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Research Article

BIOLOGICAL ACTIVITY OF SCHIFF BASES

Yılmaz Onur YİĞİT and * Hülya ÇELİK

Ağrı Ibrahim Cecen University, Faculty of Pharmacy Basic Pharmaceutical Sciences Department / Fundamental Sciences of Pharmacy 03200 Agri/Turkey.

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ABSTRACT

Compounds containing an azomethine group obtained by condensation of a primary amine and an active carbonyl (CHO or RCOR) group are called "Schiff Base". Schiff bases constitute a special class of compounds used in organic chemistry, biochemistry, physical chemistry and coordination chemistry. In studies on Schiff bases and metal complexes, it has been determined that the synthesised compounds show many biological activities such as antibacterial, analgesic, antifungal, anticancer, anti-inflammatory, anti-HIV, antimalarial. These properties have increased the interest in Schiff bases and metal complexes and encouraged intensive studies on their biological activities. Schiff base and its derivatives are widely used in medicine and pharmacy. In line with these findings, it has been determined that Schiff base and its complexes show promising activity on biological systems. It is thought that they can be used as a lead and active compound for future drug design studies and will contribute to the literature knowledge.

Keywords: Schiff bases, biological activity, biological systems.

INTRODUCTION

Schiff Base

Schiff is a very important ligan in terms of some synthesis and chemical stability. Schiff bases are formed as a result of the condensation of primary amines and ketones or aldehydes. These compounds are named after Hugo Schiff, the scientist who invented them (Schiff 2011). Hugo Schiff first synthesized the compound in 1860. It was first used as a ligand by Pfeiffer in 1930.

Schiff bases can react with all metals in the lanthanide group as they are easy to pass. Examples of metals with which it reacts are Cu, Co, Fe, Zn, Ni, and Mn (Chowdury *et al.,*2014). The range of uses of metal compounds of the Schiff base is quite wide-ranging. The complex compounds made by the Schiff base with metals have a very important place in inorganic chemistry and bioorganic chemistry (Salvat *et al.,*2001). Due to the C=N bond in its structure, they biologically exhibit many properties such as antimicrobial, antimalarial, anticancer, antibacterial and antioxidant (Schiff 1864). Because of its multi-drug resistance and bad properties, efforts to integrate new and effective drugs against cancer and various microbes have challenged researchers. Among the compounds, Schiff bases are natural mixtures used for the arrangement of a large number of biological and industrial atoms. These mixtures are used in situations such as protein hydrolysis, DNA replication, and oxygen supplementation (Prasad *et al.,*2016) (Figure 1.1).

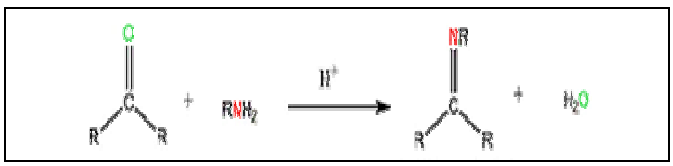

Figure 1.1 Some general reaction of Schiff

***Corresponding Author: Hülya ÇELİK,**
Ağrı Ibrahim Cecen University, Faculty of Pharmacy Basic Pharmaceutical Sciences Department / Fundamental Sciences of Pharmacy 03200 Agri/TURKEY.

Schiff bases are called imin or azotext because of the bond C = N. The proximity of the subatomic hydrogen bond and the harmony of a proton motion are justifiably described by their extraordinary physical and compound properties. Schiff bases, which occur with donor atoms such as N, O, and S, have been administered as drugs and studied to have a wide range of activities against certain types of tumors, fungi, bacteria, DNA binding and DNA cleavage activities. Aromatic primary amines may also contain additional donor functionalities. Apart from these donors, groups such as -Cl, -OH, -CH3, etc. that help to increase and regulate biological activities can be given as examples. Donors are also efficient chemicals for biological processes (Malik *et al.,*2017). Schiff bases can be defined as NO, ONO, N_2O_2, ONS, ON type ligands.

Schiff bases are important ligands with electron donor atoms in reactions. Due to its electronic and steric properties, it has properties such as dentition and chelation. In addition, it has multiplied research on the high effects of selectivity, superior catalytic effect and stability (Yoon *et al.,*2016).

Synthesis of Schiff Base

The synthesis of the Schiff base occurs in two steps, joining and leaving. In primary care, the primary amine acts as a nucleophile due to the only double atom on the nitrogen. This nucleophile opens the pi bond between carbon and oxygen and makes a nucleophilic attack on this bond. At the end of the attack, an unstable intermediate containing an acidic ammonium and a basic alkoxide anion is formed. This intermediate undergoes a rapid transfer of electrons from nitrogen to oxygen. These transfers form carbonylamines, a moderately stable intermediate. Carbonylamines amines are protonated and water outflow occurs. This step is called the joining reaction (Figure 1.2).

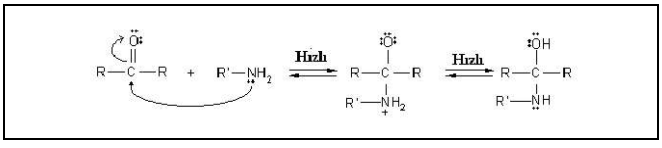

Figure1.2 Addition reaction of the Schiff base

In the second step, the separation step, the nitrogen and oxygen atom of the carbonylamine intermediate is slightly basic. A conjugated acid is formed by protonation of oxygen. Protonated carbonylamine contains water, which is a good separated group. Therefore, water is separated from the molecule. At the same time, a carbon-nitrogen π bond is formed using the unpaired electrons in the nitrogen. The resulting protonated Schiff base rapidly loses a proton, resulting in a Schiff base as the product of the reaction (Figure 1.3).

