base (-RC=N-). They were synthesised by condensing aldehyde or ketone like compounds (RCOR′), where R, R′ is an alkyl or aryl group, with primary amine (R-NH_2), where the carbonyl group is altered using an imine or azomethine group[2].A ketone or an aldehyde whose carbonyl group (C=O) has been substituted out for an imine or an azomethine group is referred to as a Schiff base [3]. Primary amines and carbonyl compounds can be combined to obtain a class of chemicals known as schiff bases [4].Schiff base ligands are essential in the field of coordination chemistry, notably in the synthesis of complexes of Schiff bases, because these substances have the potential to form stable complexes with metal ions [5].

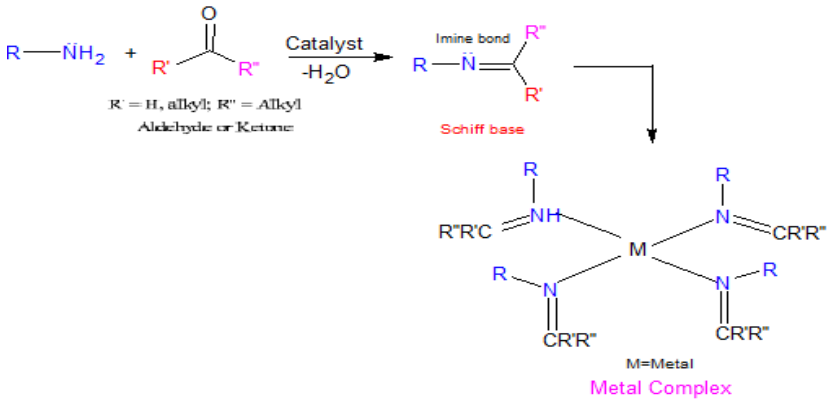


Figure 2.Bioactivity of Schiff bases and their metal complexes.

The scientist showsgrowing interest has in tiny compounds' capacity to bind to DNA, such as Schiff bases. Schiff base ligands enrich contemporary coordination chemistry because metal complexes of schiff bases are the most extensively researched coordination molecules with advanced applications [6].Numerous Schiff base complexes stand out from other compounds due to their exceptional catalytic activity in a variety of processes at high temperatures (>100^{0}C) and in the presence of moisture. Its application in both homogeneous and heterogeneous catalysis has been extensively documented in recent years [7, 8].Since there are many different ligand structures depending on the aldehydes and amines taken into consideration, the field of Schiff base complexes has quickly emerged [9,10].

It is becoming more common to use Schiff bases and their metal complexes as catalysts in many biological systems, polymers, and colours. It has also been demonstrated that these compounds can be used to make enzyme preparations [11].

Researchers were encouraged to design novel heterocyclic or aryl Schiff bases for the creation of new environmentally friendly technologies through the use of Schiff base derivatives in various processes [12]. Through ring closure, cycloaddition, and replacement reactions, Schiff bases have been used as synthons in the synthesis of a variety of physiologically and industrially active chemicals, including formazans, 4-thiazolidinines, benzoxazines, and others [13].Imines' widespread usage in new technologies, chemical catalysis, medicine, pharmacy, and other fields of human endeavor can be used to explain why there is such a high level of interest in them [14]

All d-block metals and lanthanides have been known to form complexes with Schiff bases. Due to their many biological characteristics, sulfonamide Schiff bases and their metal complexes stand out among them in medicinal chemistry. For instance, various biological features were displayed by the metal complexes of 5-chloro-2 hydroxybenzylidene)aminobenzenesulfonamides [15], 4-(2-aminomethyl)benzenesulfonamide, and sulfisoxazole [16]

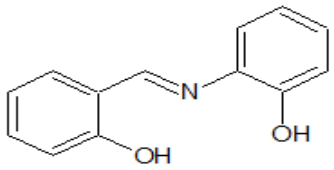
4-(2 aminoethyl)benzenesulfonamide [17]. Moreover, the metal complexes of Schiff bases derived by the reaction of 5 chlorosalicylaldehyde [18] or indole-3-carboxaldehyde [19] with various sulfonamides such as sulfanilamide, sulfaguanidine, sulfathiazole, sulfamethoxazole, 4-(2-aminoethyl)benzenesulfonamide etc. were found to have antibacterial and antifungal properties.

Schiff bases are notified as a very dominant group of organic compounds due to their capability to form complexes with transition metal ions and of their biological properties. Schiff bases and their metal complexes had been widely used for biological applications.

II. Biological Activities of Schiff Bases:

Antibacterial activity:

Bringmann, et al.[20] has been suggested that schiff bases are effective antibacterial agents. For instance, N-(salicylidene)-2-hydroxyaniline (Fig. 3) has an effective MIC value of 8μg/mL against Mycobacterium tuberculosis H37Rv. By conducting tests on J774 macrophages, the selectivity of compound (Fig.3) was verified. Compound (Fig.3) had no cytotoxic effects on J774 macrophages.



N-(salicylidene)-2-hydroxyaniline
(Antibacterial Activity)

Figure 3.

