



Analyzing the Effects of Schiff Bases on Antidepressant Use

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Abstract: Schiff bases play a major role in pharmaceutical, analytical, biochemistry, organic, and inorganic. The reported pharmacological properties of Schiff bases includes analgesic, anti-microbial, anti-convulsant, anti-tumor, anti-tuberculosis, anti-inflammatory, anti-fungal, anthelmintic, anti-glycation, anti-histaminic, anti-oxidant and anti-viral etc. depending upon the type of substituents present there. Due to the presence of –CH=N– in its structure, Schiff bases have potential to be effective against depression. The various derivatives of Schiff bases are synthesized that may have different method of preparation, mechanism of action, lesser toxic effects, more therapeutically active, more potent from the conventional antidepressants.

Keywords: Schiff bases, Imines, Carbonyl compounds, Pharmacological properties, Depressive disorder.

Introduction: Schiff base, named after Hugo Schiff, is a compound having a carbon-nitrogen double bond in its structure. Irfan Mustaq et al (2024) reported that Schiff bases are the resultant products procured by the reaction between amines and carbonyl compounds (Aldehyde/Ketone) (Dubey S.N. et al 2015).

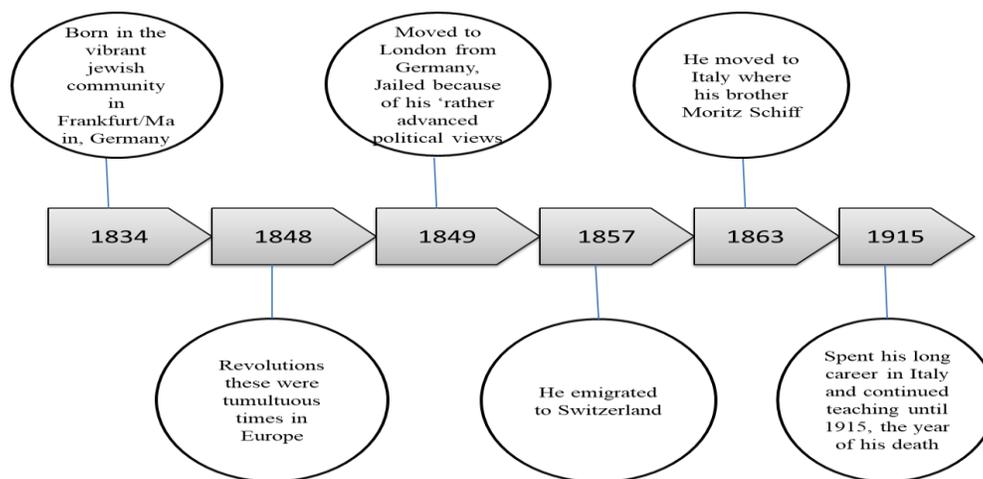


Figure 1: Introduction of Hugo Schiff

Depression is characterized by loss of pleasure or interest in almost everything for long period of time. Depression is also called as depressive disorder (Kennis M et al 2020). Suma P. et al (2023) revealed that chemically depression occurs due to the decrease in the level of serotonin (Demasi M et al 2020). Joanna Moncrieff et al (2022) reported the formation of SSRI antidepressants that first manufactured in 1990s and used for the treatment of depression (Amidfar M et al 2018). The underlying topic in depression theory nowadays is chemical imbalance and the chemical involved for the occurrence of depression is serotonin (Sadock BJ et al 2017).

Jacqui Wise et al (2023) reported that Serotonin is a neurotransmitter, having chemical formula $C_{10}H_{12}N_2O_2$, which regulates number of activities like mood, memory and gastrointestinal homeostasis (Yohn CN et al 2017). Omar A. Bamalan et al (2023) revealed Serotonin is synthesized in the raphe nuclei of the brainstem and the enterochromaffin cells (Healy D 2015). Other names of Serotonin:

- 5-HT
- 5-hydroxytryptamine
- 3-(2-aminoethyl)indol-5-ol
- Enteramine
- Thrombocytin
- Thrombotonin