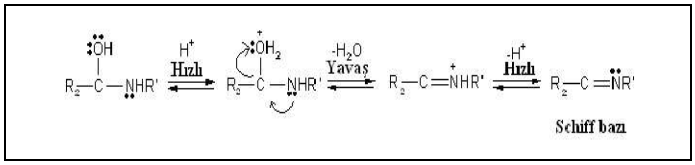

Figure 1.3 Separation reaction of the Schiff base

Since these reactions are pH-dependent reactions, pH has a very important place. If the acidity is elevated, it causes the separation events to speed up but the joining events to slow down. The optimum pH range is 3-5. This pH contains the desired sufficient level of amine (Fessender 2001).

GENERAL INFORMATION

2.1 Antibacterial Activity of Schiff Bases

2.1.1 Antibacterial property

The biggest reason for the increase in mortality rates due to infections is bacterial diseases. Effective treatments must be found to prevent these infections. At the beginning of these ways is the use of antibacterial agents. Antibacterial agents usually work by killing the bacterium or inhibiting the growth of the bacterium. In this context, Schiff bases have started to be seen as a very important antibacterial agent in recent years. Due to the chelation-forming properties of Schiff bases, it is easy for bacteria to pass through their cell membranes. This property increases the antibacterial property of Schiff bases (Biochem *et al.,* 2006). Schiff bases have a toxic effect on bacteria due to their lipophilic properties. The lipophilic property of Schiff bases, as well as their polar and polar properties, increase permeability through cells and tissues (Imran *et al.,*2007). In the synthesis of Schiff bases, many substances of natural or unnatural origin (amino acids, coumarins, sufonamides, bromocoumarins) are used to give antibacterial properties (Kulkarni *et al.,* 2009). A few examples are Schiff bases used as antibacterial agents.

2.1.2. Schiff bases with antibacterial action

Schiff base, derived from isoniazid, was found to have an effect on *M. tuberculosis* bacteria (Figure 2.1). Thus, it was used in tuberculosis disease. It has been found to bind selectively to bacteria and destroy them. The derived Schiff base has been found to be more potent and effective than normal isoniazid. In addition, no toxic effect of the Schiff base on epithelial cells has been observed. Thanks to its therapeutic and safety range, it has pioneered the discovery of many antibacterial agents (Hearn *et al.,*2004).

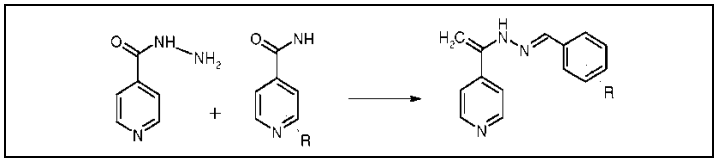

Figure 2.1 Isoniazide-derived Schiff base

It acts on many bacterial species of the Schiff base, which is formed by condensation of 5-chloro-salicylaldehyde and primary amine. The most affected type of bacteria *is Pseudomonas fluorescence*. This effect has been found to have the same effect as kanamycin. It has *been observed to act on* Bacillus subtilis, Staphylococcus aureus, Escherichia coli *bacteria depending on the MIC values (Shi et al.,* 2007).The Schiff base, derived from the compound 2,4-dichloro-5-fluorphenol, is known to inhibit bacterial growth. Examples of these bacteria are *S. aureus, E. coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* .

The Schiff base, derived from the 2-aminotiophenyl-4-bromosalisylataldehyde compound, has been observed to be effective against gram-negative and gram-positive bacteria. It has been found that the growth of bacteria inhibits the growth of bacteria by inhibiting the mechanism of synthesis of the peptidoglycan compound in the cell walls of bacteria (El Sherif *et al.,*2011).

Cellulose-based amino acid, Cu(II) cellulose fiber complex and Schiff some ligand-derived Schiff base were found. This complex compound *showed excellent efficacy on E. coli* and *S. aureus* bacteria. It has been observed that bacteria decrease as a result of contact with complex compounds. It was concluded that the cell structure of the bacteria was disrupted as a result of contact with Schiff Some (Xu *et al.,*2011).

The properties of the Schiff base on DNA and its antibacterial effect were studied. Complexes of Schiff base with 2-formilindole, salisaldehyde and N-amino rodanin were obtained (Figure 2.2). These complex compounds *have been determined to have antibacterial properties against* B. cerens E. coli, P. aeuroginosa S. aeurus bacteria (Raman *et al.,* 2011).

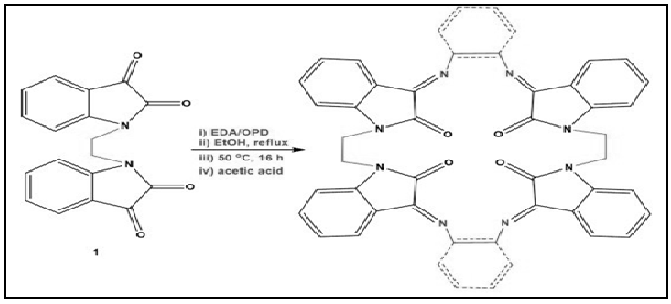

Figure 2.2 Indole-derived Schiff base

The compounds of Schiff base with 1,3,4-oxadiazoles, 1,3,4-oxadiazoles, sulfonamides, 5-imidazolinones, asomethanes, 4-thiazolidineones, 2-azetidiones, formazanes were examined (Figure 2.3). These compounds have been observed to act against *E. coli P. fluorescence B. mega B. subtilis* bacteria. It was also found to act against *A. awamori* bacteria in 50 mg/ml concentrate (Desai *et al.,* 2012).