Antifungal activity :

Schiff base antiviral action although there are numerous therapeutic alternatives for viral infections, the antiviral medications that are currently on the market are still not completely successful, most likely because of the high rate of virus mutation. They might also exhibit any of a variety of negative impacts. In order to create new antiviral medications, salicylaldehyde Schiff bases of 1-amino-3-hydroxy-guanidine tosylate are an excellent starting point [21].

In fact, it was discovered that the 2-(3-allyl-2-hydroxybenzylidene)-N-hydroxyhydrazinecarboximidamide derivative, which was derived from a variety of 1-amino-3-hydroxyguanidine tosylate-derived Schiff bases, was extremely effective against mouse hepatitis virus (MHV), inhibiting its growth by 50% when used at concentrations as low as 3.2 μM[21].

Antimicrobial activities:

Elzahany et al.[22] created transition metal complexes with schiff bases using 2-formylindole, salicylaldehyde, and N-amino Rhodanine as shown in (fig.4 and fig.5) and under the same experimental conditions, the free ligands and their metal complexes shown more action against the same organisms.

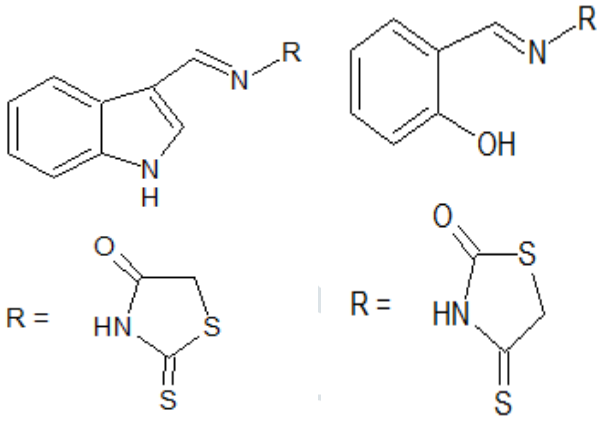


Figure 4.

Figure 5.

Antifungal activity :

Rehman, Wajid, et al.[23] reported that he majority of cruciferous crops, including broccoli, cauliflower, mustard, turnip, cabbage, rapeseed, and radish, are negatively impacted by the phytopathogenic fungus Alternaria brassicae and Alternaria brassicicola.At 500 ppm, N-(Salicylidene)-2-hydroxyaniline 4 (Fig. 6) reduced the development of these fungi by 67–68% [23].

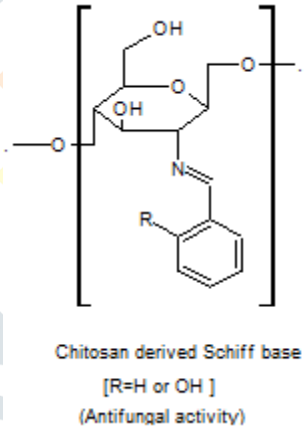


Figure 6.

The synthesis of a number of 1-(5-substituted-2-oxoindolin-3-ylidene)- 4-(substituted-pyridin-2-yl)thiosemicarbazide derivatives has been reported by Vijey Aanandhi et al [24]. These substances were tested in vitro for their ability to inhibit the growth of B. subtilis, S. aureus, E. coli, P. aeruginosa, Candida albicans, and Aspergillus niger. All of the compounds were said to have good to excellent antibacterial and antifungal activity.

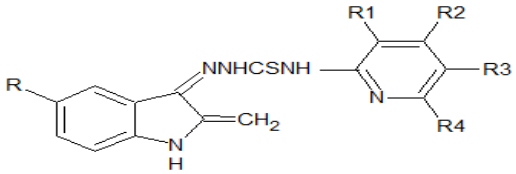


Figure 7.

Antimalarial activity:

Harpstrite, Scott; Collins et al [25] synthesized compound the Naphthalene-Schiff bases or phenols from naphthalene-amine. With a half-maximal inhibitory concentration (IC50) of 1.7 M against CQ-resistant Dd2 strains, 7 of these compounds showed substantial bioactivity.

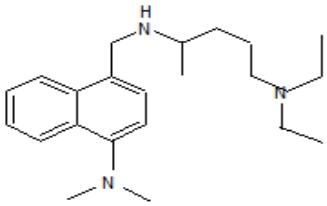


Figure 8.

Analgesic activity:

Chinnasamyet al.[26] were synthesized series of novel Schiff bases of Isatin. Using the tail-immersion method, these compounds were tested for their analgesic efficacy. When compared to typical pentazocine, 3-(4-(4-Hydroxy-3-methoxylbenzylideneamino)phenylimino) indoline-2-one had more analgesic effects. In this compounds containing electron-donating groups perform better analgesic activity than the electron-withdrawing groups. (Fig.9) shown better analgesic activity.