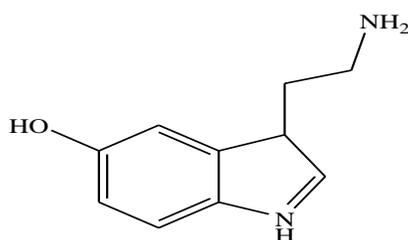
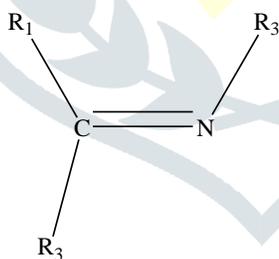


Figure 2: Chemical structure of Serotonin

From the past review studies, Schiff bases have been estimated for having its potential to treat depression. Azadeh Mesripour et al (2023) reported that N-benzylated/N-alkylated isatin derivatives bearing Schiff bases exhibit antidepressant activity. Maria Sadia et al (2021) revealed that Schiff base ligand L [1(pyridine-2-ylimino) methyl] naphthalene-2-ol] exhibit comparable results with Diazepam, against depression, because of presence of azomethine group in its structure. Ayodele Temidayo Odularu et al (2023) reported the drawbacks of synthesizing Schiff bases against depression are that synthesizing Schiff bases are time consuming process and gives small yield of product, economically high as compared to conventional process, not all materials are thermoliable, all these problems needs to be resolved.

There are number of serious adverse effects of traditional antidepressant medications have been reported in 2020 like decreased alertness, antimuscarinic effects, neuroleptic malignant syndrome, mania, suicidal feelings, gastrointestinal bleeding, erectile dysfunction, serotonin syndrome, sexual problems, SIADH (Syndrome of Inappropriate Antidiuretic Hormone Secretion), coma (loss of consciousness), diabetes etc. that surely needs to be taken into consideration. This reported data shows an urgent need to develop new antidepressants that are more potent and less toxic.

Background on Schiff Bases: China Takeda et al (2023) revealed that Schiff bases were manufactured by Hugo Schiff in 1864, when he examined the reaction of substituted amines with substituted aldehyde (Chen J. et al 2015). Further Cherifa Boulechfar et al (2023) added, that Schiff bases which involves the use of aromatic amines and aromatic aldehydes gives secured and productive results (Mahmood WH et al 2016).



R1, R2 and R3= alkyl or aryl

Figure 3: General structure of Schiff base

Applications of Schiff bases: Schiff bases have number of applications in field of dye industry, analytical chemistry, catalysis, etc.

- **Catalysis:** Schiff bases act as catalyst as they catalyse the number of reactions like polymerization, oxidation, Michael addition reaction etc (Hassan AS et al 2018). Sadia Afrin Dalia et al. (2018) reported that Schiff bases and their metal complexes have been known to act as efficient catalysts in various synthesis and other useful reactions. Schiff base complexes of palladium and ruthenium are used as catalyst in the synthetic reaction of polymers (Rao SN et al. 2007, Jammi S et al. 2008). Gupta and Sutar reported the catalytic activities of transition metal complexes. Schiff bases are reported to catalyze the reactions like hydrogenation, polymerization, oxidation and other coupling reactions etc (Tahmeena khan et al. 2015, Che CM et al. 2003). Vijay Kumar Juyal et al. (2023) reported all the catalytic applications of Schiff bases in different chemical reactions. Schiff base complexes of V(IV), Mn(II), Ni(II) and Mo(IV) are used as catalysts against the epoxidation of alkenes. Whereas Mn(II) and Cu(II) complexes are used to catalyze Henry reaction and Michael reaction is catalyzed by Co(II) complexes. Zn(II) and Ru(II) Schiff base complexes are required to catalyze the cyclopropanation reaction and Pd(II) are used for oxidation of thioanisole. Reactions like Aldol condensation, Carbonylation, Epoxidation reactions, Diels Alder reaction, Hydroformylation, Hydrosilylation, Heck reaction, Henry reaction, Allylic alkylation, Oxidation and Reduction reactions Homogenous and Heterogenous reactions etc (Vijay Kumar Juyal et al. 2023).
- **Food industry:** As Schiff bases are antimicrobial in nature; they prevent the growth of micro-organisms so they can also be used in food packaging films to preserve the food products. Ramhari meena et al. (2022) reported that Chitosan-derived Schiff bases films not only enhance the safety of foods but also lengthen their shelf life. Schiff's base modified zirconium dioxide reinforced PLA bio-composite film is reported as alternative packaging film to displace the synthetic manufactured materials that pollute our surroundings (Natesan S et al. 2022, Mr SN et al. 2021). Schiff's base (SB) modified polylactic acid (PLA) film provide improved antimicrobial, antifungal qualities (Singh S et al 2021).
- **Analytical chemistry:** Schiff bases have its applications in field of analytical chemistry, for the analysis purpose, such as in UV-Visible spectroscopy, as spectrometric reagent, in Fluorimetry etc. (Oiyee EN et al 2019). Schiff bases have been reported to be used as analytical probes. They are used to analyze carbonyl compounds, amines and functional groups. In case of complexes, azomethine bonds are formed during complex formation. Thus changes take place in their spectroscopic properties. Schiff bases are highly known for their chelating properties. N,N-bis(3-methylsalicylidene)-ortho-phenylene diamine, Schiff base that is reported useful in the spectrophotometric detection of nickel. Schiff base are reported to be helpful in the quantification analysis of nickel in natural food samples. Schiff bases are highly used as analytical reagents due to their chelating property. Schiff bases made of salicylaldehyde are used in spectrophotometric analysis and this reagent is also reported to be used for the spectrophotometric detection of Ni(II). Also 4-(1-phenyl-1-methylcyclobutane-3-yl)-2-(2-hydroxy-5-bromobenzylidene)aminothiazole Schiff base is used to detect Cu²⁺ ions. Md. Hasibul Islam et al. (2024)

