Schiff bases – interesting range of applications in various fields of science

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Introduction
Schiff bases are condensation products of primary amines and carbonyl compounds and they were discovered by a German chemist, Nobel Prize winner, Hugo Schiff in 1864 [1].

Structurally, Schiff base (also known as imine or azomethine) is an analogue of a ketone or aldehyde in which the carbonyl group (C=O) has been replaced by an imine or azomethine group (Fig. 1) [2]. Schiff base ligands are essential in the field of coordination chemistry, especially in the development of complexes of Schiff bases because these compounds are potentially capable of forming stable complexes with metal ions [3].

![Fig. 1. General structure of Schiff bases](image)

A large number of Schiff base complexes are characterized by an excellent catalytic activity in a variety of reactions at high temperature (>100°C) and in the presence of moisture. In recent years, there have been numerous reports of their use in homogeneous and heterogeneous catalysis [5, 6].

Schiff bases and their metal complexes are increasingly being used as catalysts in various biological systems, polymers and dyes. Moreover, it is confirmed that these compounds can act as enzyme preparations [7].

Due to the excellent selectivity, sensitivity and stability of Schiff bases for specific metal ions such as Ag(II), Al(III), Co(II), Cu(II), Gd(III), Hg(II), Ni(II), Pb(II), Y(III) and Zn(II), a large number of different Schiff base ligands have been used as cation carriers in potentiometric sensors. Studies in terms of catalytic properties of Schiff bases exhibit the catalytic activity in the hydrogenation of olefins. One of the more interesting applications of these compounds is the possibility to use them as effective corrosion inhibitors. This phenomenon is the spontaneous formation of a monolayer on the surface to be protected [1].

The interest in metal complexes in which the Schiff bases play a role as the ligands are increasing as evidenced by the number of publications appearing annually (approximately 500) [8]. So much interest in imines can be explained by the fact that they are widely distributed in many biological systems and they are used in organic synthesis and chemical catalysis, medicine, pharmacy and chemical analysis, as well as new technologies [9].

Application in medicine and pharmacy
Imine complexes have a broad range of biological properties: antitumor, antiviral, antifungal, antibacterial [10]. They are also used in the treatment for diabetes and AIDS. As biological models, they help in understanding the structure of biomolecules and biological processes occurring in living organisms. They participate, inter alia, in photosynthesis and oxygen transport in organisms. They are involved in the treatment of cancer drug resistance, and often tested as antimalarials. It also could be used for the immobilization of enzymes [11, 12].

Biological activity
Schiff bases are characterized by an imine group –N=CH–, which helps to clarify the mechanism of transamination and racemization reaction in biological system [1].

It exhibits antibacterial and antifungal effect in their biological properties [13, 14]. Metal-imine complexes have been widely investigated due to antitumor and herbicidal use. They can work as models for biologically important species [13].

Antibacterial properties
Mortality increase caused by infectious diseases is directly related to the bacteria that have multiple resistance to antibiotics. The development of new antibacterial drugs enriched by innovatory and more effective mechanisms of action is clearly an urgent medical need [15].

Schiff bases are identified as promising antibacterial agents. For example, N-(Salicylidene)-2-hydroxyaniline (Fig. 2) is active against Mycobacterium tuberculosis [4].

![Fig. 2. N-(Salicylidene)-2-hydroxyaniline as the example of bioactive Schiff base](image)

Schiff bases containing 2,4-dichloro-5-fluorophenyl moieties also take part in effective inhibition of bacterial growth [16]. On the other hand, the compounds obtained from furylglyoxal and p-toluidene show antibacterial activity against: Escherichia coli, Staphylococcus aureus, Bacillus subtilis and Proteus vulgaris. Isatin derived Schiff bases present anti-HIV and antibacterial activity. Other Schiff bases derivatives, which possess antibacterial activity are: benzimidazole, thiazole, pyridine, glucosamine, pyrazolone, hydrazide, thiazolidiones, indole, thiosemicarbazone, p-fluorobenzaldehyde [7].

Antifungal properties
Fungal infections usually are not only limited to the contamination of surface tissues. Recently, there was a considerable increase in the incidence of systemic fungal infections, which are potentially life-threatening [17]. Exploration and development of more effective antifungal agents is necessity, and the individual Schiff bases are considered to be promising antifungal medicines [18].

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Some of them, such as imine derivatives of quinazolinones possess antifungal properties against *Candida albicans*, *Trichophyton rubrum*, *T. mentagrophytes*, *Aspergillus niger* and *Microsporum gypseum*. Schiff bases and their metal complexes formed between furan or furylglycoxal with various amines exhibit antifungal activity against *Helminthosporium gramineum* — causing leaf stripe in barley, *Synchelidium racemosus* — contributing to fruit rot in tomato and *Colletotrichum capsici* — causing anthracnose in chillies.

### Biocidal properties

Schiff bases obtained by the synthesis of o-aminobenzoic acid and \(\beta\)-keto esters have found biocidal use against *S. epidermidis*, *E. coli*, *B. cinerea* and *A. niger* [2].

By contrast, Schiff bases of isatin derivatives are used in the destruction of protozoa and parasites [19].

