

Review on the Production, Utilization, and Pharmacological Activity of Schiff Base Compounds

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ABSTRACT

Hugo Schiff gave the extremely reactive chemical compounds known as Schiff bases his name. Among the uses are catalysts, polymer stabilizers, organic synthesis intermediates, pigments and dyes, and catalysts. The literature has documented Schiff bases', anti-inflammatory, anti-fungal, anti-bacterial, anti-fungal, and antiviral properties. Schiff bases are renowned for their capacity to combine with a variety of metals to produce complexes. Both Schiff base complexes along with Schiff bases and metals by themselves have been found. Frequently demonstrated anticancer activity. We'll concentrate on the most prominent examples of this class of compounds that have been written about in the literature.

KEYWORDS: -Biological Activity, Synthesis, Reaction, and Schiff bases.

INTRODUCTION

Compounds bearing the functional group Schiff bases include azomethine ($-C=N-$) or imine [1]. They are produced when a carbonyl molecule condenses utilizing a primary amine [2- 4]. This kind of molecule was first created in 1864 Hugo Schiff, a German scientist, therefore the name Schiff base [5-7]. The fundamental formula for Schiff bases is $CR'R''=RN$, where R H [8]. The general structure of aromatic Schiff bases is $R-CH=N-R$, and they are more stable than the unstable and polymerizable aliphatic Schiff bases. [9].

Schiff bases are essential in the synthesis of a variety of bioactive chemicals. There have also been reports of antibacterial, antifungal, anticancer, and herbicidal properties [10, 11, 12, 13, and 14]. On the other hand, they play a critical part in the creation of certain ligands for Schiff bases that are employed as chiral auxiliary compounds in asymmetric synthesis. Additionally, oxidation procedures have made use of metal complex Schiff bases. [15].

These findings indicate the significance of Schiff bases in both chemical synthesis and medicinal chemistry. There are numerous techniques to construct Schiff bases. To determine which method is the simplest, we'll examine three distinct ones in this essay. We used a straightforward substance to produce p-Toluidine, 3, 4, and 5 trimethoxybenzaldehyde, and a Schiff base, figure (1) in order to make comparing the results easier.

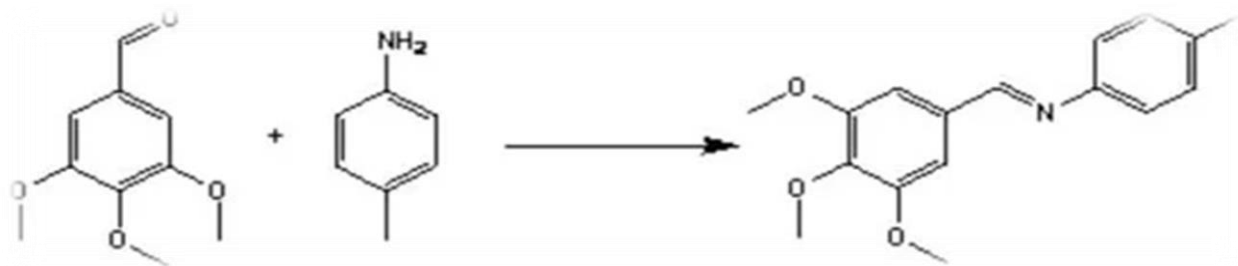


Figure 1: Schiff base Synthesis

Schiff base derivatives are a significant class of compounds with numerous uses in medicinal chemistry due to their wide many different pharmacokinetic characteristics and importance in programs to develop new drugs. [16]

The Schiff bases 2,2', N-(aryl) diimino, 3,3', and 4,4'-3,3'-bithiophene are created by reacting aromatic amines with 3,3'-bithiophene-2,2'-dicarbaldehyde and 3,3'-bithiophene-4,4'-dicarbaldehyde [17],figure (2).

