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Synthesis and biological evaluation of 4-dimethylaminobenzaldehyde derivatives of Schiff bases metal complexes: A review

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ABSTRACT

Schiff bases are considered as valuable compounds because of their versatility in the field of medicine and pharmaceuticals. A new Schiff base was formed by condensation of 4-dimethylaminobenzaldehyde with benzamide in 1:1 M ratio. The catalytic activity of Schiff base is raised by making its complex with metals. Different transition metals (Ni, Co, Zn, Pb) were used to form the metal complex with the newly formed Schiff base. Metal complexes of Schiff bases derived from 4-dimethylaminobenzaldehyde was processed for good yield of product. The Schiff bases show strong biological activities that includes antifungal, anticancer, antibacterial activities etc. The complexes of Schiff base metal are in the wide range of study. They have high thermal power and have useful effects in many fields. This effect of metal has increased the biological activities of such compounds and therefore the scientists have changed their behavior towards coordination chemistry. The new complexes were also characterized by using UV, IR, XRD and molar conductive techniques. This article throws light on the formation of 4-dimethylaminobenzaldehyde derivatives of different Schiff base metal complexes, its importance and use of Schiff bases along with its metal complexes. The investigation of antibacterial activities of ligand and complexes were done against bacteria like *Staphylococcus Aureus*, *Bacillus subtilis and Escherichia Coli*. It was found that the complexes showed marvelous result as compare to ligand against bacteria.

1. Introduction

There are some new class of compound, Schiff base exhibit versatile characteristics in various fields such as anti-fungal, anti-cancer, anti-bacterial and anti-oxidant activities [1,2]. It has affected the lives by enhancing the infectious diseases worldwide and are used in different biological activities [3]. The dominant cause of these illnesses is bacteria that are impermeable to many antibiotics. To hold on this hazardousness the coordinated complexes are considered effective agents. They help to adapt affinity against life-threatening diseases and provide systematic antimicrobial activities.Fig. 2Fig. 3Fig. 4Fig. 5Fig. 6Fig. 7Fig. 8Fig. 9 Fig. 10Fig. 11Fig. 12Fig. 13Fig. 14Scheme 1Scheme 2Scheme 3Scheme 4Scheme 5Scheme 6Scheme 7Scheme 8Scheme 9Table 1Table 2

In Inorganic chemistry, azomethine group contains(C═N) as a functional group are called Schiff base [4]. The discovery of coordination chemistry, as a Schiff base ligand has increased the thirst for the scientists to discover their importance in biological activities [5]. Coordination compounds have gained utmost interest with transition metal complex formation [6]. The complexes of transition metals with nitrogen and oxygen atom are used as functional groups in the Schiff base and show structural liability [7]. They are considered as a vital group of ligands because they can form complexes with metals [8–10]. The development of coordination chemistry in metal complexes along with Schiff base is playing a marvelous role. This base ligand was not known until 19th century. But with the advancement of the science, a lot of work has done on Schiff base metal complexes in their synthesis and characterization to make further complexes which is the need of today. The redesigned bio-ligands have expanded its character in coordination

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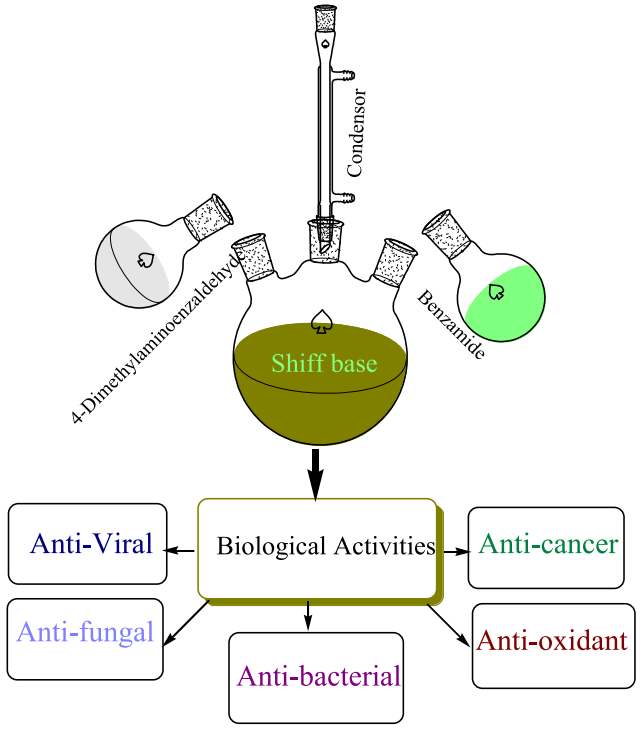


Fig. 1. Condensation reaction for production of ShBL with biological activities.

