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Bio-Active Schiff Bases: A Short Review

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Abstract

Due to the numerous biological and medicinal applications for these compounds, medicinal chemistry and Schiff base chemistry have garnered a lot of interest. Schiff bases are chemical compounds that typically have an azomethine (–C=N–) functional group that is created when primary amines and aldehydes or ketones condense. Significant biological potential and exceptional structural flexibility are imparted by the imine bond and several substituent groups. The antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, antitubercular, and anticancer properties of bio-active Schiff bases and their metal complexes have made them attractive candidates in pharmaceutical and medical research in recent years. Their pharmacological characteristics and biological efficacy are further improved by their capacity to coordinate with transition metal ions.

Primary biological activities of bio-active Schiff bases described in recent literature are highlighted in this review. Their therapeutic significance, mode of action, and uses in coordination chemistry and drug development are given particular attention. The role of Schiff base derivatives as chelating agents, enzyme inhibitors, and possible leads for the creation of new medications is also briefly covered in the review. Schiff bases remain an important family of molecules in contemporary medicinal chemistry and bioinorganic research

because of their easy synthesis, structural variety, and wide range of biological activity.

Introduction

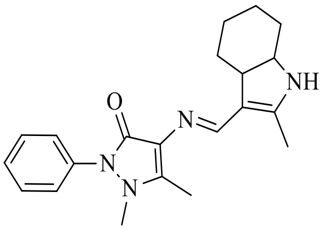
Biological application of Schiff bases

Hugo Schiff made the discovery of the condensation of carbonyl compounds with primary amines in 1864. As a result, this type of chemical is referred to as the Schiff base [1, 2]. It refers the process by which certain compounds having aldehydes react with other compounds that have amino groups to form imine groups(-C=N-)[3, 4]. The Schiff base has a broad spectrum of biological activities including anti-fungal, anti-bacterial, anti-malaria, anti-proliferation, anti-inflammatory and anti-viral properties In addition to being utilized as a pigment, dye, catalyst, intermediate in chemical synthesis, supercapacitor and so on [1, 4, 5].

Antioxidant activity of Schiff bases

Natural chemical compounds called antioxidants protect the body from damage caused by harmful molecules called free radicals. Body cells produce these (antioxidants) in reaction to free radicals [6] .

Some foods include antioxidants which work by neutralising free radicals to prevent some of the damage they cause. These include the minerals copper, zinc and selenium as well as the nutritional antioxidants, vitamins A, C and E. The creation of novel drugs and treatments for a variety of diseases including cancer, diabetes, liver damage, autoimmune disorders, heart disease, antherosclerosis and ageing, which is greatly influenced by free radicals may benefit from the utilization of Schiff bases showing promising antioxidant potential. The antioxidant potential of Schiff bases with pyrazole and indazole moieties (**1-2**) is considerable [7-9] (shown in **Figure 1**).



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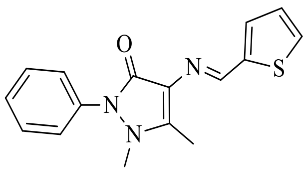

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Figure 1 Structure formulae of antioxidant Schiff bases (**1-2**)

Anti-inflammatory application of Schiff bases

Anti-inflammatory drugs or other medicines reduce inflammation which is the body response to damage to tissue or injury. Inflammation is a complicated process that involves the inflammation of several cells, enzymes and cytokines if left untreated. Chronic disease and tissue damage may arise if they are not managed. Among the various types of medications are steroids, biologics and non-steroidal anti-inflammatory drugs (NSAIDs) [10, 11].

Schiff bases (**3**) anti-inflammatory properties have also been studied and a number of studies have described the synthesis and evaluation of Schiff bases as possible anti-inflammatory medications (shown in **Figure 2**). Based on the benzopyran substitutions coumarins have a variety of biological actions including growth control, antioxidant, antiviral, antibacterial, anti-inflammatory and anticancer properties. P-amino benzoic acid, aminothiadiazole and thiosemicarbazide have anti-inflammatory properties. [12, 13].