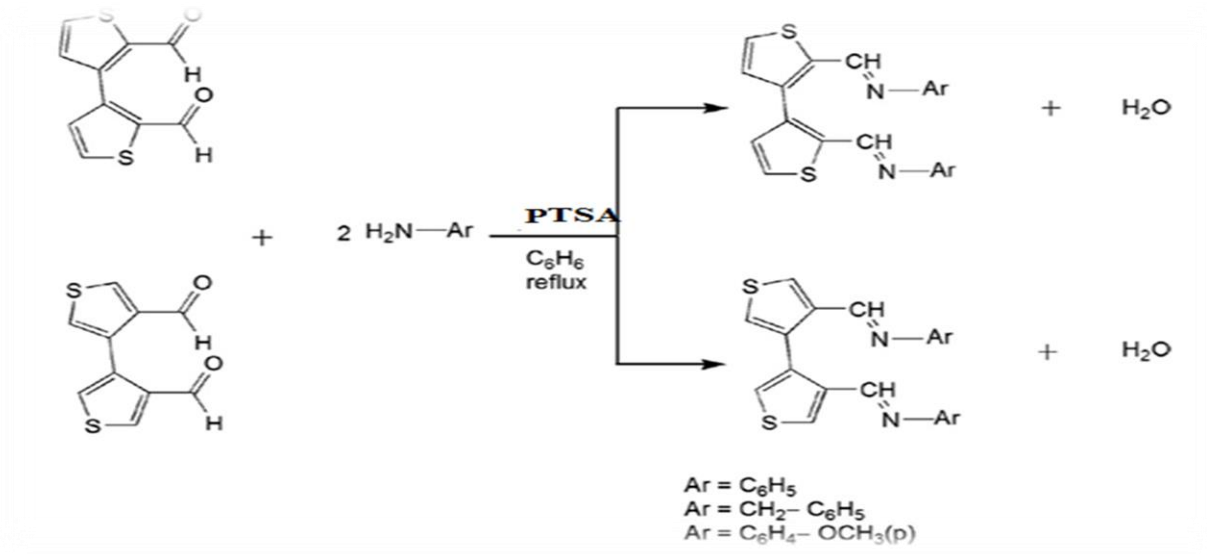


Figure 2: Schiff base Synthesis

Mohammed and colleagues [18] produced by combining aniline and 5-bromo-2-hydroxybenzaldehyde, you can make a Schiff base, as shown in equation,figure (3).

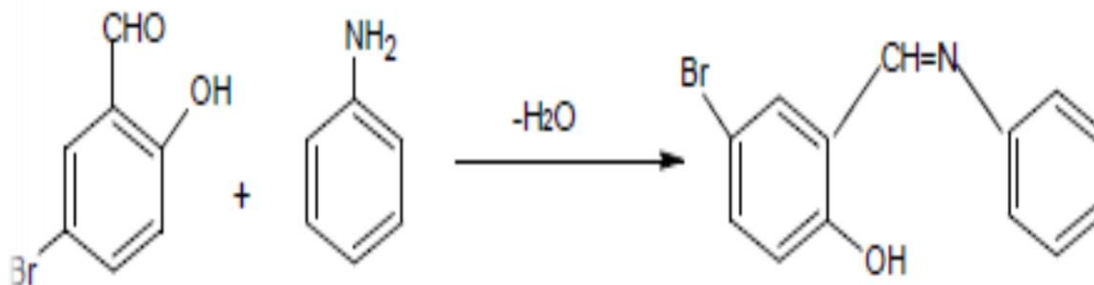


Figure (3):Schiff base Synthesis

General Schiff Base Procedures:

Schiff's bases are typically prepared by a combination of a carbonyl chemical being refluxed (derivatives of aliphatic and aromatic aldehydes or ketones) and a primary amine (aromatic or aliphatic) in the presence of a few drops of an acid a suitable solvent, and a base (piperidine) or acid (glacial acetic acid), and by removing one water molecule [19-20].