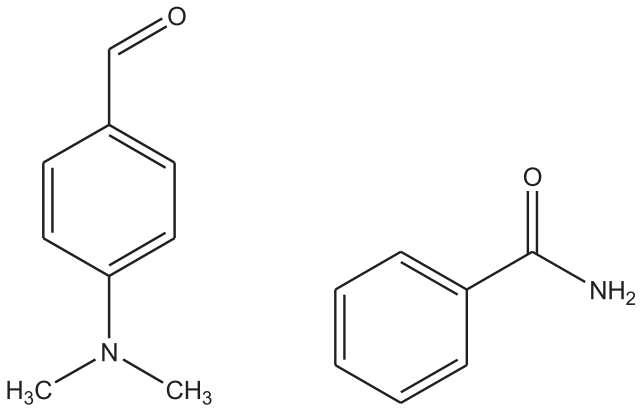


Fig. 2. Structure of 4-Dimethylaminobenzaldehyde and Benzamide.

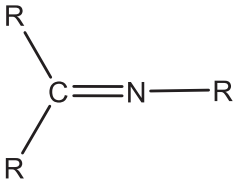


Fig. 3. A Schiff base.

complex formation. The complexes of Schiff base ligands play exceptional role in the study of biological activities like anti-fungal, anti-oxidant, anti-diabetic and antibacterial [11]. The Schiff bases have played an interesting role in the chemistry of coordinated compound synthesis of different donor atoms with regard of transition metals. There were different applications of these coordinated compounds were studied in fields of polymer, pigments and paints [12].

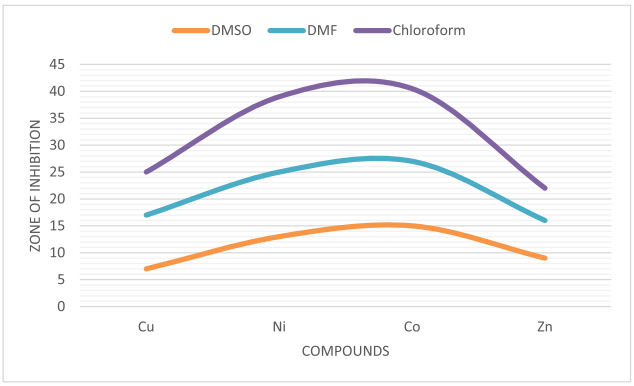


Fig. 4. Antibacterial activity of complexes in polar and non-polar solvents against *N. Asteroids.*

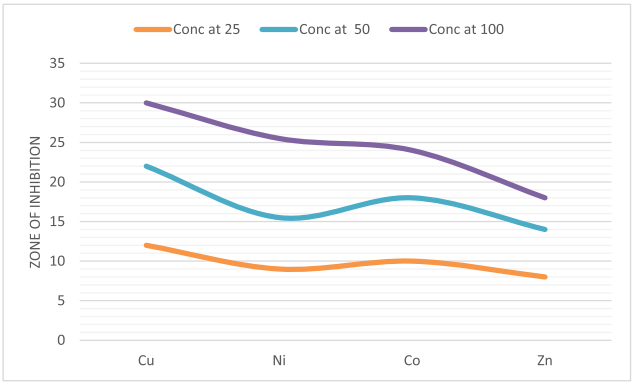


Fig. 5. Antibacterial activity of complexes in polar and non-polar solvents against *Pseudomonas putida.*

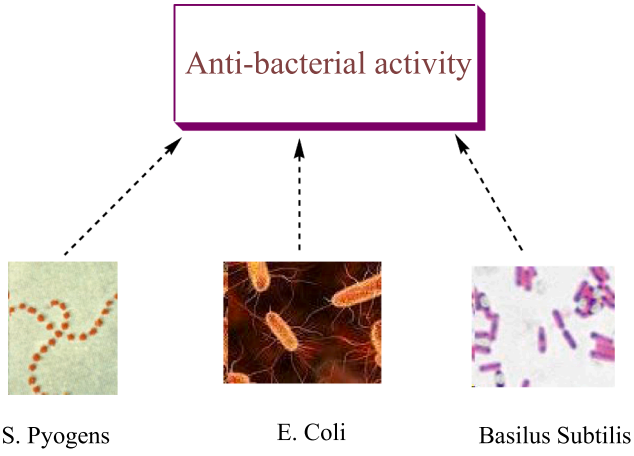


Fig. 6. Antibacterial activity (*S. pyogens, E. coli, Basilus Subtilis*).

