# SCHIFF BASES: A SHORT REVIEW ON THEIR BIOLOGICAL ACTIVITY

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## Abstract: -

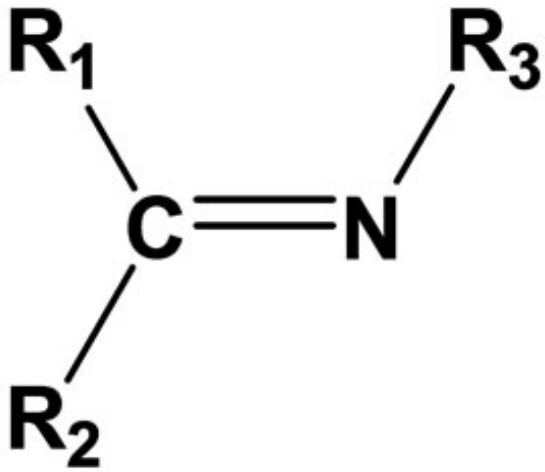
A **Schiff base** (named after Hugo **Schiff**) is a compound with the general structure $R_2C=NR'$ ($R' \neq H$). They can be considered a sub-class of imines, being either secondary ketimines or secondary aldimines depending on t **Schiff bases** are some of the most widely **used** organic compounds. They are **used** as pigments and dyes, catalysts, intermediates in organic synthesis, and as polymer stabilisers heir structure.In present review I discussed about its biological activity.

Keywords: - Schiff base, Antimicrobial, Antibacterial, Medicinal property.

## Introduction: -

Schiff bases are condensation products of primary amines with carbonyl compounds gaining importance day by day in present scenario. Schiff bases are the compounds carrying imine or azomethine (–C=N–) functional group and are found to be a versatile pharmacophore for design and development of various bioactive lead compounds. Schiff bases exhibit useful biological activities such anti-inflammatory, analgesic, antimicrobial, anticonvulsant, antitubercular, anticancer, antioxidant, anthelmintic, antiglycation, and antidepressant activities. Schiff bases are also used as catalysts, pigments and dyes, intermediates in organic synthesis, polymer stabilizers, and corrosion inhibitors.

Schiff bases are the compounds carrying imine or azomethine (–C=N–) functional group. These are the condensation products of primary amines with carbonyl compounds and were first reported by Hugo Schiff [1-3]. Schiff bases form an important class of the most widely used organic compounds and have a wide variety of applications in many fields including analytical, biological, and inorganic chemistry. Schiff bases have gained importance in medicinal and pharmaceutical fields due to a broad spectrum of biological activities like anti-inflammatory [4-7], analgesic [5-8], antimicrobial [9,10], anticonvulsant [11], antitubercular [12], anticancer [13,14], antioxidant [15], anthelmintic [16], and so forth. The nitrogen atom of azomethine may be involved in the formation of a hydrogen bond with the active centers of cell constituents and interferes in normal cell processes [17,18]. Apart from biological activities, Schiff bases are also used as catalysts, intermediates in organic synthesis, dyes, pigments, polymer stabilizers [3], and corrosion inhibitors [19]. Studies enlightened that metal complexes show greater biological activity than free organic compounds [20]. Augmentation of biological activity was reported by implementation of transition metals into Schiff bases [21]. Schiff bases played an influencing role in development of coordination chemistry and were involved as key point in the development of inorganic biochemistry and optical materials [22]. Schiff bases have been utilized as synthons in the preparation of a number of industrial and biologically active compounds like formazans, 4-thiazolidinines, benzoxazines, and so forth, via ring closure, cycloaddition, and replacement reactions [23]. Schiff base derivatives in various processes promoted the researchers for designing of novel heterocyclic/aryl Schiff bases for development of new environmental-friendly technology [24].