Drug-activating properties of Schiff base:

The biological effects of Schiff base include antiviral, antifungal, antibacterial, and anticancer capabilities, to name some of its pharmaceutical activities [21]. They work well in the management of diabetes mellitus as well. We can better comprehend biomolecule structure and biological processes in living things thanks to the Schiff bases. They are frequently investigated as antimalarial agents and help treat cancer [22-23].

The azomethane group (N=C) that the Schiff rules include, which modifies the activity of enzymes internally to the biological system, gives them a biological and pharmaceutical perspective action. Schiff base derivatives exhibit antibacterial properties, as seen in figure (4) [24-25].

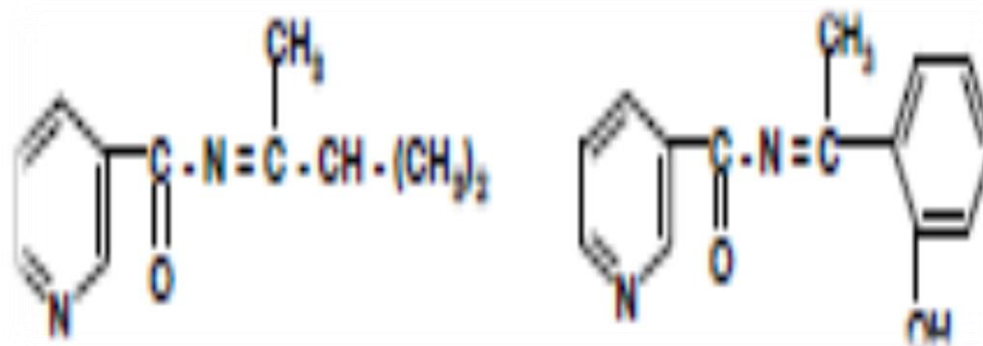


Figure (4):Schiff base Derivatives' Antimicrobial Activity

Potential antibacterial medications known as Schiff bases include N-(Salicylidene)-2-hydroxyaniline (Figure 5), which is effective against *Mycobacterium tuberculosis* [26].

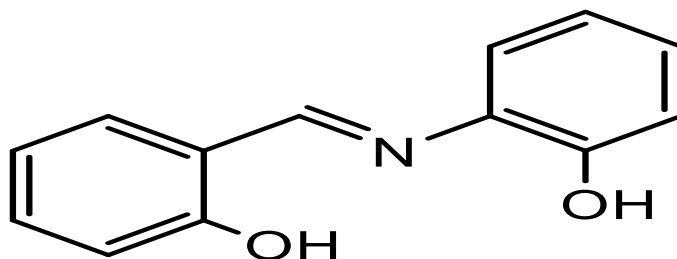


Figure (5):Antibacterial characteristics are seen in Schiff base derivatives

The Schiff base compounds below ,have antioxidant capabilities, as seen in figure (6) [27].

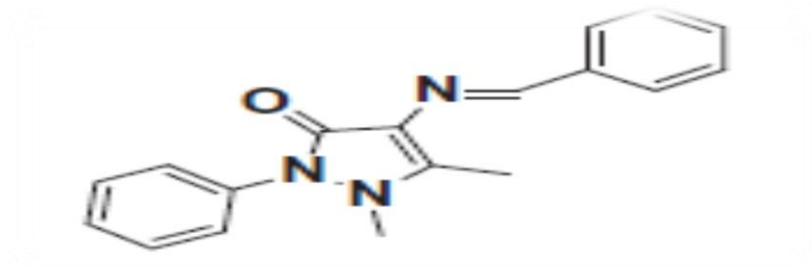


Figure (6):Characteristics of Schiff base molecules that are Antioxidant

Schiff bases with antifungal action against several fungus species, quinazolinones imine derivatives, for example, are thought to be promising antifungal agents [28]. Schiff bases identified a number of promising antifungal drugs that show promise for the future of antifungal activity evaluation and development [29].

Schiff bases, as Ancistrocladidine figure (7), also show antimalarial activity.