1.1. Schiff base derivatives

When aromatic or any aliphatic aldehydes are condensed with amines, Schiff bases are formed. A new Schiff base was synthesized by condensing 4-dimethylaminobenzaldehyde with benzamide. They form stable complexes with different metals of transition series.

The study of metal complexes has attracted a lot of researchers because they are now the base of many biological evaluations and have pharmacological uses such as anti-tumor, anti-bacterial and anti-fungal [13]. In the structural and synthetic research Schiff bases and their

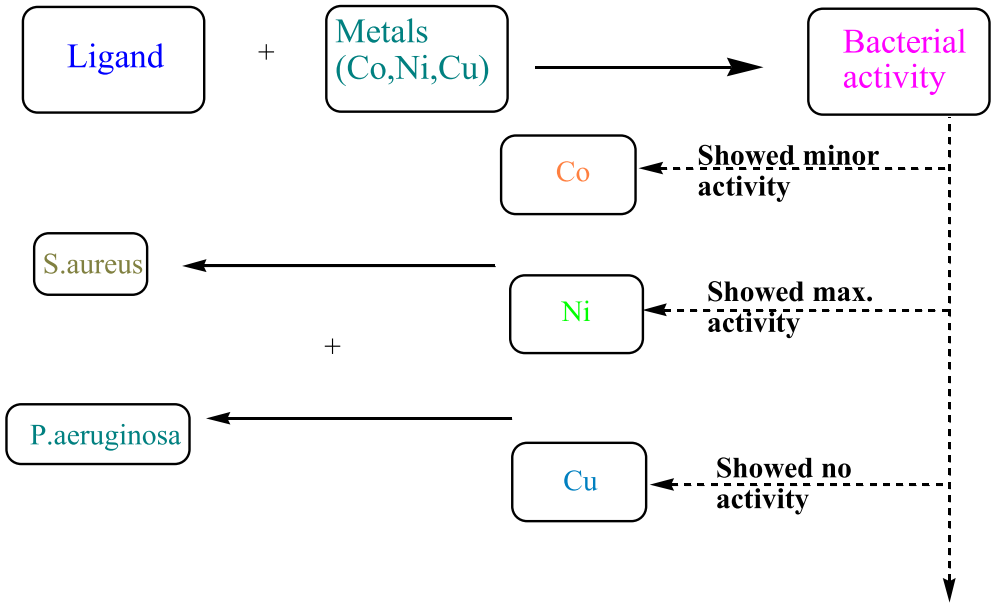


Fig. 7. Bacterial activity by ligand potassium 2-N(4-N,*N*-dimethylaminobenzaldehyde)-4-trithiocarbonate 1,3,4-thiadiazole and metals Ni, Co, Cu.

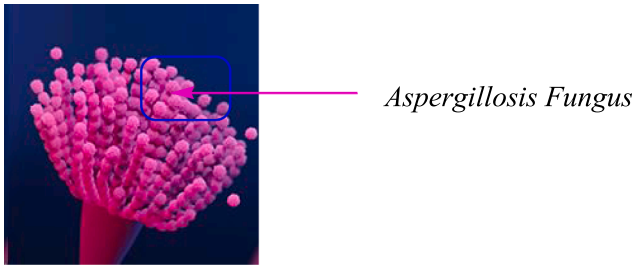


Fig. 8. Aspergillosis….type of fungus.

complexes of metals are playing a promising role in the uplifting of inorganic chemistry. These complexes are extensively scrutinized, because of their prodigious chemical characteristics [14–17]. The biological applications and ability to form chelates have also shown awful attraction. They can also work as specimens for different biological species [18–20]. Imino functional group containing Schiff bases show an extensive range of biological interest that includes antifungal, antibacterial, antitumor, anticancer and anti-inflammation enterprise [21–23]. It is thought that H-bonding in imino group is involved in biological activities [24].

Almost all metals can be used to form complexes with Schiff base. The most widely used metals are from transition series (Zn, Cd, Ni, Cu, Co, Pb etc.). Currently, there is a great expansion in the research field due to these metal complexes because researches are paying a great allure on the Schiff base metal complexes[25]. They are trying to expand the areas of organometallic compounds with different points of bio-inorganic chemistry [26]. The antimicrobial activities of complexes were investigated by using different methods one of them is by diffusion method. The results showed that Schiff bases in free form are less reactive than that of its metal complexes. The biological activities of all these complexes were found by using different pathogenic organisms. The Schiff bases have a wide range of implementations viz. detection of aldehyde or ketones group, purification of organic compounds as well as protection of all these compounds in case of complications. They are also a central part of some dyes. These bases could be in bio or trio form, therefore they form many types of complexes with metals of transition series. In case of organic synthesis, Schiff bases are used to form C—N bond which is very useful.