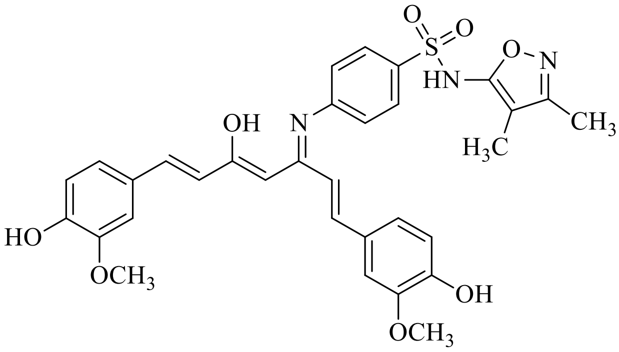

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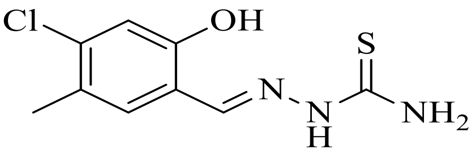
Figure 2. Anti-inflammatory Schiff base **(3***)*

Anti-cancer activity of Schiff bases

Cancer is a general term used to describe a variety of disorders (tumor, malignant neoplasm). Nearly every organ or tissue in the body is susceptible to the tumor process, which is characterized by the uncontrolled proliferation of malignantly altered cells within the tumor. Consequently new tissue grows invades the surrounding body area or spreads to other organs and tissues [14-16]. Anti-cancer drugs or compounds are used to treat cancer. Uncontrolled proliferation and spread of abnormal cells is known as cancer. As a complex disease with several environmental, genetic and lifestyle factors. Cancer is treated using radiation, chemotherapy, surgery and other targeted therapies [17, 18].

Schiff bases have reportedly been created and evaluated for their cytotoxic and anti-proliferative effects on cancer cells. Schiff bases have been investigated for their potential as anti-cancer [19, 20]. These Schiff bases have the potential to be anticancer agents. Thioamide moieties and thiazole (**4-7**) are examples of Schiff bases that exhibit strong anticancer action against a range of cancer cell types including HepG2, A549, MCF-7 and HCT116 as well as leukaemia, breast cancer and colon cancer [21-23]. It act by blocking the enzyme ribonucleotide reductase which is necessary for the production of DNA [24, 25] (shown in **Figure 3**).



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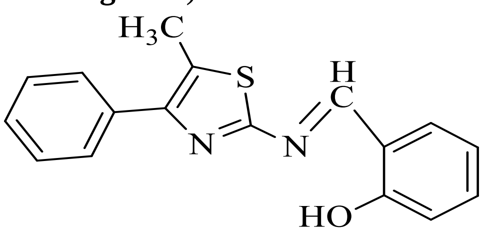

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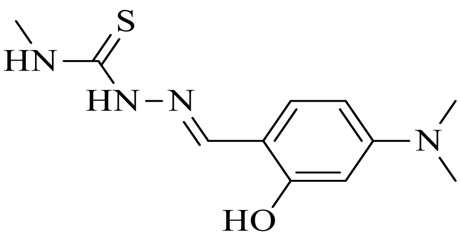

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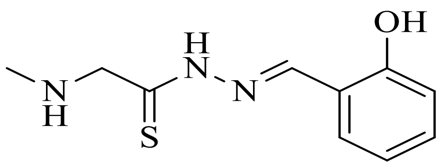


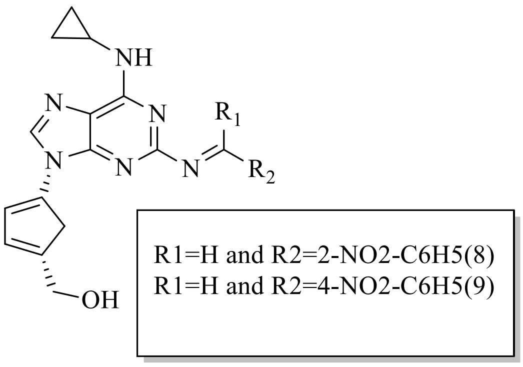
(7)

Figure 3. **Structure formulae of anti-cancer Schiff bases** (4-7)

Antiviral activity of Schiff bases

To treat a variety of viral illnesses the antiviral activity of Schiff bases is being studied [26]. Numerous studies have shown that Schiff bases can inhibit the growth of many viruses including the human immunodeficiency virus (HIV) and the herpes simplex virus (HSV) [27, 28].