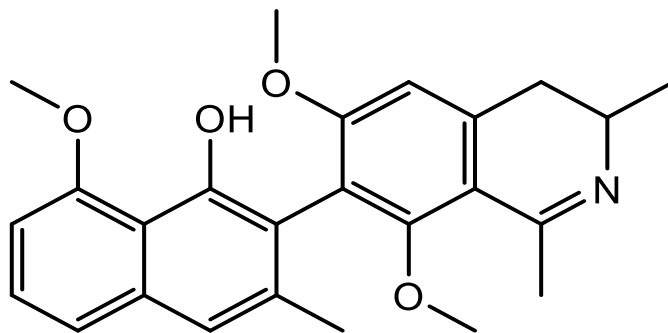


Figure (7):compounds with ancistrocladidine characteristics that are Schiff bases

Imine derivatives of different Schiff bases, such as Figure (8), reveal that N-hydroxy-N'-amino guanidine has powerful anticancer effects and can be used to treat leukemia by inhibiting ribonucleotide reductase in tumor cells [30].

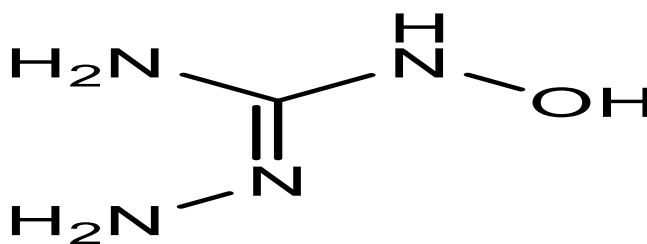


Figure (8):Substances with Schiff bases that have Anticancer Properties

New open (Figures 9–11) and macrocyclic (Figure 12) there has been synthesis of Schiff bases, and their antimicrobial properties have been tested. O-vanillin and salicylaldehyde were combined in conjunction with 4, 4'-diaminodiphenylmethane and 4, 4'-diamino diphenyl sulfide, and terephthalic acid's diethyl ester, respectively to create open bases for Schiff.