While overlooking the enzymatic reactions, it was found that these bases are essentially used as intermediate in a number of reactions. Among these reactions one of the most effective was the biochemical mechanism that is the condensation of primary amines with carbonyl groups to form Schiff base or imine.

Metal complexes are also considered as powerful materials for their use against the anticancer cells. The use of metal complexes is also considered valuable in all type of chemical analysis. It is a potential tool for thousands of studies from past century. It also suggests that amount of pollution can be indicated by using metal complexes and all this was possible due to discovery of coordinated complex compounds. The chemical and physical properties of Schiff base was studied by Layer a chemist in 1963 [27]. The chelating properties of Schiff bases was shown on a monograph by Mellor [28] and Dwyer. An excellent review was presented by Holmes and his workers [29]. Bayer tried to work elaborately on the Schiff base characteristics and find its chelating agents. In organic analysis Jungies *et al.* found the extensive applications of Schiff bases. A new compound was formed when thiosemicarbazide was condensed with a reliable aldehyde or may be Ketones. The obtained product was Thiosemicarbazones. These are one of the best obtained products of inorganic chemistry. This compound has sulfur and nitrogen as a set of donor [30,31]. This formed complex has been studied by chemists from last many years because of its application in medicine and it has capability to bind with transition metals to form complexes [32–37]. Due to its various applications thiosemicarbazones show their characteristics in bonding, biological activations etc. [38–41].

1.2. Schiff base ligand synthesis

- L_a: In a reaction synthesis, characterization as well as antimicrobial activities was investigated by Morad *et al.* He used two reactants one was aldehyde and other was amine derivate and condense them to form a new Schiff base ligand. A water molecule was released in this synthesis.
- L_b: Gopal Krishna *et al* studied the synthesis of Schiff base of 4-Hydroxy 6-carboxyhydrazinobenzofuran [42].
- L_c: When rectified spirit is used, it produces 4-Chloro-2-oxo-2H-chromene-3-carbaldehyde on reacting with anilines of different type and produces Schiff base of the substituted-phenylimino methyl type. Its characteristics were identified on their spectra's and their values