**$R_1$, $R_2$ and / or $R_3$=alkyl or aryl**

General structure of Schiff Base

## Synthesis of schiff bases: -

The first preparation of imines was reported in the 19th century by Schiff (1864). Since then a variety of methods for the synthesis of imines have been described [25]. The classical synthesis reported by Schiff involves the condensation of a carbonyl compound with an amine under azeotropic distillation [26]. Molecular seives are then used to completely remove water formed in the system [27]. In the 1990s an *in-situ* method for water elimination was developed, using dehydrating solvents such as tetramethyl orthosilicate or trimethyl orthoformate [28]. In 2004, Chakraborti et al. demonstrated that the efficiency of these methods is dependent on the use of highly electrophilic carbonyl compounds and strongly nucleophilic amines. They proposed as an alternative the use of substances that function as Brönsted-Lowry or Lewis acids to activate the carbonyl group of aldehydes, catalyze the nucleophilic attack by amines, and dehydrate the system, eliminating water as the final step. Examples of Brönsted-Lowry or lewis acids used for the synthesis of Schiff bases include ZnCl2, TiCl4, MgSO4-PPTS, Ti(OR)4, alumina, H2SO4, NaHCO3, MgSO4, Mg(ClO4)2, H3CCOOH, Er(OTf)3, P2O5/Al2O3, HCl.

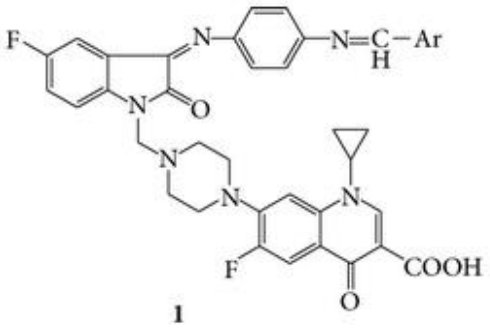
In the past 12 years a number of innovations and new techniques have been reported, including solvent-free/clay/microwave irradiation, solid-state synthesis, K-10/microwave, water suspension medium, [bmim]BF4/molecular sieves, infrared irradiation/no solvent, NaHSO4·SiO2/microwave/solvent-free, solvent-free/CaO/microwave, and silica/ultrasound irradiation . Among these innovations, microwave irradiation has been extensively used due to its operational simplicity, enhanced reaction rates, and great selectivity. The use of microwave irradiation commenced with the independent studies of Rousell and Majetich groups. Microwave irradiation is less environmentally problematic than other methods because it abolishes the excessive use of aromatic solvent and the Dean-Stark apparatus for azeotropic removal of water. Another feature of this technique is that the reactions achieve high efficiency in a shorter period of time.

## Biological activities of Schiff bases: -

### 1-Antimicrobial activity: -

A series of some novel 5-substituted Schiff and Mannich bases of isatin derivatives, that is, 7-(4-((3-(4-(substituted benzylideneamino) phenylimino)-5-fluoro-2-oxindolin-1-yl)methyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 1[a-1], [PIC-1] were synthesized and characterized for *in vitro* antibacterial activity. Antimicrobial activity of synthesized compounds

was assessed by minimum inhibitory concentration (MIC) in comparison with standard antimicrobial drugs, that is, ciprofloxacin and ketoconazole. Compound [1c] was reported to be more active than both of the standard drugs against tested microorganisms which proves the significance




1

| 1 | Ar | 1 | Ar |
|---|---|---|---|
| a | $-C_6H_5$ | g | $-4CH_3-C_6H_4$ |
| b | $-4Cl-C_6H_4$ | h | $-3,4,5(OCH_3)_3-C_6H_4$ |
| c | $-4OH-C_6H_4$ | i | $-4OH, 5-OCH_3-C_6H_4$ |
| d | $-4OCH_3-C_6H_4$ | j | $-5NO_2-C_6H_4$ |
| e | $-4NO_2-C_6H_4$ | k | $-4N(CH_3)_2-C_6H_4$ |
| f | $-6OH-C_6H_4$ | l | $-CH=HC-C_6H_4$ |