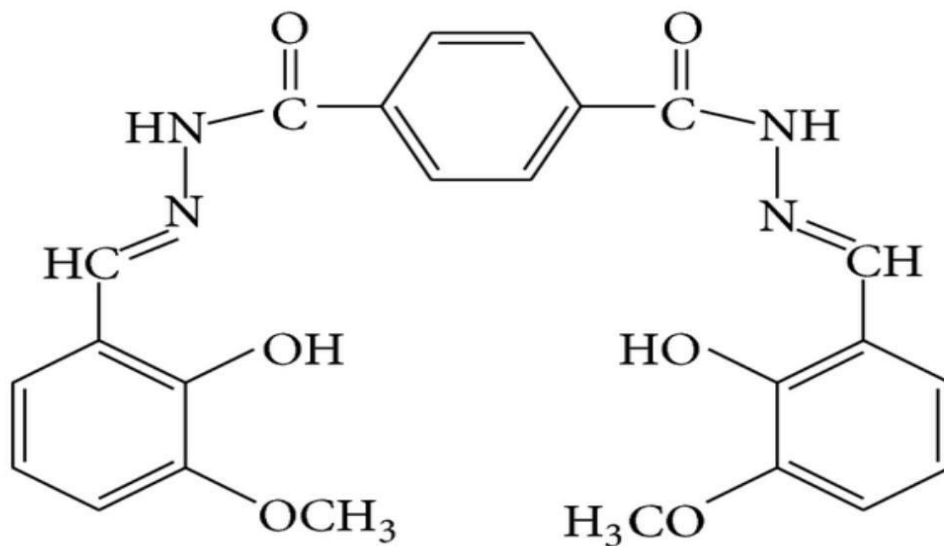


Figure (9):Schiff base Derivatives' Antimicrobial Activity

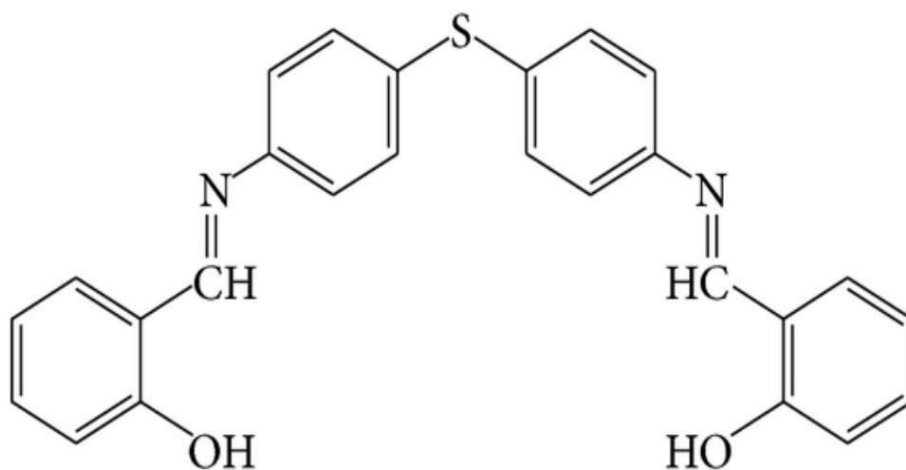


Figure (10):Schiff base Derivatives' Antimicrobial Activity

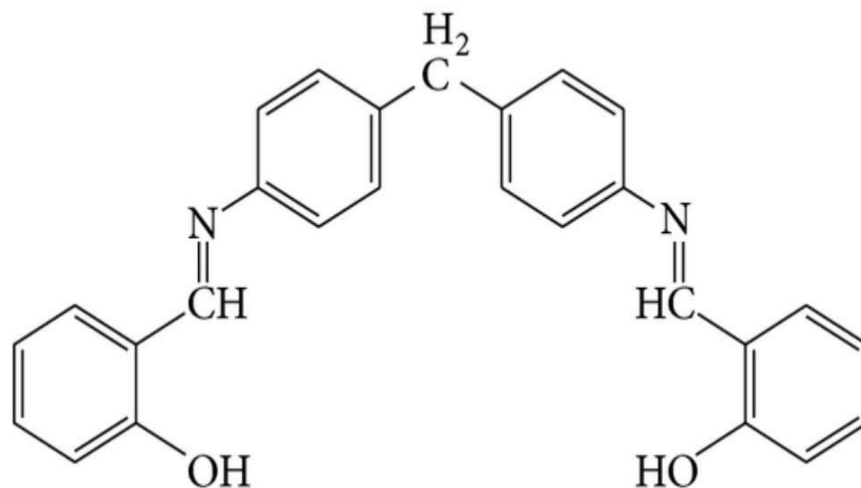


Figure (11):Schiff base Derivatives' Antimicrobial Activity

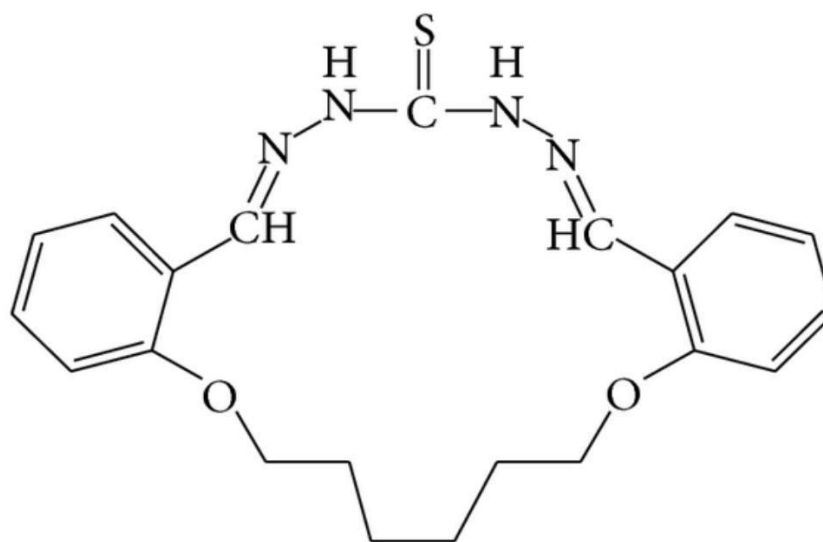


Figure (12):Schiff base Derivatives' Antimicrobial Activity

2, 2-formylphenyl-1, 6-bis(hexane) was found to condense into macrocyclic Schiff bases when it was combined with thiocarbonylhydrazide. Four microorganisms were used to investigate physiologic function of

the produced substances: *S. aureus*, *K. pneumoniae*, *E. coli*, and *S. typhimurium*. Every molecule that was produced was determined to be moderately to significantly active [31].

Diclofenac acid, 2-[(2,6-dichloroanilino) phenyl] acetic acid a collection of Schiff bases and S-substituted phenacyl 1,3,4-oxadiazoles (Figure 13) were created, testing for their analgesic, and anti-inflammatory, nonulcerogenic properties. For testing analgesic and anti-inflammatory effects, respectively, carrageenan-induced