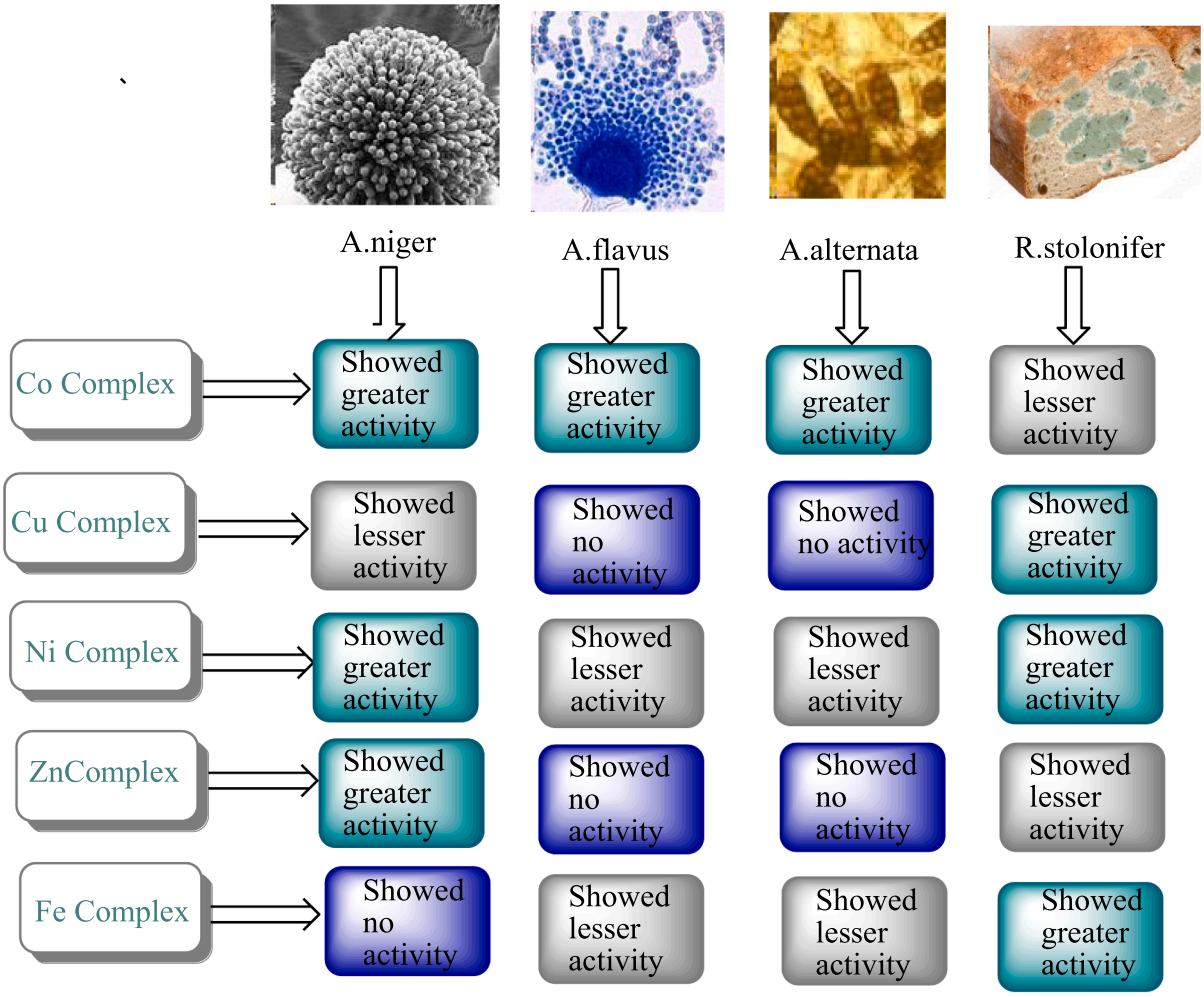


Fig. 9. Metal complexes showing anti-fungal activities against *A. niger*, *A. flavus*, *A. alternata* and *R. stolonifer* fungus.

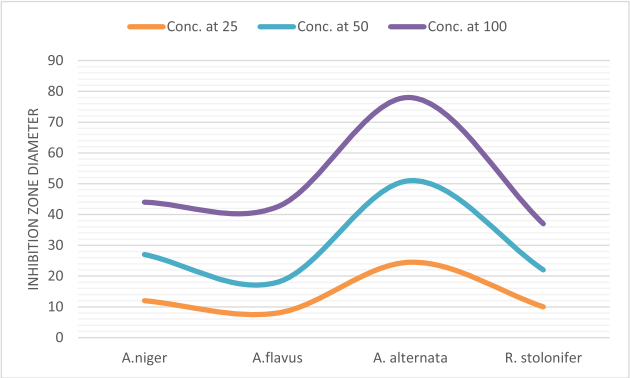


Fig. 10. Consequence of CoCl2.6H2O on different fungi.

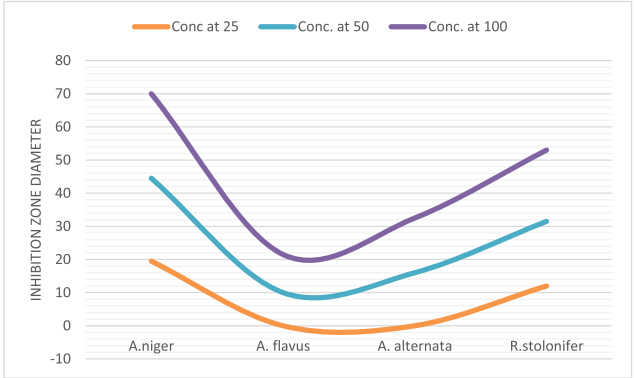


Fig. 11. Consequence of NiCl2.6H2O on different fungi.

were used to identify antimicrobial activities of gram positive and negative bacteria.

- L_d: By using 2-formylindole, *N*-amino Rhodanine along with salicylaldehyde metal complexes with Schiff base were synthesized by Elzahany *et al.* He also made elemental characterization of ligands of Schiff base as IR, NMR as well as electronic spectra. The antimicrobial activities were studied against many bacteria's such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* etc. by use of free ligands and their metal complexes. The imitation shows the non-activity of ligands against these bacteria. But if we closely observe complexes of metal it shows that by handling some experimental conditions activity of these bacteria can be found more reliably.
- L_e: The synthesis of a number of 1–5-substituited-2-oxoindolin-3-ylidene and 1–4-substituited-pyridin-2-yl was reported by Vijey Aanandhi *et al.* All these compounds were tested for antibacterial as well as antifungal activities against *B. subtilis*, *E. coli*, *A. niger* etc. the result was clear that showed a good response for these activities.