The compound (**8**) and (**9**) are marketed under the trade name ziagen and are used to treat HIV and AIDS [26, 29]. Compound (**10**) is used to combat type 1 HIV (human immunodeficiency virus). [30-32] (shown in **Figure 4**).



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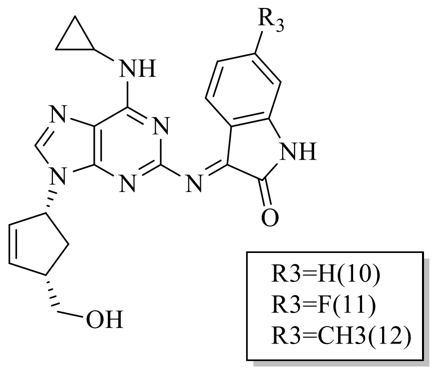
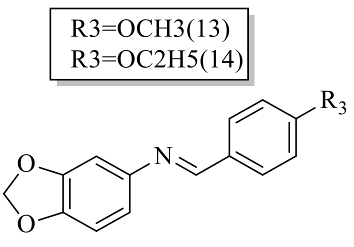


(10-12)

Figure 4. Structural formulae of anti-viral Schiff bases **(8-12)**

Anti-fungal activity of Schiff bases

Because of their ability to obstruct fungus enzymes rupture fungal cell membranes and obstruct the development and expansion of fungal cells. Schiff bases have antifungal properties [2, 33]. According to some study Schiff bases such as piperonyl derivatives can prevent the growth and multiplication of Schiff bases in a variety of fungal species (**13-14**). Schiff bases are against *Tricophyton rubrum*, which contains pyrimidine derivatives (**15-17**) has great ability to combat many fungal strains [34-36] (shown in **Figure 5**).



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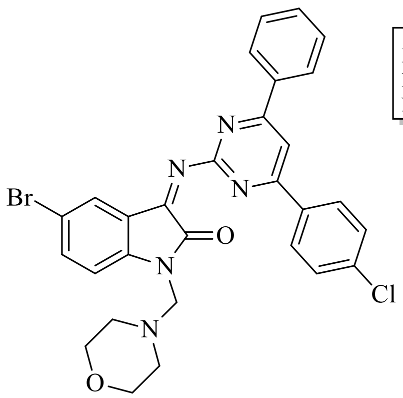

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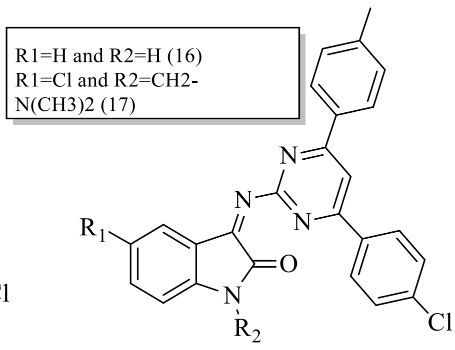
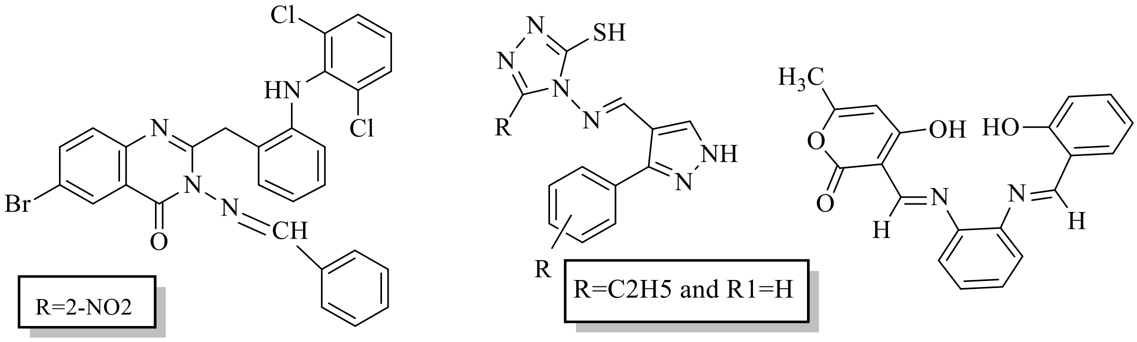


(16-17)

Figure 5. *Anti-fungal Schiff bases* ***(13-17)***

Antibacterial activity of Schiff bases

Antibacterial Schiff bases are Schiff bases that combat bacterial infections. A variety of bacterial species are tested to determine the antibacterial activity of Schiff bases [2]. The antibacterial activity of Schiff bases is associated with interactions with bacterial cell membranes, suppression of bacterial growth, disruption of bacterial DNA and enzymes [34, 37]. The nitrogen rich Schiff base species (**18-20**) have antibacterial action against *Pseudomonas aeruginosa, Bacillus subtilis* and *Staphylococcus aureus* as well as against gram positive and gram negative bacteria [38-40] (shown in **Figure 6**).