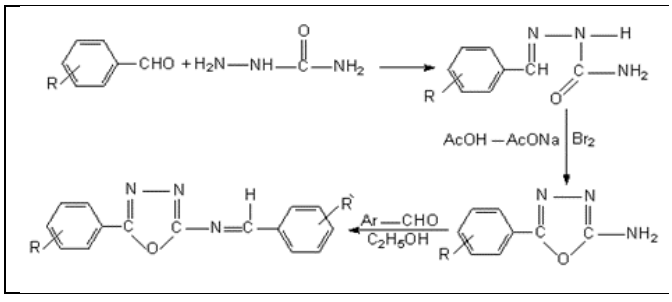

Figure 2.3 Oxadiazole-derived Schiff base

Copper(II), zinc(II), nickel(II), cobalt(II) complexes of Schiff's base consisting of 4-hydroxybenzaldehyde and L-alanine were synthesized. The antibecterial effects of Schiff base and metal complexes *against E. coli, S. aureus* and *P. aeruginosa* bacteria have been studied. As a result of this study, it was determined that the metal complexes of Schiff bases were more effective than Schiff bases (Chohan *et al.,* 2002).

Schiff's base was obtained as a result of the reaction of o-phenylenediamine and p-phenylenediamine with salicylaldehyde and 2-furaldehyde o-phenylenediamine and p-phenylenediamine (Figure 2.4). The antibacterial effects of the obtained ligands and metal complexes *against E. coli*, B. subtilis*, P. aereuguinosa*, S. aureus *bacteria, A. niger, A.* fluves*, C. albican, S.* cervisiea *bacteria were observed (Gaballa et al.,* 2007)

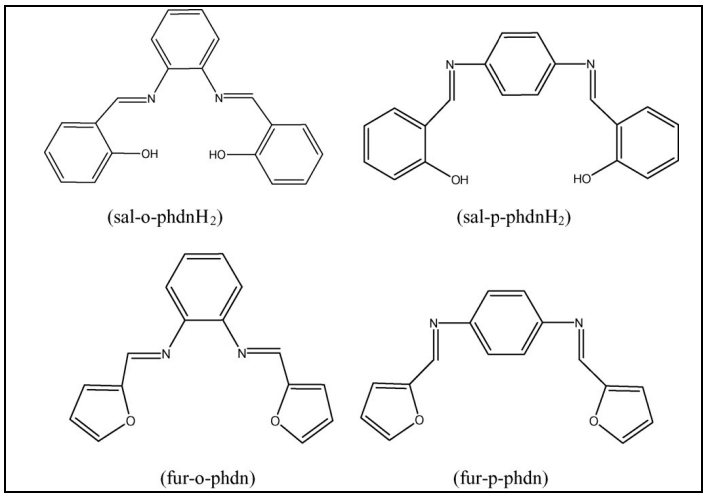

Figure 2.4 Phenylenediamine-derived Schiff base

Some Schiff bases that are 4-(4-aminophenyl)morpholine derivatives *have been found to have very good antimicrobial properties against* Staphylococcus aureus, *Staphylococcus epidermidis*, *Bacillus cereus*, *Micrococcus luteus* and *Escherichia coli bacteria (Pannerselvam et al.,* 2005).As a result of the reaction of 2-furancarboxyaldehyde and o-phenylenediamine, the reaction of 2-thiophencarboxyaldehyde and 2-aminotiophenol, Schiff bases and metal complexes were synthesized. The antimicrobial activity of synthesized Schiff bases and metal complexes *using Escherichia coli, Pseudomonas aeruginosa, Staphylococcus pyogones* bacteria was determined (Mohamed *et al.,* 2006).

2.2. Anticancer Activity of Schiff Bases

2.2.1. Anticancer property

The human body is in constant renewal. It regenerates old and dead cells. In the specified process, everything takes place within control. Some old cells do not die and continue to grow. These cells grow out of control and begin to grow very quickly, and this growth is called abnormal growth (Ronconi *et al.,* 2018). Genes that regulate cellular growth, reproduction, and cell turnover mutate and turn normal cells into cancerous cells (Hyndman *et al.,*2016). Such cells bypass cell checkpoints, escape apoptosis, produce larger populations, grow their mass, and begin to invade nearby and accessible tissues (Kim 2015). Cancer disease, which affects almost all body systems, organs and tissues except dead cells, is constantly detected in individuals of all age groups. After affecting a particular body part or system, the disease progresses to other parts of the body. Cancer can be effectively managed and treated if diagnosed early, but can be fatal if left undiagnosed and the disease progresses to the final stage (Virnig *et al.,*2009). Schiff ligands and their metal complexes show strong antitumor activity against human cancer cells. Their anticancer activity is due to their ability to break down DNA and get between DNA base pairs, so Schiff bases are also potential anticancer drugs. Schiff bases are versatile and flexible ligands that can combine various metals and thus are one of the most widely used ligand types in metal coordination chemistry in terms of forming complexes with common structure and properties. Therefore, Schiff bases are expected to be used as pioneering ligands for the rational design of novel metal complexes with antitumor activities (Obeid *et al*., 2017).

2.2.2 Schiff bases with anticancer action

Nanochitosan is a new type of nano-chitosan Schiff-based Cu with a particle size of 350 nm by combination of Cu and Schiff base. Nano-chitosan and their Schiff-based Cu complexes inhibited the in vitro growth of the liver cancer cell lines SMMC-7721. The rate of inhibition of Schiff-based Cu complexes was higher than that of nano-chitosan. Schiff base and nanochitosan combined with Cu have developed anticancer activities attributed to the synergistic effect between the chitosan matrix and the planar structure of Cu complexes (John *et al.,* 2007).