reported that Schiff bases coordinate with metal ion, thus their fluorescent properties changes and can be used for detection of metal ions in sample. Because of changes in pH Schiff base undergo protonation or deprotonation. Their fluorescent properties change and can be used for pH sensing applications. Schiff bases are reported to be able for detection of biological entities in sample. Schiff base probes are also used for environmental monitoring (Aksuner N et al. 2009, Kumar J et al. 2015).

- **Agrochemical industry:** Schiff bases are used as pesticidal, insecticidal in field of agrochemical industry (Kazemnejadi M et al 2017). Schiff base and their metal complexes are used widely in field of agrochemical industry because of their applications as pesticidal, insecticidal and nematicidal. Faeza Alkorbi et al. (2024) reported the synthesis of indole derivatives that are 4-((2-Oxo-1,2-dihydro-3H-indol-3-ylidene)hydrazono)methyl}phenyl 4-methylbenzenesulfonate, 4-((1-Methyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)hydrazono)methyl}phenyl 4-methylbenzenesulfonate, 4-((5-Chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)hydrazono)methyl}phenyl 4-methylbenzenesulfonate, 4-((5-Chloro-1-methyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)hydrazono)methyl}phenyl 4-methylbenzenesulfonate, 4-[[[(3-Oxo-3,4-dihydroquinoxalin-2-yl)carbonyl] hydrazono}methyl]phenyl 4-methylbenzenesulfonate, 4-[[[(1-Methyl-3-oxo-3,4-dihydroquinoxalin-2-yl)carbonyl]hydrazono}methyl]phenyl 4-methylbenzenesulfonate. After synthesis, compounds were tested for its potential as insecticidal. The tested data revealed that all of the synthesized compounds exhibited strong to moderate insecticidal activity (Elkanzi et al. 2023, Abd El-Lateef et al. 2023, Abd El-Lateef et al. 2024).
- **Environmental applications:** Schiff bases also used to identify the metals present in water, plants, soil etc. that can be harmful for biological system. Most of the firms need metals like copper, aluminium, cobalt and silver etc. So there are high chances that these metals can be present in all nearby environmental sources and dairy products. Schiff bases control the quality of sources present in environment (Sakthivel A et al 2020). As Schiff bases have ability to form complex with metal ions. Due to this property, Schiff bases are also used for wastewater treatment. Schiff bases form complex with heavy metal contaminants and does helpful in the removal of any contaminants from sample (Farg AA et al. 2022, Paul A et al. 2022).
- **Dye industry:** Schiff bases are also considered helpful in field of dye industry. (Fatima B et al 2020). Transition metal complexes such as iron (III), nickel (II), cobalt (II) and copper complexes are reported to be prepared as dyes from a variety of Schiff bases. These dyes are also used by textile industries for coloring purposes. Md. Hasibul Islam et al. (2024) reported that Schiff base's dyes can act as sensitizers DSSCs, absorbing light across a broad spectrum of wavelengths. The imine linkage in Schiff base dyes provides a pathway for efficient electron transport, contributing to the generation of a photocurrent in the solar cell. Schiff base dyes can also increase the stability and durability of DSSCs, ensuring prolonged and efficient performance under varying environmental conditions.