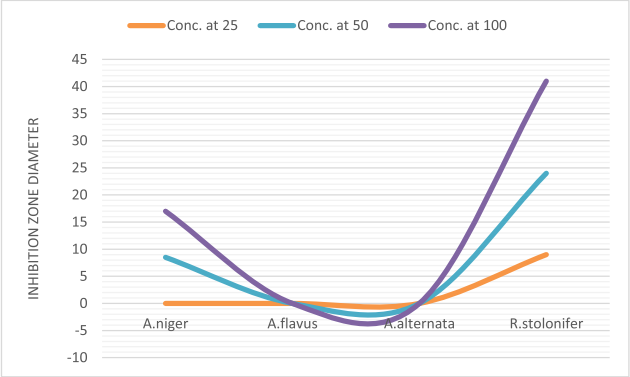


Fig. 12. Consequence of CuCl2.6H2O on different fungi.

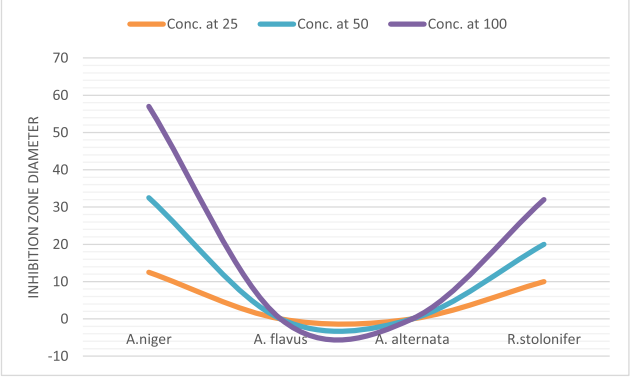


Fig. 13. Consequence of ZnCl2 on different fungi.

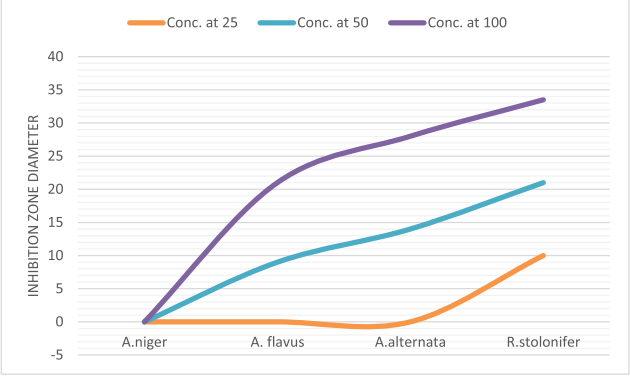
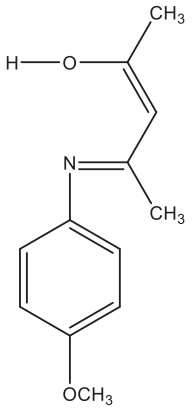


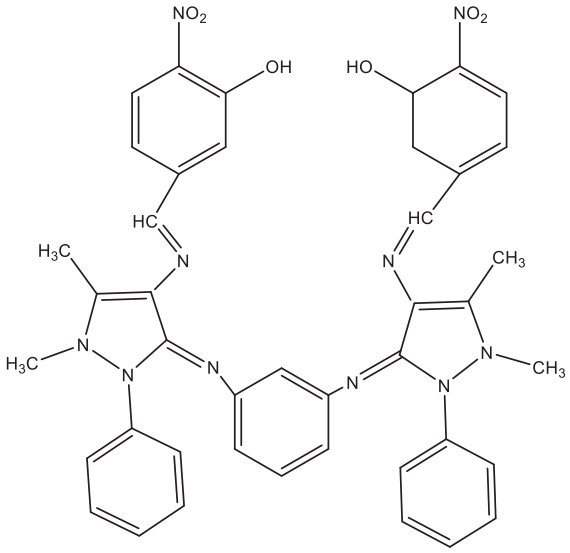
Fig. 14. Consequence of FeCl3.6H2O on different fungi.

- ***L*$_f$:** Biological activities of some other metal complexes along with Schiff base were also studied by Baluja *et al.* He prepared a Schiff base ligand and used it for the study of many biological activities against different bacteria.
- ***L*$_g$:** Raman and his Colleagues worked on the Synthesis and characterization of Cu, Co, Ni and Zn complexes that were identified in acetylacetone and anisidine [43,44]. The result showed the greater antimicrobial activities.