### Antiviral properties

The use of vaccines may lead to the eradication of pathogens known viruses, such as smallpox, poliomyelitis (polio), whether rubella. Although there are many therapeutic ways to work against viral infections, currently available antiviral agents are not fully effective, which is likely to cause a high rate of mortality from the virus and the possibility of side effects. Salicylaldehyde Schiff bases derived from 1-amino-3-hydroxyguanidine tosylate are good material for the design of new antiviral agents [4].

Isatin Schiff base ligands are marked by antiviral activity, and this fact is very useful in the treatment of HIV [19]. In addition, it was also found that these compounds have anticonvulsant activity and may be included in the anti-epileptic drugs [20].

Gossypol derivatives also present high antiviral activity. Increasingly, gossypol, used in medical therapy is replaced by its derivatives, because of their much lower toxicity [21]. Schiff bases have obtained acceptable results for *Cucumber mosaic virus*, whose effectiveness was estimated at 74.7% [7].

### Antimalarial properties

Malaria is a disease which when is neglected causes serious health problems. Human malaria is largely caused by four species of the genus *Plasmodium* (*P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*). The search for new drugs, vaccines and insecticides for the prevention or treatment of this disease is a priority. Schiff bases are interesting compounds, which could be part of antimalarial drugs.

For example, the compound with such effect is Ancistrocladinine (Fig. 3), which is a secondary metabolite produced by plants of the family Ancistrocladaceae and Dioncophyllaceae, and presenting an imine group in a molecular chain [4].

![Fig. 3. Ancistrocladaceae – antimalarial activity of bioactive Schiff base](image)

Cryptolepine, valid indolchinoline alkaloid, isolated from African plant *Cryptolepis sanguinolenta*, also used in the treatment of malaria, is the product of multi-stage reaction, in which Schiff base is involved [22].

### Anticancer properties

Some Schiff bases have a high antitumor activity. Imine derivatives of N-hydroxy-N’-aminoguanidine block ribonucleotide reductase in tumor cells, so that they are used in the treatment of leukemia [23]. Schiff bases of PDH [N-(1-phenyl-2-hydroxy-2-phenyl ethylidene)-2’,4’-dinitrophenyl hydrazine], PHP [N-(1-phenyl-2-hydroxy-2-phenyl ethylidene)-2’-hydroxy phenyl imine] and HHP [N-(2-hydroxy benzylidene)-2’-hydroxy phenyl imine] reduce the average tumor weight (reduction in tumor growth increases with increasing dose) and decrease the growth of cancer cells in mice EAC cells. In addition, they have ability to rebuild depleted haematological parameters, such as hemoglobin, red blood cells (RBC) and white blood cells (WBC) towards the right content. They also show protective effect on hematopoietic system [24].

### Application in modern technologies

Photo- and thermochromic properties of Schiff bases as well as their biological activity make them applicable in modern technology. Among others, they are used in optical computers, to measure and control the intensity of the radiation, in imaging systems, as well as in the molecular memory storage, as organic materials in reversible optical memories and photodetectors in biological systems [25, 26].

Due to photochromic properties, Schiff compounds could behave as photostabilizers, dyes for solar collectors, solar filters. They are also exerted in optical sound recording technology [25].

Among others, worthy of interest in the properties associated with Schiff rules include: properties of liquid crystal [27], chelating ability [28], thermal stability [29], optical nonlinearity [30] and the ability to create the structure of a new type of molecular conductors using electrical properties to proton transfer [31]. Because of its thermal stability Schiff bases can be used as stationery phase in gas chromatography [29]. The optical nonlinearity of these compounds allows us to use them as electronic materials, opto-electronic (in optical switches) and photonic components [30].

Imine derivatives can be exerted to obtain conductive polymers. Schiff bases as an electrical conductor possess a variety range of uses: as catalysts in photoelectrochemical processes, electrode materials and micro-electronic equipment, organic batteries or electrochromic display device (graphical output devices) [7].

Due to the presence of the imine group, the electron cloud of the aromatic ring and electronegative nitrogen, oxygen and sulfur atoms in the Schiff bases molecules, these compounds effectively prevent corrosion of mild steel, copper, aluminium and zinc in acidic medium [32].

### Application in synthesis and chemical analysis

Schiff bases are a group of organic intermediates, which are very often used in the synthesis and chemical analysis. They are exerted in the production of pharmaceutical and agrochemical industry. In the reaction with hydrogen cyanide Schiff bases may form \(\alpha\)-amino acid precursors (Strecker synthesis). Moreover, chiral Schiff bases are used as initial substrates for the asymmetric synthesis of \(\alpha\)-amino acids, and as catalysts in asymmetric synthesis. Furthermore, the imines obtained by the condensation reaction of arylamines and carbonyl compounds have determined a group of intermediates used in the preparation of important compounds (arenediazonium nitrates, N-arylamene carboxamides, the appropriate amines and cyanamides, \(\beta\)-lactams) [13].

Otherwise, Schiff bases are precursors of reaction of polycyclic derivatives of quinoline and isoquinoline receiving by oxidative ring closure under the influence of ultraviolet light. They are also used for the preparation of acrylic and macrocyclic compounds, such as: cryptats, coronates and podates [25].

These compounds lead to the formation of Ruhemann’s purple (reaction between an amino acid and ninhydrin), which allows to detect and assist in the identification of fingerprints [33].
Summary
Schiff bases have been widely explored for industrial applications. However, the biological activity of this class of compounds still requires further investigation. Both Schiff bases and their metal complexes are interesting research subject that constantly provides us with new information about newly created compounds.

Literature
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