- **Biologically active:** Schiff bases are biologically active as they exhibit number of properties like anti-microbial, anti-tumor and so on.

Lijie Wei et al. (2021) reported the synthesis of chitosan derivatives bearing active halogenated aromatic imines via Schiff bases. The antifungal activity against three common plant pathogenic fungi, including *Botrytis cinera*, *Fusarium oxysporum* f. sp. *Cucumerinum* and *Fusarium oxysporum* f. sp. *niveum* was reported. The results showed that double Schiff bases of chitosan derivatives exhibited enhanced antifungal activity compared with chitosan, especially at 1.0mg/ml.

Cristian Cezar Login et al. (2019) reported the synthesis of Schiff base 4-(3-bromobenzylideneamino)-5-(4-methyl-2-phenylthiazole-5-yl)4H-1,2,4-triazole-3-thiol. Further the antibacterial and antifungal ability of the Schiff base was evaluated against Gram-positive and Gram-negative bacteria and against three *Candida* strains. Schiff base showed good antibacterial activity against *L. monocytogenes* and *P. aeruginosa*; it was reported two times more active than ciprofloxacin. Anti-*Candida* activity was twofold higher compared with that of fluconazole. The effect of the Schiff base on cell viability was evaluated by colorimetric measurement on cell cultures exposed to various Schiff base concentrations. The data revealed that the newly synthesized Schiff base had antibacterial activity, especially on Gram negative *P. aeruginosa*, and antifungal activity.

- **Biosensing applications:** Schiff bases have been used as biosensor to detect the presence of particular hormone, enzyme that can further develop disease condition (Krishan U et al 2022). Sheta et al. created an ultrasensitive method of detecting human creatinine using a cerium (III)-isatin Schiff base complex as an optical sensor (Sheta SM et al. 2020). Schiff base compounds are reported to be used as biosensors for H_2O_2 , glucose and Oncomarker CA-125. Evaluation of the sensitivity and specificity of the gold Schiff base complex-doped sol gel nano optical sensor for the detection of CA-125 in ovarian cancer patient sample was performed (Abou-Omar MN et al. 2020).
- **Chemo-sensing:** Schiff bases can also be used to detect the presence of hazardous chemicals or analytes in our biological system (Bharali B et al 2020). It is reported that Schiff base compounds with nitrogen-oxygen-rich coordination as a receptor site provide a stable platform for fluorescence. Nowadays detection of metal ions in a sample by the use of Schiff base-based sensors is taking attention. Schiff base probes based on fluorescence live-cell imaging have been reported to detect metal ions like Hg^{2+} , Al^{3+} , Co^{2+} , Cu^{2+} , Ag^+ etc (Yuan C et al. 2016).

Senthil Kumar Raju et al (2022) reported that Schiff bases are known for having number of applications especially in field of its biomedical applications like anti-microbial activity, anti-tumor activity, anti-oxidant activity, anti-fungal activity, anti-viral activity, anthelminthic etc. From the review studies, Schiff bases have been estimated to be potent anti-depressants.

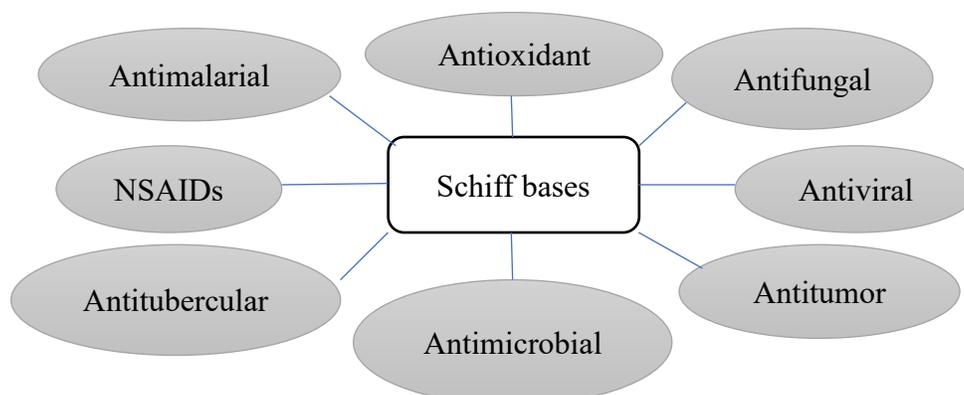


Figure 4: Pharmacological Profile of Schiff bases

Effect of Schiff bases on biological system:

- 1) **Inhibition of cell wall of microorganisms:** Schiff bases are involved in the inhibition of cell wall synthesis of microorganisms. So Schiff bases can also be said as antimicrobial for having its potential against microorganisms. An antimicrobial is an agent that kills microorganisms or stops their growth. One of the most discussed issues in antibiotic therapy is resistance. There are number of reasons for the antibiotic resistance. Schiff bases are reported for having anti-microbial activity. Schiff bases having anti-microbial property are prepared by the direct condensation of isatin and amino acids. For example, Macrocyclic Schiff bases are considered having anti-microbial activity

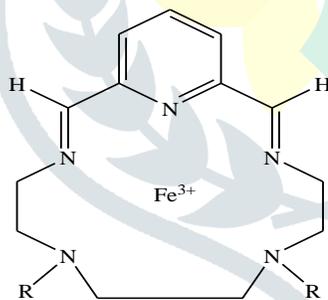


Figure 5: Schiff base having anti-microbial activity

- 2) **Reduction of free radicals:** Free radicals are highly unstable and highly reactive molecules. Free radical damage is responsible for oxidative stress and may lead to damage at cellular molecular levels. So it becomes necessary to aprevent the formation of free radicals in biological system as it can cause damage and further responsible for cancer. Schiff bases are reported to prevent or reduce the growth of free radicals, so they are also used as antioxidant. Antioxidants are the group of agents that avoids the formation of free radicals. Antioxidants restrict the growth of cancerous cells to avoid cancer.

Antioxidants also restrict the growth of micro-organisms, so can also be used as packaging films for various food products to protect them from any kind of micro-organism. As the name suggests, Antioxidants prevents the oxidation process (Hassan AS et al 2018).

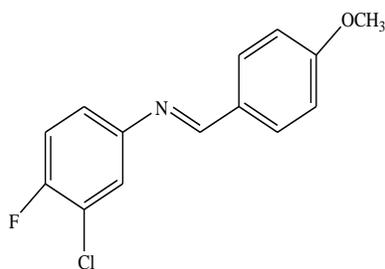


Figure 6: Schiff base having anti-oxidant property

- 3) **Inhibit the growth of malaria parasite in liver and red blood cells:** Schiff bases are reported to interfere with the growth cycle of malaria parasite thus inhibit the development of malaria in an individual. Thus Schiff bases are also categorized under anti-malarial medication. Anti-malarial drugs are used for the treatment and prevention of malarial infection. Schiff bases are said to be effective against malaria. Malaria is an infectious disease caused by plasmodium species and transmitted by the bite of infected mosquitoes. Malaria spread through the bite of infected female mosquitoes i.e. Anopheles. Plasmodium species causing malaria are: P. Vivax, P. Ovale, P. Malariae, P. Falciparum, P. Knowlesi (Ragi K et al 2017).

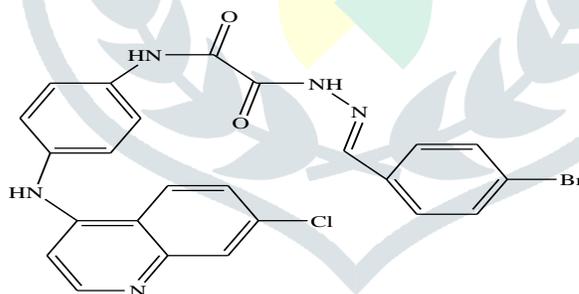


Figure 7: Schiff base having anti-malarial activity

- 4) **Increase sodium excretion:** There is a condition when pressure on the blood vessels is increased, then that is called as hypertension. It can occur because of various reasons and one of them is too much salt in diet, which further increase the uptake of water which further leads to increased blood volume. To resolve this problem, one of the solutions is increased sodium excretion from body. Schiff bases are found to be responsible for increased sodium excretion and thus regarded as antihypertensive. Anti-

hypertensives are drugs that are used to cure hypertension. Hypertension is a condition in which the force of the blood against the artery walls is too high i.e. above 120/80 mmHg. Schiff bases are also reported for having anti-depressant activity (Rawat A et al 2022).