They synthesized 2-hydroxy-1-naphthaldehyde-derived Schiff base (Figure 2.5). Proliferative activity has been observed against the breast and lung cancer cell lines MCF-7 and H-460. Studies on growth inhibition caused by Schiff bases have shown that the amine group in the molecular structure of these compounds is responsible for the inhibitory effect on cell lines. As a result of the experiments, Schiff determined that some complex ligands had anticancer properties. (Sadi *et al.,*2002).

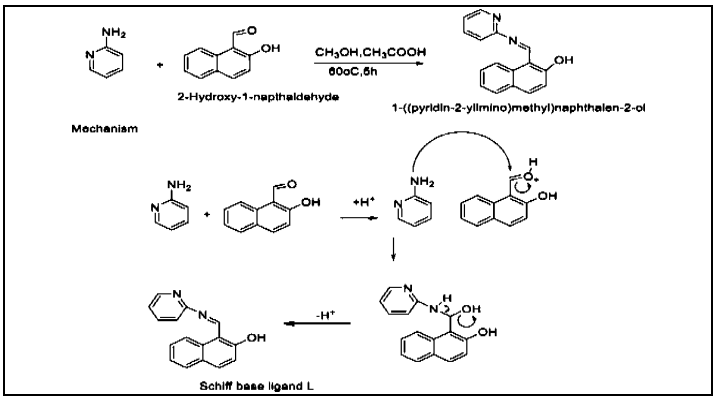

Figure 2.5 Naphthaldehyde-derived Schiff base

Schiff base was synthesized from the 2-acetylpyridine-L-tryptophan compound (Figure 2.6). Of these, the complex compound formed by the metals Cu, Cd and Zn has been observed to inhibit proteasome activity. This inhibition has also been found to affect the mechanism of apoptosis. It has been found to change the apoptic morphology of cells. It has been observed that Schiff bases can inhibit cell prophylation, but the most effective complex of these is the Schiff base, which contains the compound cadminium. It was found that complex compounds with cadium induced MDA-MB-231 cell apoptosis in breast cancer (Goldfarb *et al.,*1998).

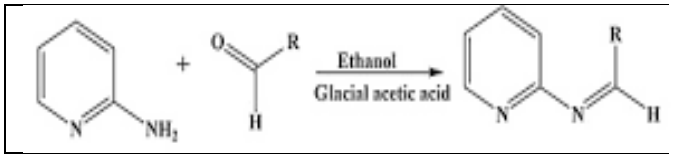

Figure 2.6 Acetylpyridine-derived Schiff base

A new schiff base was synthesized by condensation of glycinglisine and 4-nitrobenzaldehyde (Figure 2.7). The Schiff base has been determined to be effective against Cu and its complex compounds HCT116 and HeLa cells. It was found to affect the profileration against both cells. It has been observed that the complex obtained with Cu metal affects the oxidative stress mechanism of cancer cells. In addition to the Cu complex, complex compounds formed with the metals Co and Ni showed the same effects. Due to the uncoordinated bonds between carbonyl oxygen and hydrogen in the compounds, it has been found to reduce activity by adhering to the components of cancer cells and lead to the death of cancer cells, but noscopan has been less effective than anti-cancer drugs such as estramustine and etoposide (Aquirre *et al.,*2009).

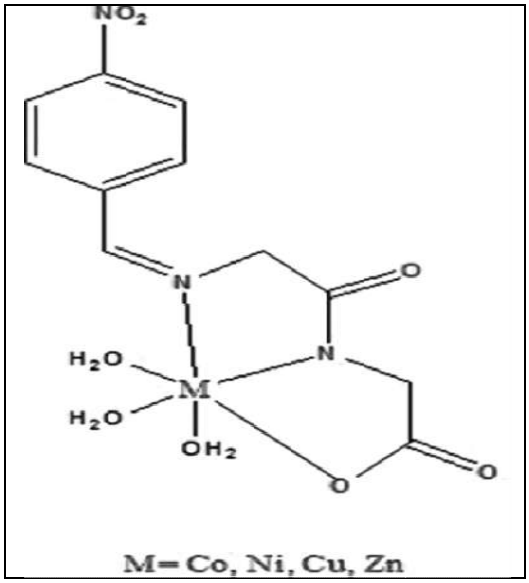

Figure 2.7 Glycinglysine derived Schiff base

The schiff base derived from 4-hydroxycoumarin has been found to stop the growth of cancerous cells. In particular, the complex compound formed with cis-platinum metal, one of the transition metals, has been very effective. The cis-platinum complex compound has played a very important role in testicular, ovarian, uterine and bladder cancer. It has also been observed to cause the death of cancer cells, but it has been shown to have toxic effects while killing cancer cells. It has been discovered that it has side effects such as vomiting, nausea, decrease in blood cell and platelet production. Although it has side effects, many Pt(II) complex compounds have been synthesized in this area. Complex compounds with palladium metal have been used in kidney toxicity. Although palladium and platinum complex compounds have similar effects, complex compounds with palladium have been found to be more effective (Nicholson *et al.,*2001)

2.3. Antimalarial Activity of Schiff Bases

2.3.1. Antimalarial effect

Malaria, also known as malaria, is a febrile disease caused by the plasmodium parasite. Approximately 500 million people are exposed to this disease every year, and close to 3 million of the patients exposed to the disease result in death. Children account for 90% of deaths. The biggest cause of death is negligence and wrong treatment methods. Malaria is seen in nearly 100 countries, the most important of which are Africa and Latin America. Malaria is caused by 4 types of plasmodium. These are P. *falciparum, P. vivax, P. ovale* and *P. malariae*, in addition the female anopheles mosquito can be seen as a vector (Bohac *et al.,*2007). Schiff bases have also been used as antimalarial agents because they act on these species.