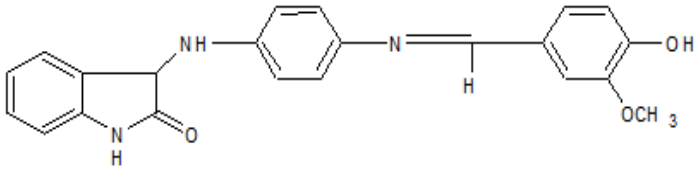
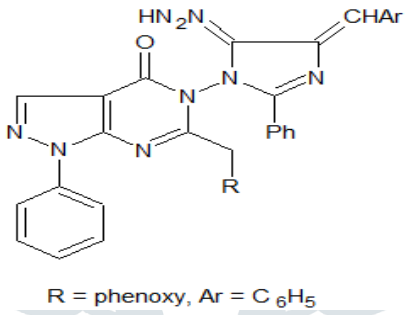


Figure 9.

Anti-inflammatory:

Hussein et al.[27] reported the synthesis of series of novel Schiff bases bearing Pyrazolo[3, 4-D]Pyrimidine-4-ones. Some of the newly synthesized compounds showed good anti inflammatory activities and safer on liver enzymes in rats.

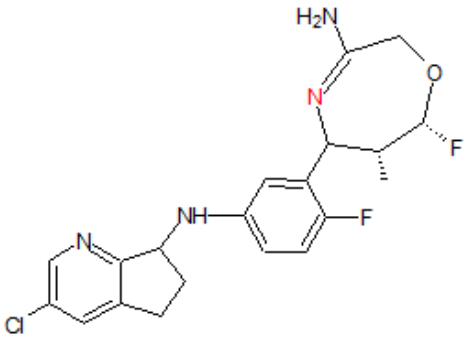


R = phenoxy, Ar = C_6H_5

Figure 10.

Anti-diabetes :

Gabellieri E, Guba W, Hilpert H, et al.[28] reported thata versatile metal complexing agent, Schiff bases Compound had strong inhibitory activity in the bioactivity experiment, with IC50 values for BACE1 and BACE2 of 0.070 μM and 0.024 μM, respectively. BACE2 inhibitors also contribute significantly to the proliferation of β -cells, which reduce type 2 diabetes complications.

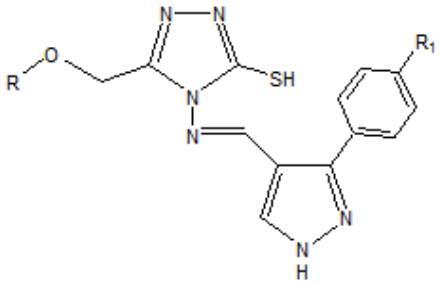


β-Secretase (BACE1 and BACE2) inhibitors.

Figure 11.

Anti-tumor activity:

Sunil, D., Islooret al.[29] were studied the three Schiff bases, 4-({[3-(4-fluorophenyl)-1*H*-pyrazol-4-yl]methylene}amino)-5-[(2-methylphenoxy)methyl]-1,2,4-triazole-3-thiol (SB-3).The mean survival time of infected mice was shown to be improved at a dose of 100 mg/kg body weight. Swiss albino mice having Ehrlich ascites carcinoma (EAC) were used to test three Schiff bases at two different doses for their anti-tumor effects.



SB 1 R=4methyl benzene, R_1 = Cl SB 2 R=4methyl benzene, R_1 = F
SB 3 R=4methyl benzene, R_1 = F
Figure 12.

Antiglycation activity:

Al-Resayes SI, Warad I, Al-Nuri MA, et al[30] reported that by using the bovine serum albumin-methylglyoxal (BSA-MG) assay in vitro, these compounds' antiglycation capability was assessed, and their IC50 values were compared to that of rutin (IC50 = 292.21 ± 1.5 µM). The strongest antiglycating agent discovered so far is Schiff base (fig.13) IC50 = 397.21 2.2 µM).

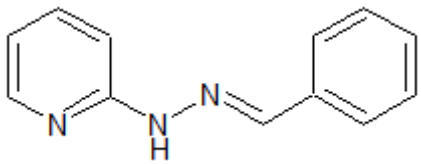


Figure 13.

RESULT AND DISCUSSION:

The Schiff bases are one of the important biological molecules which are having number of applications in Chemistry, Biology, Physics and technology. This organic molecule is confirmed with the help of advance characterification techniques such as IR Spectroscopy to identify the (-C=N-) functional group,^{1}H NMR for identification of protons and surrounding environment with aromaticity of molecules, mass spectroscopy for determination of molecular mass as well as in retroanlysis. UV spectroscopy to for identification of unsaturation in molecules.With this we can also used other analytical techniques for identification and analysis of Schiff bases and their derivatives.

As Schiff base is having heteroatom and aromatic character, this type of organic molecule is widely use in biological systems and in medicinal field for identification of biological or microbial activity of these type of compound microbiologist may use different methods such as disc diffusion technique and agar well diffusion method use to evaluate the antimicrobial activity. With help of zone inhibition, we can identify antimicrobial or antifungal activity of schiff bases and their derivatives.

CONCLUSION

One of the most significant chemical groups of molecules that share an essential characteristic with numerous therapeutic medicines is the schiff base. This review highlights how Schiff bases helped design and create new lead with possible biological functions. Researchers have remained interested in learning more about numerous Schiff bases that are significant for medicine due to its bioactive core because it offers the most suggestive and conclusive information. This paper aims to examine all biological actions for Schiff bases that have been described.

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