- 5) **Apoptosis of abnormal cells:** Schiff bases causes apoptosis. Apoptosis is a type of cell death which is useful to get rid of the abnormal or unnecessary cells that can further cause cancer. Cancer is disease primarily caused due to the abnormal growth of cells. Usually, when cells grow old, they become damaged, they die and new cells take place. But sometimes, cells start growing abnormally and unusually and these cells causes cancer. Drugs to treat cancer are called anti-cancer drugs. Nilotinib and Capacitabine are reported as anti-cancerous Schiff bases (Alshaheri AA et al 2017).

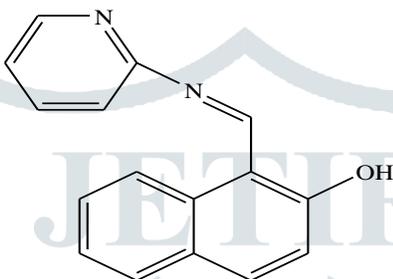


Figure 8: Schiff base having anti-cancer activity

- 6) **Inhibition of ergosterol synthesis:** Ergosterol serves as an important structural role in in the cell membrane of fungi. To kill or stop the growth of fungi first we need to disrupt its cell membrane by inhibiting the growth of ergosterol. Schiff bases that inhibit the ergosterol synthesis, comes under anti-fungal category. Anti-fungal drugs are the type of drugs used to treat infections caused by fungus. A fungus that invades the tissue can cause a disease that is confined to the skin, spreads into tissue, organs or whole body. Drugs like Fluconazole, Itraconzole are considered effective against fungal infection.

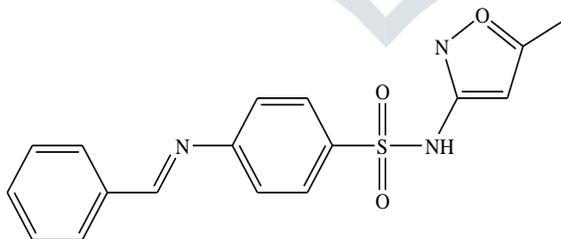


Figure 9: Schiff base having anti-fungal activity

- 7) **Inhibition of cholinesterase:** Cholinesterase is a family of enzymes present in the central nervous system, particularly in nervous tissue, which catalyzes the hydrolysis of the neurotransmitter acetylcholine into choline and acetic acid. Inhibition of cholinesterase is necessary to decrease the breakdown of acetylcholine. This increases the amount and duration of acetylcholine in the synaptic cleft that can bind to muscarinic receptors, nicotinic receptors and others. Due to its effect as anticholinesterase, Schiff bases can also be used as anti-alzheimer. Anti-alzheimer drugs are the drugs that are used to treat Alzheimer. Alzheimer is a condition that causes a steady decline in memory and thinking. In this disease, basically brain cell connections degenerate and die, leading to the loss of memory. This can be due to various reasons like lifestyle, genetic cause, diet and environmental factors etc. Schiff bases that are synthesized by direct condensation of amines and aldehydes exhibit anti-alzheimer activity (Iacopetta D et al 2020).