2.3.2 Schiff bases with antimalarial action

The Schiff base was synthesized from the Ancistrocladadine compound obtained from the family Ancistrocladaceae and *Dioncophyllaceae* (Figure 2.8). This Schiff base has been determined to be effective against *the P. falciparum* parasite.

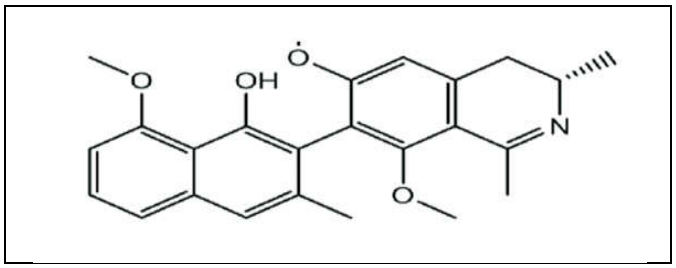

Figure 2.8 Ancistrocladine compound

They synthesized a Schiff base from 5-nitroisoquinoline (Figure 2.9). They observed that the schiff base they synthesized *acted in vitro against the parasite Plasmodium falciparum*. They found that this effect stopped the growth of the bacterium *Plasmodium falciparum* by almost 50% (Rathelot *et al.,* 2010).

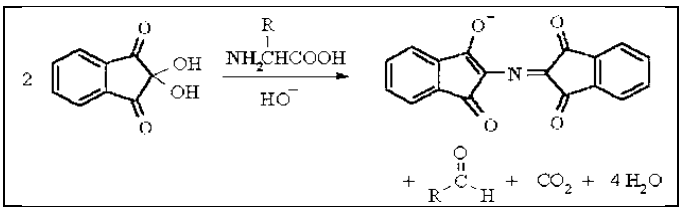

Figure 2.9 Isokinoline derived Schiff base

Hydrazine-derived Schiff bases have been found to have antimalarial effects (Figure 2.10). This schiff base has been observed to be highly effective compared to chloroquine compared to another chloroquine. When used in combination with sulfonamide-derived Schiff bases, it turned out to be a more effective antimalarial and potent inhibitor. It has been determined that the aromatic aldehyde group has an effect on the emergence of these properties.

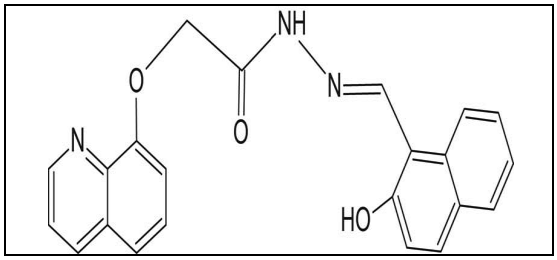

Figure 2.10 Hydrazine-derived Schiff base

2.4. Antioxidant Activity of Schiff Bases

2.4.1. Antioxidant property

Free radicals have a very important place in the human body because free radicals have the potential to disrupt the human body. The formation of free radicals causes the formation of chain reactions. Free radicals can disrupt the structure of matter by transferring electron pairs. The deteriorating substance can also disrupt the structure of other substances. As a result of these deteriorations, diseases such as cardiovascular, cancer, ulcers may occur in our

body. These harmful effects of free radicals are called oxidative stress. Antioxidants should be used to prevent these deteriorations and diseases. Antioxidants give free radicals electron pairs, preventing free radicals from disrupting the structure of substances. Schiff bases were thought to be a better antioxidant due to their chelating effect, so Schiff bases were used to produce antioxidants that were more effective than normal antioxidants. Some synthesized Schiff bases have been observed to be more effective.

2.4.2. Schiff bases with antioxidant action

Schiff base, derived from cinnamaldehyde, has been found to be a better antioxidant than normal cinnamaldehyde (Figure 2.11). The reasons for this situation have been shown such as significantly increasing the activity of hydroxyl groups at position 2 of the phenyl ring, which increases the chelating property of the phenyl ring, increasing the activity of the groups at position 3 that will contribute to the chelating structure in compounds with hydroxyl in position 2 of the phenyl ring, and electron donor groups in the phenyl ring showing better antioxidant properties than electron attracting groups (Imran *et al.,* 2005).

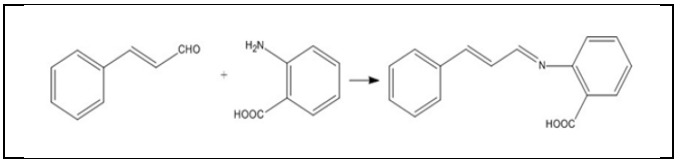

Figure 2.11 Cinnamaldehyde-derived Schiff base

Thiosemicarbazone-derived Schiff bases have been found to have a high antioxidant property (Figure 2.12). In particular, complex compounds formed by Cd (II) metal have been observed to cause oxidative stress, decrease in vitamin A and E levels, increase MDA levels and damage to testicular tissue. The Cu(II) complex has been found to have the same effects. Not all compounds caused any damage to tissues such as the kidneys, lungs and adren (Reina *et al.,* 2017).