rat, Acetic acid-induced writhing test and paw edema were used. The experiments led researchers to the conclusion that synthetic drugs lacked gastrointestinal toxicity. The most effective anti-inflammatory molecule discovered so far is N-(4-bromo-benzylidene)-2,6-dichloroaniline-2,2-benzyl carbazide [32].

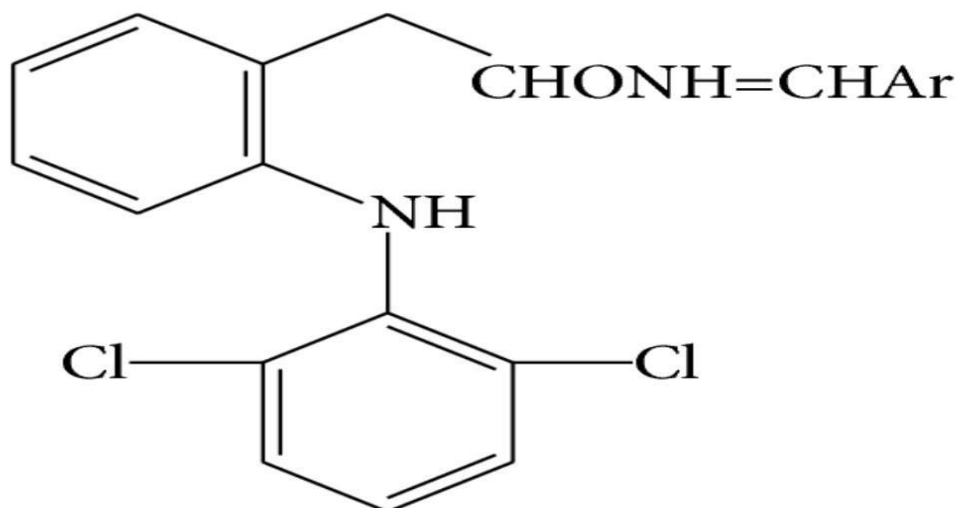


Figure (13): Schiff base Derivatives' Anti-inflammatory Activity

Conclusion:

Bases on the Schiff have been extensively studied for use in industries. On the other hand, more research is needed to understand the biological action of this class of chemicals. When plant pathogens are taken into consideration, this is made evident. The quantity of studies demonstrating the impact of Schiff bases on pathogens of therapeutic relevance has recently risen, despite the fact that this field of study is still in its infancy. Schiff base compounds have been noted as having great potential for the development of fresh antibiotics. Research into the Structure-activity of Schiff bases correlations and their method of action will be necessary to further this field.