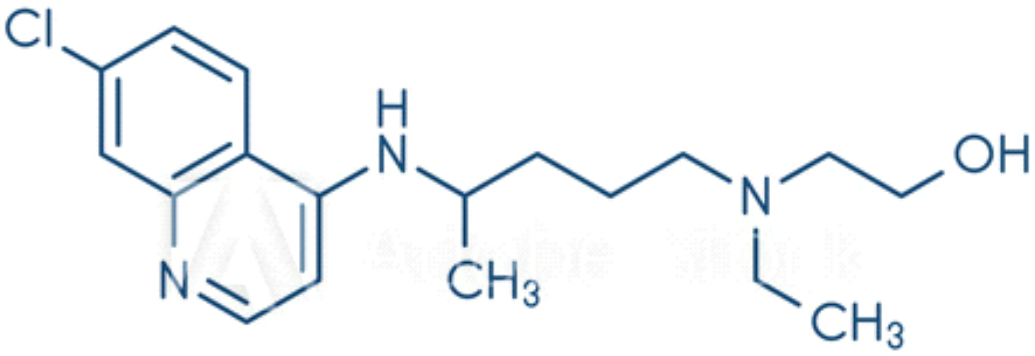
PIC-1

Of substituted electron-donating groups in improving the antimicrobial activity [29].

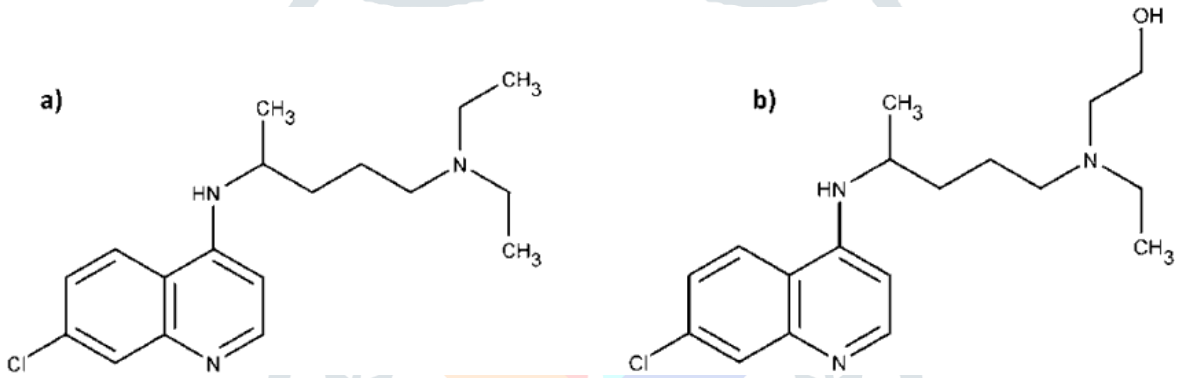
**Antimalarial activity: -**

Malaria is a neglected disease that still causes serious public health problems. Every year, approximately 500 million people are afflicted by the disease, of whom around 1–3 million die, 90% of who in sub-Sahara Africa are primarily children [30]. Malaria is currently found in more than 100 countries throughout Africa, Latin America, Asia, and Oceania. Human malaria is mainly caused by four species of *Plasmodium* (*P. falciparum*, *P. vivax*, *P. ovale,* and *P. malariae*). The female mosquito of the *Anopheles* genus is the vector of *Plasmodium* [31]. The search for new drugs, vaccines, and insecticides to prevent or treat this disease is clearly a priority.

Schiff bases have been shown to be interesting moieties for the design of Antimalarial agents. Ancistrocladidine is a secondary metabolite produced by plants from the families Ancistrocladaceae and Dioncophyllaceae that present an imine group in its molecular scaffold. Compound 1 has been shown to be active against *P. falciparum* K1 and 3D7. The minimum inhibitory concentrations (MIC values) of ancistrocladidine necessary to completely abolish *P. falciparum* K1 and 3D7 growth were 0.3 and 1.9 µg/mL, respectively. Interestingly, compound 1 was 90- and 10-fold more selective to *P. falciparum* K1 and 3D7, respectively than to rat skeletal mytoblast L-6 cells. Rathelot et al. described the synthesis of Schiff base-functionalised 5-nitroisoquinolines and investigated the *in vitro* activity of these compounds against an ACC Niger chloroquine resistant *P. falciparum* strain. Schiff base was the most effective antimalarial agent among the synthesised 5-nitroisoquinoline derivatives. The concentration of compound 5 necessary to inhibit *P. falciparum* growth by 50% ($IC_{50}$) was 0.7 µg/mL. Under the same experimental conditions, the $IC_{50}$ value for chloroquine was 0.1 µg/mL.