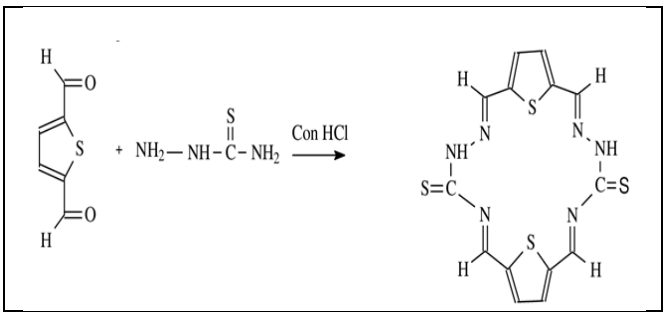

Figure 2.12 Thiasesemicarbazone-derived Schiff base

The antioxidant properties of spiro-izatin derivative Schiff bases have been determined (Figure 2.13). It has been found to eliminate free radicals. It has been established that this antioxidant property is due to a strong interaction between the anion radical and the strong oxygen bonds. Schiff base has proven to be more effective than standard ascorbic acid-derived Schiff bases (Güneşli *et al.,* 2018).

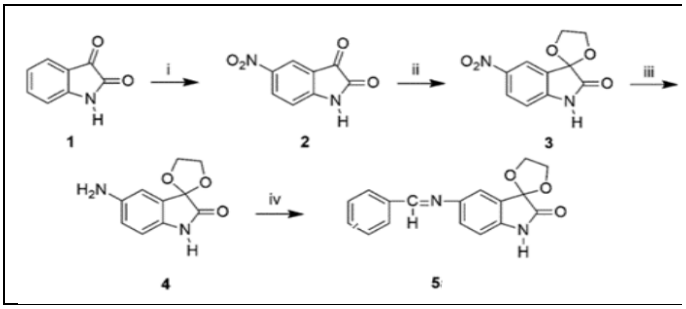

Figure 2.13 Spiroizatin-derived Schiff base

4-Methyleniminophenazone-derived Schiff bases have been found to have antioxidant properties (Figure 2.14). It has been observed that it is quite strong compared to other normal ligands in terms of its high affinity for binding to DNA and its ability to retain free radicals. It has also been found to be a highly successful Schiff base in removing the hydroxyl group from the environment. Thanks to these properties, it has been determined to be both a very good anticancer and antioxidant agent (Taha *et al.,* 2014).

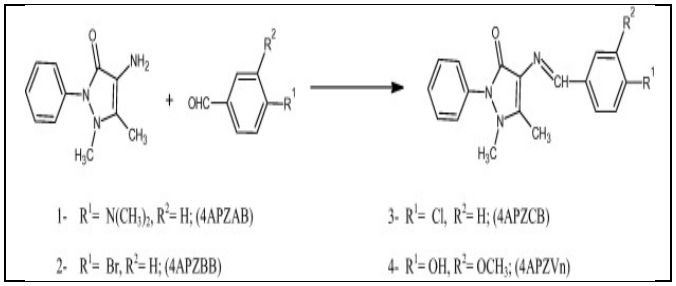

Figure 2.14 Methyleniminophenazone-derived Schiff base

2.5. Schiff Bazlarının Antifungal Aktivitesi

2.5.1. Antifungal property

Fungal infections caused by some types of fungi pose a constant and serious threat to human health. Approximately 1.5 million people worldwide die each year from fungal infections. It is most commonly seen in patients undergoing chemotherapy, weakened immune systems and organ transplantation.

2.5.2. Schiff bases with antifungal action

Schiff base, synthesized by glycine and 2,3-butanedione condensation, has been found to have an antifungal effect (Figure 2.15). Schiff base has been shown to be effective against the fungal species Candida *parapsilosis* and *Candida albicans*. It has been found that it inhibits the growth of this species.

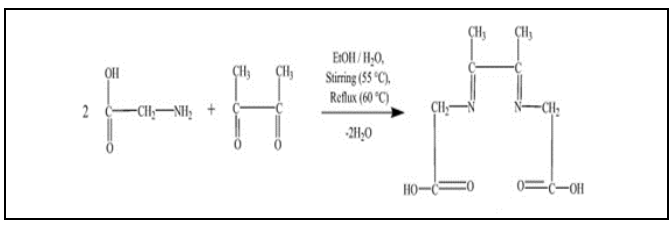

Figure 2.15 Glycine and benzadione derived Schiff base

Cinnamaldehyde-derived Schiff bases have been found to have antifungal effects (Figure 2.16). *It* turns out that it affects 4 species of fungi from the Cryptococcus family. Especially among these fungal *species, it has been noted to act on C. neoformans* and *C. gattii* species. The biggest reason for its antifungal effect is the presence of

the nitro group. It is known that this group changes its antifungal effect on the way it is attached. The absence of any toxicity in the kidneys and lungs has also shown to be a good antifungal agent (Kahraman *et al.,* 2010).

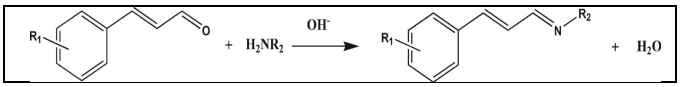

Figure 2.16 Cinnamaldehyde-derived Schiff base

Inulin-derived Schiff bases have been found to have antifungal effects (Figure 2.17). *It has been found to be effective against B. cinerea, F. oxysporum f. sp. cucumerium owen, F. oxysporum f. sp. niveum and P. asparagi fungi.* It has been determined that the effect of inulin-derived Schiff bases is higher than that of normal inulin. The location and shape of the substituents on some of Schiff's have been shown to be important in the antifungal effect. It has been observed that halogens enhance the antifungal effect. It is a Schiff base that also has an effect against fungi that affect the environment badly and is thus very important for environmental protection (Tripodo *et al.,* 2010).