(18) **(19)** **(20)**

Figure 6. A**nti-bacterial Schiff bases** (18-20)

Vanillin Schiff bases

Schiff base chelates are made from vanillin a naturally occurring dietary ingredient present in plants. [41]. A phenolic chemical vanillin is a member of the 3-methoxy-4-methoxybenzaldehyde class. Ether, aldehyde and phenol make up its functional group [42]. Vanillin with its strong milky scent and vanilla bean aroma is an essential ingredient in many foods, beverages, medications and cosmetic products [43]. Biologically vanillin is an organic molecule with numerous uses including antiviral, antifungal, anticancer, antidepressant and anti-inflammatory properties [41] (shown in **Figure 7**).

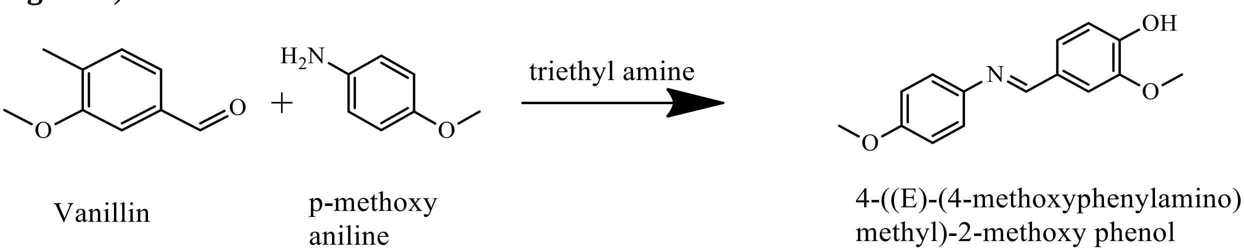


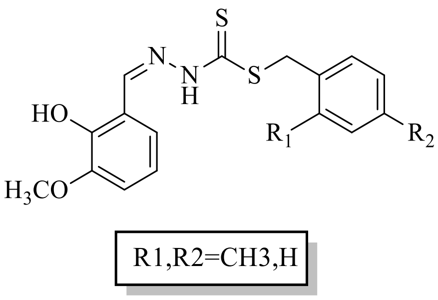
Figure 7. Synthesis of vanillin Schiff bases

Biological application of vanillin Schiff bases

The broad pharmacological and biological properties of vanillin based Schiff bases make them useful in a wide range of biological applications across multiple fields. Several uses for Schiff based on vanillin include

Antioxidant activity of vanillin Schiff bases

Vanillin has a phenolic group. Schiff bases based on vanillin have strong antioxidant a ctivity they can prevent oxidative cellular and tissue damage and neutralize free radica ls [44]. Antioxidant activity has been assessed using vanillin Schiff bases with thioamide and hydrazide moieties (**21-23**) [45-47] (shown in **Figure 8**).



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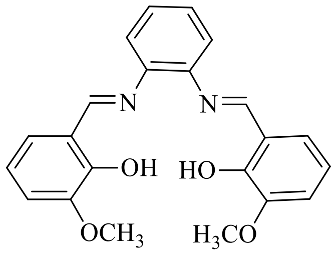

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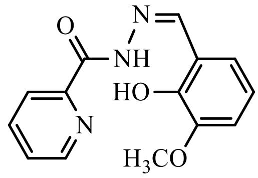

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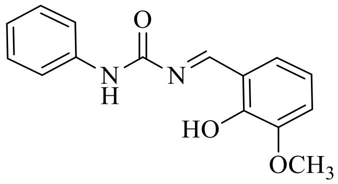
Figure 8. **Anti-oxidant vanillin based Schiff bases** (21-23)

Anticancer activity of vanillin Schiff bases

By inducing apoptosis and inhibiting the growth of cancer cells the vanillin Schiff base has shown strong anticancer efficacy [48, 49]. When tested on the murine melanoma cell line B16F10, compound (**24**) and (**25**) exhibit minimal cytotoxicity against HeLa. When tested against human colon cancer cell (HCT-116) and breast cancer cell line (MCF-7) compound (**26**) exhibits minimal cytotoxicity. [19, 20, 50, 51] (shown in **Figure 9**).