References

1. Kajal A., Bala S., Kamboj S., Sharma N. and Saini V., Schiff bases: a versatile Pharmacophore. *J. Catalysts*, 1-14 (2013).
2. El-Shafiey Z. A., Synthesis, spectroscopic characterization, thermal investigation and antimicrobial activity of S, O and N-donor heterocyclic Schiff base ligands and their Co(II), Cd(II), Hg(II), Fe(III) and UO₂ (II) metal complexes. *Egypt. J. Chem.*, 53 (1), 137 - 162 (2010).
3. Pradhan A. and Kumar A., A review: an overview on synthesis of some Schiff bases and their metal complexes with anti-microbial activity. *Chemical and Process Engineering Research*, 35, 84-86 (2015).
4. Chaurasia M., Tomar D., Chandra S., BSA binding studies of Co(II), Ni(II) and Cu(II) metal complexes of Schiff base derived from 2-hydroxy-4-methoxybenzaldehyde and 2-amino-6-methylbenzothiazole, *Egypt. J. Chem.*, 62 (2), 357 - 372 (2019).
5. Hossain M. S., Roy P. K., Zakaria C. M. and Zahan M. K-E., Selected Schiff base coordination complexes and their microbial application: a review. *Int. J. Chem. Stud.*, 6 (1), 19-31 (2018).
6. Manju, Mishra N. and Kumar D., Coordination chemistry of Schiff base tin complexes. *Rus. J. Coord. Chem.*, 40 (6), 343-357 (2014).
7. da Silva C. M., da Silva D. L., Modolo L. V., Alves R. B., de Resende M. A., Martins C. V. B., de Fatima A., Schiff bases: a short review of their antimicrobial activities. *J. Adv. Res.*, 2, 1-8 (2011).
8. Hameed A., al-Rashida M., Uroos M., Ali S. A. and Khan K. M. Schiff bases in medicinal chemistry: a patent review (2010-2015). *Expert Opin. Ther. Pat.*, 27 (1), 63-79 (2017).
9. Al Zoubi W., Al-Hamdani A. A. S. and Ko Y. G., Schiff bases and their complexes: recent progress in thermal analysis. *Sep. Sci. Technol.*, 52 (6), 1052-1069 (2017).
10. Jarrahpour, A. A.; Jalbout, A. F.; Rezaei, S.; Trzaskowski, B. *Molbank* 2006, M455.
11. Taggi, A. E.; Hafez, A. M.; Wack, H.; Young, B.; Ferraris, D.; Lectka, T. *J. Am. Chem. Soc.* 2002, 124, 6626.
12. Jarrahpour, A. A.; Shekarriz, M.; Taslimi, A. *Molecules* 2004, 9, 29-38.
13. Chohan, Z. H.; Arif, M.; Shafiq, Z.; Yaqub, M.; Supuran, C.T. *J. Enzyme. Inhib. Med. Chem.* 2006, 21(1), 95-103.
14. Ren, S.; Wang, R.; Komatsu, K.; Bonaz-Krause, P.; Zyrianov, Y.; McKenna, C.E.; Csipke, C.; Tokes, Z.A.; Lien, E.J. *J. Med. Chem.* 2002, 45(2), 410-419.
15. Jarrahpour, A. A.; Rezaei, S. *Molbank* 2006, M456.
16. F.A. El-Saied, T.A. Salem, M.M.E. Shakhofa, A.N. Al-Hakimi, A.S. Radwan Antitumor activity of synthesized and characterized Cu (II), Ni (II) and Co (II) complexes of hydrazone-oxime ligands derived from 3-(hydroxyimino) butan-2-one Beni-Suef Univ. *J. basic Appl. Sci.*, 7 (2018), pp. 420-429.
17. N .Bhanvesh, and K. R. Desai, "Novel approach for rapid and efficient synthesis of heterocyclic Schiff bases and azetidines under microwave irradiation". *Ind. J. chem.* :45(B), 267-271 (2006)
18. M.Y. Mohammad et al. "Synthesis and characterization of Schiff base aniline with 5-bromo-2-hydroxy benzaldehyde and their metal complexes". *Int. J. of Rec. Sci. Res.* 9(4), 26026-26030 (2018).
19. A.P. Dobbs, and S. Rossiter, Imines and their N-substituted derivatives: NH, NR, and N-Haloimines. In *Comprehensive Organic Functional Group Transformations II*; Alan, R.K., Taylor, R.J.K., Eds.; Elsevier: Oxford, UK, pp. 419-450 (2005).
20. Chakraborti, A. K., Bhagat, S., & Rudrawar, S., Magnesium perchlorate as an efficient catalyst for the synthesis of imines and phenylhydrazones. *Tetrahedron letters*, 45(41), 7641-7644, 2004.