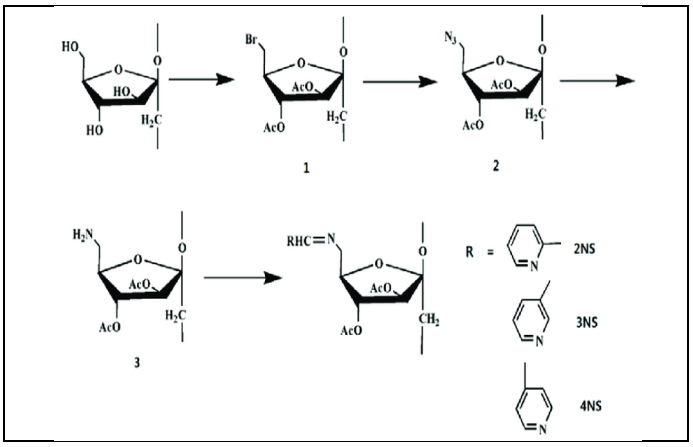

Figure 2.17 Inulin-derived Schiff base

1,2,4 – Triazole-derived Schiff bases have been shown to have antifungal effects (Figure 2.18). *Its effect against Pythium solani, Gibberlla nicotiancola, Fusarium oxysporium f. sp. niveum, Gibberlla saubinetii* and *Alternaria iycopersici* fungal species has been found to be over 50%. *Phytophthora capsici, Physalospora piricola, Cercospora arachidicola hori* and *Fusarium oxysporium f. sp. Cucumber have* been found to have weak effects against fungal species. The type of fungus with which it acts best is *Alternaria iycopersici*. These effects have shown to be a good antifungal agent (Jasmine *et al.,* 2010).

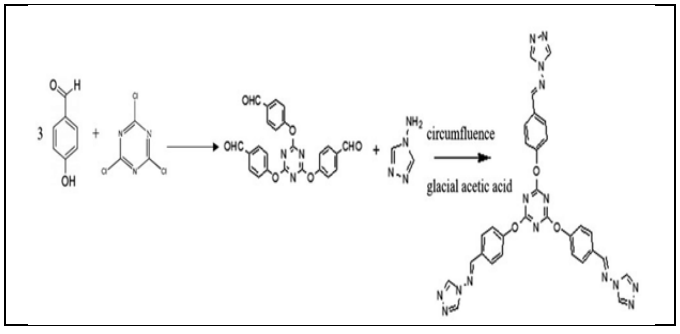

Figure 2.18 Triazole-derived Schiff base

The N-2-aminotiophenol derivative Schiff bases have been shown to have antifungal effects. *It has appeared to have an effect on C. albicans, A. niger* mushroom species. The complex compounds formed by Co(II), Cu(II) and Zn(II) metals were also effective on fungal species. It has been determined that its antifungal property is due to the imin group and metals. The most effective complex compound is the Schiff base, which is formed by the metal Cu(II) (Jin *et al.,* 2008).

The antifungal effect of Schiff base, synthesized by condensation of 1,2-diaminoethane and creatinine, has been identified (Figure 2.19). Complex compound formed by the synthesized Schiff base with Co(II) and Cu(II) metals *Aspergillus niger* and *Candida albicans* It has been observed to act on fungal species. Schiff bases formed with metals have been found to be more effective than normal Schiff bases (Venkittapuram *et al.,* 2011).

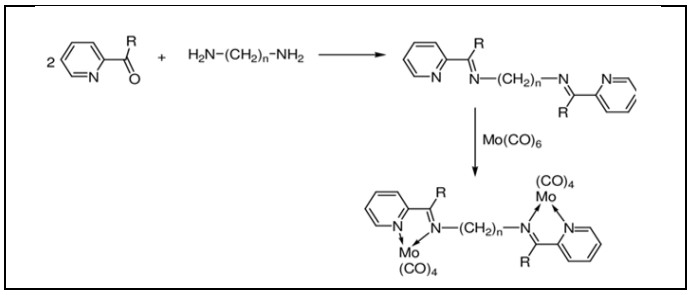

Figure 2.19 Diaminoethane and creatine-derived Schiff base

CONCLUSION

In this study, Schiff bases and their antimicrobial, antimalarial, anticancer, antifungal and antioxidant properties were investigated. With the developing technology, Schiff bases are expected to occupy a great place in today's chemistry. In addition to its biological properties, the fact that Schiff base has a stable structure as a chemical property has made it worthy of study. However, it has an increasing importance especially in analytical chemistry and biochemistry. With the synthesis of new Schiff bases in today's chemistry, many properties are expected to emerge in addition to the properties we mentioned. Schiff base compounds are considered to be promising precursors for the design of more effective biological agents. Advances in this field will require analyses of the structure-activity relationships of Schiff bases as well as the mechanisms of action of these compounds.

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REFERENCES

Abbo, H.S., Titinchi, S.J.J., Prasad, R., Chand, S., 2005. Synthesis, characterization and study of polymeric iron(III) complexes with bidentate p-hydroxy Schiff bases as heterogeneous catalysts Journal Molecular Catalys A: Chemistry, 225, 225-232.