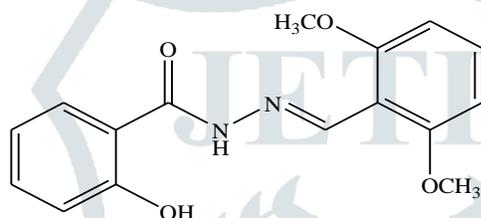


Figure 10: Schiff base having anti-alzheimer activity

- 8) **Increase the cell permeability towards ions:** This has been reported that Schiff bases increase the permeability of the membrane of schistosome cells towards calcium ions, so Schiff bases can also be used as anti-schistosomal. Anti-schistosomal is the type of drugs that are used to treat the condition schistosomiasis. Schistosomiasis is a disease caused by parasitic worms. Schistosomiasis is also called as bilharzia. Schistosomiasis is a parasitic disease caused by blood flukes (trematode worms) of the genus Schistosoma. Schiff bases are also reported to treat Schistosoma (Amorim CA et al 2020).
- 9) **Interference with viral DNA synthesis:** Schiff bases are considered anti-viral as they are reported of inhibiting the DNA synthesis of virus. Anti-viral drugs are used to cure viral infections. A virus is an infectious agent that replicates only inside the living cells. Schiff bases derivatives that are aminophenoxy ethane are considered as anti-viral drugs (Asfandiyarova NS et al 2020).
- 10) **Binding to parasitic muscle cells:** Schiff bases bind to nerve and muscle cells causing paralysis and death of the parasite, called anthelmintic activity. Anthelmintics are the drugs used to treat worm infections. Schiff bases are reported for having anthelmintic activity.
- 11) **Opening of Chloride channel:** Schiff bases are responsible to increase the duration of time for opening of chloride channels that leads to depressing of central nervous system. Anti-epileptic drugs are the drugs used to treat epilepsy. Epilepsy is a disorder in which nerve cell activity in the brain gets disturbed. Epilepsy can occur due to brain injury, genetic cause etc (Adebayo JO et al 2020).

12) **Inhibition of CoX enzyme:** CoX stands for cyclooxygenase. Schiff base inhibit CoX. Cyclooxygenase is required to convert arachidonic acid into thromboxanes, prostaglandins and prostacyclins. Prostaglandins are hormones-like substances that affect several body functions and one of them is inflammation. So because of inhibition of CoX by Schiff bases, anti-inflammatory activity is reported. Anti-inflammatory drugs used to cure inflammation. For this, traditionally, we use NSAIDs because of its activity against fever, pain and inflammation. NSAIDs can also be used to treat other syndromes like menstrual cramps, gout, arthritis, body pain etc. Schiff bases that are synthesized by direct condensation of aldehydes with pyrazole derivatives exhibit anti-inflammatory activity (Higuera L et al 2015).

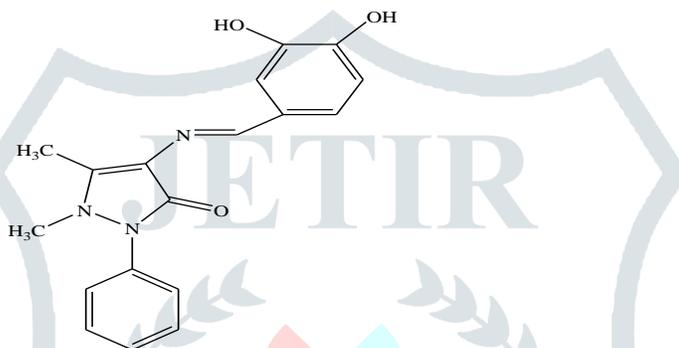


Figure 11: Schiff base having anti-inflammatory activity

Antidepressants and their Mechanisms: Antidepressant medications that are used conventionally are classified as:

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Tricyclic antidepressants (TCAs)
- Monoamine oxidase inhibitors (MAOIs)
- Atypical antidepressants

Nancy Schimelpfening (2024) reported that Antidepressants work by altering the level of neurotransmitters like serotonin, dopamine, and norepinephrine. SSRIs antidepressants specifically work by preventing the reabsorption of neurotransmitters into the body. SNRIs work in a similar way to SSRIs except that they block the reuptake of both norepinephrine and serotonin. Whereas TCAs block the absorption of serotonin and nerve cells and MOAIs is responsible for breakdown of monoamines.

Potential side effects of conventional antidepressants are dry mouth, gastrointestinal issues, sexual dysfunction, irregular heart rhythm, nausea, drowsiness, fatigue, constipation, blurry vision, drowsiness, low blood pressure, seizures, weight gain and insomnia etc.

Interaction between Schiff Bases and Antidepressants:

Azadeh Mesripour et al. (2023) reported the antidepressant activity evaluation of isatin derivatives bearing Schiff bases. The synthesis was initiated by N-alkylation and N-benylation of isatin to give N-substituted isatins. The synthesis of 2-(Benzyloxy)benzohydrazide derivatives was done by treating methyl-2-hydroxybenzoate with benzyl bromide or 4-chlorobenzylbromide which was followed by a reaction with hydrazine hydrate to provide acid hydrazide derivatives. The final compounds were obtained by condensation of N-substituted isatins with 2-(benzyloxy) benzohydrazide derivatives as Schiff-base products. Further tests were performed for their antidepressant potential where it was reported that N-Benzylated-isatin and N-acetic acid ethyl ester-isatin derivatives showed more effective antidepressant activity compared with N-phenyl acetamide isatin derivatives.