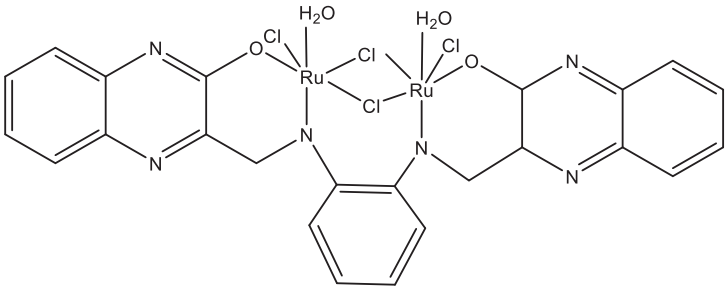
(I)

- ***L*$_h$:** When hetero aromatic aldehyde was condensed with 2-acetohydrazides a new type of Schiff base was formed. This Schiff base was 2, [4-methyl-2-oxo-chromen-7-yl)oxy]-N1 type [45]. This base was characterized by 1H NMR, IR and mass spectra. The compound which was synthesized in this reaction was used to determine the antimicrobial activities.
- ***L*$_i$:** Many other Scientists have also worked on the synthesis of metal complexes. Ramen *et al* also worked and formed another Scheme of the Schiff base ligand [46]. He tried to work on the cleavage of DNA and antimicrobial activities of these Schiff base complexes.



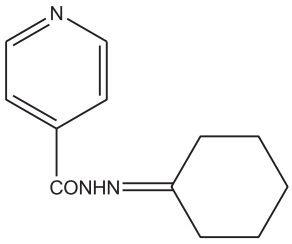
(II)

- ***L*$_j$:** The synthesis, characterization and biological activities of another Schiff base containing Ruthenium that was emerged from 3-hydroxy quinoaxiline-2-carboxaldehyde and salicylaldehyde was studied by Chittilappilly.



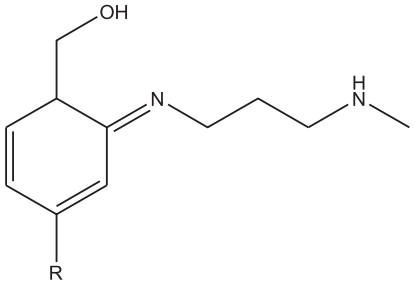
(III)

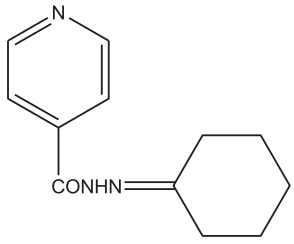
- ***L_k*:** The given type of Schiff base was studied by Hearn and coworkers against biological activities. They studied the biological activities against different bacteria like Escherichia coli.



(IV)

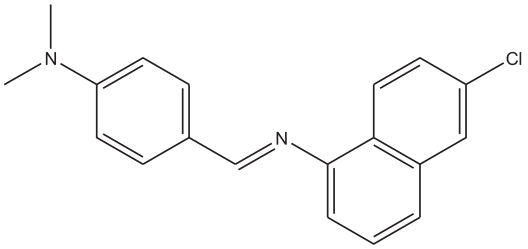
- ***L_l*:** Schiff base ligands of trisalicylidene(imino)propyl)amine was reacted with hydroxysalicylideneimino-propylamine [47] and prepared a ligand that was characterized by using many techniques such as UV,IR,NMR etc.





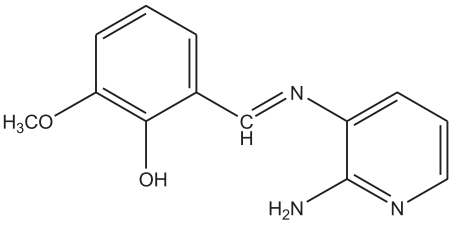
(V)

- ***L_m*:** The synthesis and structural features of another Schiff base was studied by Dong-Hoon and his colleagues [48]. It was having thiopene in its structure.
- ***L_n*:** Synthesis and characterization of some other Schiff bases were studied by Samira [49].
- ***L_o*:** A new Schiff base [50] was made by condensation of reactants (1,2 diaminocyclohexane and 2-hydroxyacetophenone).
- ***L_p*:** The characterization of Schiff base was made by Sharif and Ibrahim [51]. This can be regarded as best material in the study of flurometric reagents.