Aguirre, J.D., Angeles-Boza, A.M., Chouai, A., Turro, C., Pellois, J.P., Dunbar, K.R., 2009. Anticancer activity of heteroleptic diimine complexes of dirhodium: a study of intercalating properties, hydrophobicity and in cellulo activity Dalton Trans. 48

An, B., Goldfarb, R.H., Siman, R., Dou, Q.P., 1998. Novel dipeptidyl proteasome inhibitors overcome Bcl-2 protective function and selectively accumulate the cyclindependent kinase inhibitor p27 and induce apoptosis in transformed, but not normal, human fibroblasts, Cell Death Differ. 5

Ashraf, M.A., Mahmood, K., Wajid, A., 2011. Int. Proc. Chem. Biol. Environ. Eng., 10,1

Chen, Y.,Tan, W., Li, Q., Dong, F., Gu, G., Guo, Z.,2018, "Synthesis of inulin derivatives with quaternary phosphonium salts and their antifungal activity" Int. J. Biol. Macromol.

Cleare, M. J., Hoeschele, J. D., 2002. Studies on the antitumor activity of group VIII transition metal complexes. Part I. Platinum(II) complexes. Bioinorg. Chem. 2

Florea, A.M., Büsselberg, D., 2011. Cisplatin as an Anti-Tumor Drug: Cellular Mechanisms of Activity, Drug Resistance and Induced Side Effects, Review: Cancers 3

Gunesli, Z., Kurt, B.Z., Gazioglu, I., Avci, D., Kucukislamoglu, M., 2018. Synthesis, antioxidant activity and SAR study of novel spiro isatin based Schiff bases Mol. Div. 23

Hearn, MJ, Cynamon, MH., 2004. Design and synthesis of antituberculars: preparation and evaluation against Mycobacterium tuberculosis of an isoniazid Schiff base Antimicrob Chemother

Ikram, M., Rehman, S., Khan, A., Baker, R. J., Hofer, T. S., Subhan, F., Qayum, M,, Schulzke, C., 2015. Synthesis, characterization, antioxidant and selective xanthine oxidase inhibitory studies of transition metal complexes of novel amino acid bearing Schiff base ligand vol 428, 117

Imran, M., Iqbal, J., Iqbal, S., Ijaz, N., 2007. Turk. J. Biol., 31, 67-73

Jian-ning, L., Bo-wan, W., Bing, Z., Yongchun, L., Turk J. Chem., 2006

Jin, Y. Jin, Sun XH., Liu, YF, Ma, HX,2013. Synthesis, characterization and biological activities of 4-amino-5-substituted-1,2,4-triazolethione Schiff base Huaxue Tongbao,76, 849-852.

Kulkarni, A, Patil, SA, Badami, PS., 2009.Synthesis, characterization, DNA cleavage and in vitro antimicrobial studies of La(III), Th(IV) and VO(IV) complexes with Schiff bases of coumarin derivatives.Eur J Med Chem 44

Kulkarni, A.A., Wankhede, S.B. , Dhawale, N.D., Yadav, P.B., Deore, V.V., Gonjari I.D.. Arabian J., 2017. Chem., 10, S184

Mahmoud, W.H., Deghadi, R.G., G.G. Mohamed, J., 2020. Organomet. Chem., 917, 121113

Malik, M.A., Dar, O.A., Gull, P., Wani, M.Y., Hashmi, A.A.,2018.Heterocyclic Schiff base transition metal complexes in antimicrobial and anticancer chemotherapy MedChemComm 9 409-436.

Nicholson, K.M., Phillips, R.M., Shnyder, S.D., Bibby, M.C., 2002.In vitro and in vivo activity of LS 4477 and LS 4559, novel analogues of the tubulin binder estramustine Eur. J. Canc. 38

Raman, N., Joseph, J., Kumara, A.S., Pothiraj, C., 2006. Mycobiology, 34, 214

Raman, N., Ravichandran, S., Thangaraja, C., J., 2004. Chem. Sci., 116, 215–219.

Rathelot, P., Vanelle, P., Gasquet, M., Delmas, F., Crozet, MP., David, T., 1995.Eur J Med Chem 30:503-8

Reina, M., 2017. "Copper or free radical scavenger?," Comput. Theor. Chem., vol. 1104, 1-11

Salvat. A., Antonnacci, L., Fortunato, R.H., Suarez, E.Y., Godoy, H.M.,2001. Lett. Appl. Microbiol.32, 293

Schiff, H., 1864. Ann. Chem. Pharm., 131, 118

Taha, M., Ismail, N.H., Jamil, W., Rashwan, H., Kashif, S.M., Sain, A.A., Adenan, M.I. , Anouar, E., Ali, M., Rahim, F., Khan, K.M.,2014. ''Synthesis of novel derivatives of 4-methylbenz imidazole and evaluation of their biological activities'' Eur. J. Med. Chem. 84

Tripodo, G., Perteghella, S., Grisoli, P., Trapani, A., Torre, M.L., Mandracchia, D., 2019 Drug delivery of rifampicin by natural micelles based on inulin: Physicochemical properties, antibacterial activity and human macrophages uptake Eur. J. Pharm. Biopharm.,136, 250-258

Wong, E., Christen, M., 1999. Giandomenico Current Status of Platinum-Based Antitumor Drugs Chem. Rev. 99

Wong, E., Giandomenico, C.M., 1999. Current status of platinum-based antitumor drugs. Chem. Rev. 99

Yang, YL., Wan, NN., Wang, WP., Xie, ZF., Wang, JD., 2011. Synthesis of bis(indolyl) methanes catalyzed by Schiff base-Cu(II) complex. Chin Chem Lett 22:1071-4.

Zhang,, J., Xu, L., Wong, W.Y., 2018. Energy materials based on metal Schiff base complexes. Coordination, Chemistry Reviews, 355, 180-195

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