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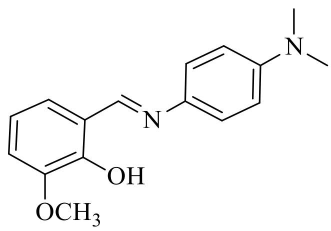

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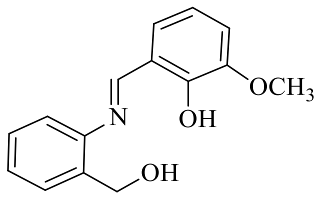

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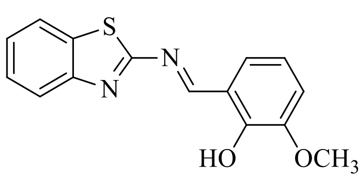
Figure 9. **Anti-cancer vanillin based Schiff bases** (24-26)

Antifungal activity of vanillin Schiff bases

The ability of Schiff base vanillin to prevent the growth of fungal cell walls. These compounds further enhance their fungal efficacy by inhibiting both the fungal enzyme and the fungal DNA creation [45, 52]. Because of their antifungal properties it impair the integrity of the fungal membrane. *Candida albicans* is well inhibited by aniline, sulphonamide, and benzothiazol that contain vanillin Schiff bases (**27-29**) *[53-55]* (shown in **Figure 10**).



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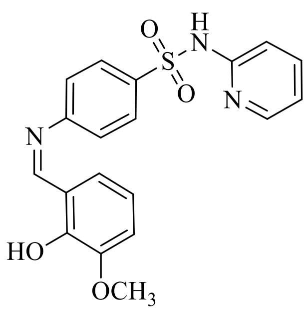

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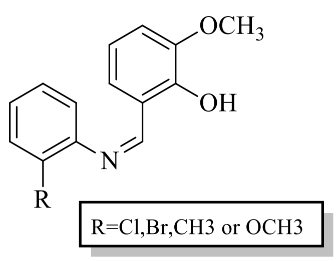

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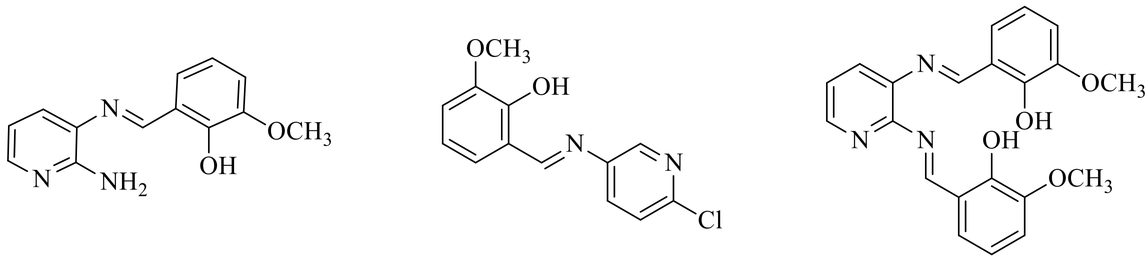
Figure 10. **Anti-fungal vanillin based Schiff bases compounds** (27-29)

Antibacterial activity of vanillin Schiff bases

The Schiff bases of vanillin exhibit strong antifungal action. Vanillin Schiff bases function by rupturing the bacterial cell membrane, which prevents the bacterial cells from proliferating and growing [49, 56]. It exhibits strong antifungal activity against *Escherichia coli* and *Pseudomonas aeruginosa* as well as other gram positive and gram negative bacteria [57, 58]. Schiff bases (**30-32**) found in amino pyridine and aniline exhibit antibacterial action against *Pseudomonas aeruginosa* [20, 59] (shown in **Figure 11**)



(30) **(31)** **(32)**

Figure 11. **Anti-bacterial vanillin based Schiff bases** (30-32)

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