Maria Sadia et al. (2021) reported the antidepressant activity evaluation of Schiff base ligand L [1(pyridine-2-ylimino)methyl)naphthalene-2-ol] against breast (MCF-7) cell lines. The Schiff base ligand was synthesized by reacting 2-hydroxy-1-naphthaldehyde with 2-amino-pyridine. Further tests were performed for their antidepressant activity evaluation. A dose dependent response was reported for the synthesized ligand when tested as antidepressant in elevated plus maze model. It was reported that synthesized ligand L exhibited good antidepressant activities and could be used as alternative drug to treat the related health complications.

Depression is a mental disorder that completely and negatively affects our daily life. Depression further causes feeling of persistent sadness and loss of interest in everything (APA 2024). The population suffering from depression doubles annually. Christopher H. van Dyck et al (2021) reported that depression is further associated with low levels of serotonin (as a result of tryptophan-depleted diet), and elevated amyloid-beta ($A\beta$) (Mackin R.S. et al 2021). High level of amyloid-beta (further causes amyloid angiopathy and inflammation) protein is reported as the cause for depression to occur in elder population. (Krell-Roesch J et al 2018, Donovan NJ et al 2018).

Speranta Avram et al (2021) revealed that depression nowadays is a center of interest in terms of its pathophysiology, diagnosis and its treatment (Weller J et al 2018). To cease the evolution of depressive disorder, treatments should be followed to interfere with the cause causing depression (Bordei AT et al 2019). Literature survey shows that there is relationship between amyloid-beta and depression in elderly patients (Fantoni E et al 2020). So for the treatment of high level of amyloid-beta, passive immunotherapy has also been evolved (Byman E et al 2018). Anti-amyloid treatment may work by three ways:

- By inhibiting the enzyme responsible for the production of $A\beta$, with the help of inhibitors.

- By γ -secretase inhibitors.
- By α -secretase activators.

In a literature survey, it has been reported that a person needs to try atleast four different treatments before depression can be truly considered treatment-resistant (Smitha Bhandari et al 2023). This clearly indicates that there are chances of synergistic effect which can occur due to administration of multiple medications at a time. This can lead to severe adverse effects for long term, suicidal thoughts and persistent depression. Schiff bases shows possibility to overcome the adverse effects (because of presence of azomethine group in its structure) exhibited due the intake of conventional anti-depressants.

Clinical Implications and Future Research: The common side effects exhibited by the utilization of traditional SSRIs antidepressant are swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs, severe muscle stiffness, loss of coordination, agitation, fever, diarrhea etc. The side effects of SNRIs antidepressant are difficulty in sleeping, feeling dizzy, dry mouth, blurred vision etc. The side effects of TCA antidepressant are urinary retention, tachycardia, delirium, acute angle glaucoma etc. The common side effects of MAOIs antidepressant are chills, overactive reflexes, cold sweats etc. There is review studies that states the adverse effects of traditional antidepressants can be lowered by the use of newly developed Schiff bases as antidepressant. There is also possibility that administration of Schiff bases with drugs that shows the synergistic effects against depression which can be resolved out only by incorporating Schiff bases into clinical practice.

Future work will entail a research to fully understand the potential of Schiff bases to treat depression. Also there is an urgent need to fully understand the pharmacokinetics and pharmacodynamics of Schiff bases. If we acknowledge the pharmacology of Schiff bases, we can easily recognize the outcomes of Schiff bases that can be affected due to the administration other medications and can cause synergistic and antagonistic effects. Synergistic effects refers to the interaction or cooperation of two or more organisms or substances to produce a combined effect greater than sum of their separate effects. Antagonistic effects refers to the interaction or cooperation of two or more organisms or substances to produce a combined effect lesser than the sum of their individual effects.

Conclusion: Schiff bases are the class of compounds that exhibits variety of pharmacological properties because of presence of $-\text{CH}=\text{N}-$ in its structure. This review concludes the Schiff bases for having its potential against depression. This review summarizes that there is need for continuous research and further development in the same area to completely acknowledge their mechanism of action and efficacy in different patient populations.

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