21. Radecka-Paryzek W., Pospieszna-Markiewicz I., Kubicki M.: Self-assembled two-dimensional salicylaluminum(III) nitrate coordination polymer. *Inorg. Chim. Acta*, 2007, 360, 488–496.
22. Boghaei D. M., Askarizadeh E., Bezaatpour A.: Molecular and Biomolecular Spectroscopy. *Spectrochim. Acta Part A*, 2008, 69, 624–628.
23. Prashanthi Y., Kiranmai K., Subhashini N. J. P., Shivaraj: Synthesis, potentiometric and antimicrobial studies on metal complexes of isoxazole Schiff bases. *Spectrochim. Acta Part A*, 2008, 70, 30–35.
24. A.P.Mishra ,N.Sharma ,R.K.Jain . "Microwave Synthesis,spectral, thermal and antimicrobial studies of some Ni (II), and Cu (II) Schiff base complexes" .*J .Syn.Theor..Appl.*, 2, 56-62(2013).
25. S.Tiwari ,V.Mujalda ,V.Sharma ,P.Saxena ,M.Shrivastava. "Synthesis and evaluation of 4-Quinazolinone analogues as antimicrobial agents". *Asian J Pharm Clin Res* 5,(1),98-100(2012).
26. Da Silva, Cleiton M., et al. "Schiff bases: A short review of their antimicrobial activities." *Journal of Advanced research* 2.1 (2011): 1-8.
27. M.Kumar ,T.Padmini ,K.Ponnuvel. "Synthesis, characterization and antioxidant activities of Schiff bases are of cholesterol".*J. of Saudi Chem.Soc.*21, S322-328(2017).
28. Kumar S., Dhar D. N., Saxena P. N.: Applications of metal complexes of Schiff bases – a review. *J. Sci. Ind. Res.*, 2009, 68, 181–187.
29. Rehman W., Baloch M. K., Muhammad B., Badshah A., Khan K. M.:Characteristic spectral studies and in vitro antifungal activity of some Schiff bases and their organotin (IV) complexes. *Chin. Sci. Bull.*, 2004, 49, 2, 119–122.
30. Jesmin M., Ali M. M., Khanam J. A.: Antitumour activities of some Schiffbases derived from benzoin, salicylaldehyde, amino phenol and 2,4 dinitrophenyl Hydrazine. *Thai J. Pharm. Sci.*, 2010, 34, 20–31.
31. H. H. Essa, F. Kandil, and A. Falah, "Synthesis and identification of schiff bases and biological activity new study," *Iraqi Journal of Science*, vol. 53, no. 2, pp. 230–240, 2012.
32. S. V. Bhandari, K. G. Bothara, M. K. Raut, A. A. Patil, A. P. Sarkate, and V. J. Mokale, "Design, synthesis and evaluation of antiinflammatory, analgesic and ulcerogenicity studies of novel S-substituted phenacyl-1,3,4-oxadiazole-2-thiol and Schiff bases of diclofenac acid as nonulcerogenic derivatives," *Bioorganic and Medicinal Chemistry*, vol. 16, no. 4, pp. 1822–1831, 2008.