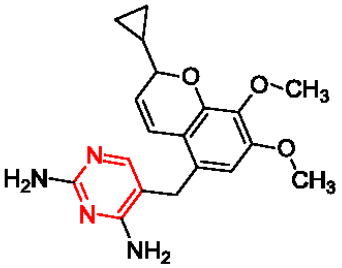

hydroxychloroquine #179186060



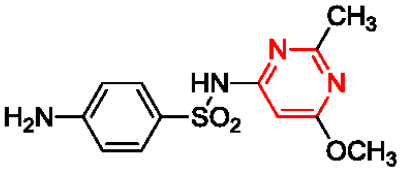

Chloroquine Hydroxychloroquine

**Anthelmintic Activity: -**

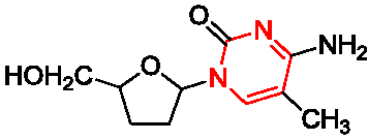
A series of new Schiff bases, containing 4(3H)-quinazoline ring system was synthesized by the condensation reaction of 3-amino-2-methyl-4(3H) quinazolinone (AMQ) with different substituted aromatic aldehydes in methanol. The compounds were also evaluated for their anthelmintic, antioxidant, and antimicrobial activities. Indian adult earthworms (*P. posthuma*) were employed for the anthelmintic activity. Piperazine citrate was used as a reference standard while DMSO as a control for comparison. Results revealed that all the synthesized compounds were moderately active except compound which was found to be the most potent anthelmintic agent due to presence of chloro group. Chloro group may improve the conductance of worm muscle membrane that causes reduction in hyperpolarization and excitability which leads to flaccid paralysis that results in expulsion of worm by peristaltic movement.[32]



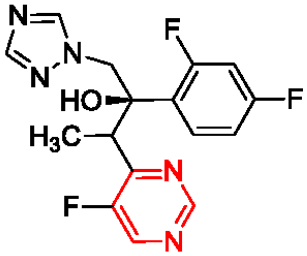
**Iclaprim**
(Dihydrofolate inhibitor)



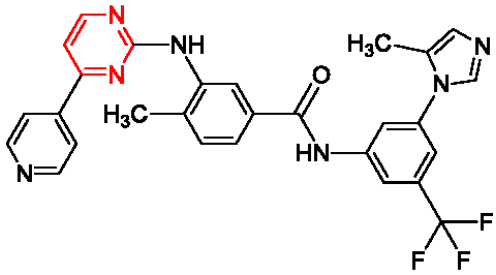
**Sulfamethomidine**
(Antibacterial)



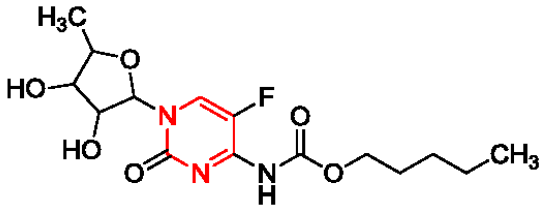
**Zalcitabine**
(Antiviral)



**Voriconazole**
(Antifungal)



**Nilotinib**
(Anticancer)



**Capecitabine**
(Anticancer)

irketed preparations of pyrimidine molecules

## Antiviral activity of Schiff base: -

A new synthesized derivative of substituted salicylaldehyde Schiff bases of aminophenoxy ethane were selected as new biological agents. The results indicate that none of the tested compounds was found to be an antiviral agent for DNA (bovine herpesvirus 1) and RNA (parainfluenza-3 viruses) viruses used, but they possess highly cytotoxic effects.

## Anticancer activity of Schiff base: -

Nilotinib a derivative of Schiff base act as anticancer compound. Capecitabine also reported as anticancer Schiff base compound.

## Antifungal activity of Schiff base: -

Voriconazole is treated as antifungal Schiff base derivative. It is highly active against fungal infections.

## Conclusion: -

Schiff bases are one of the most important chemical classes of compounds having a common integral feature of a variety of medicinal agents. This review reflects the contribution of Schiff bases to the design and development of novel lead having potential biological activities with fewer side effects. This bioactive core has maintained the interest of researchers in gaining the most suggestive and conclusive access in the field of various Schiff bases of medicinal importance from last decades. The present paper is an attempt to review all the biological activities reported for Schiff bases in the current literature with an update of recent research findings.

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