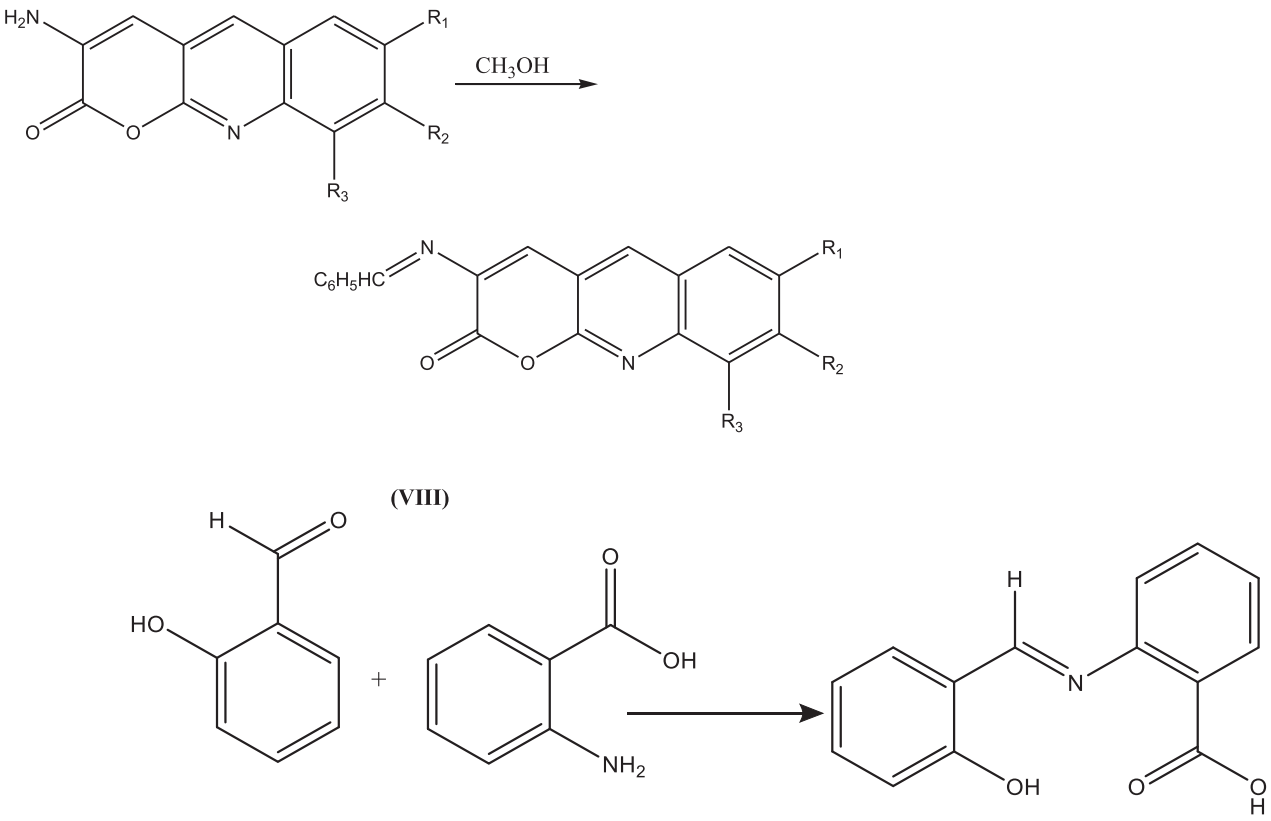
(VI)

- ***L_q*:** Dioxouranium and thorium complexes were made from acetophenones and 2-amino pyridine. The characterization and synthesis of this reaction was studied by Gudasi *et al* [52].
- ***L_r*:** The following(XI) Schiff base was reported by More *et al* [53]. The proton stability of the base was studied by these authors as well as they gave the concept of formation of constants in Schiff bases.
- ***L_s*:** Some other Schiff bases were also reported by condensation of o-vanillin and diminopyridine [54]. The following Schiff base shows biological activities such as antifungal, antibacterial, etc.



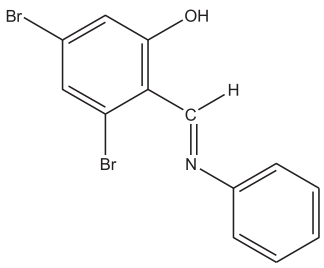
(VII)

- ***L_t*:** The formation of Schiff base was reported by Rajendran [55] who worked on the condensation 3-amino-2,Hpyrano[2,3-*b*]quinolin-2-ones. The formed product was used to screen the antifungal activities against some fungi that were Aspergillus niger.



Scheme 1. Synthesis of Schiff base ligand ShBL(L_a).

- ***L_u*:** The Cu complexes were formed after the condensation of terepthalic aldehyde with 4-aminopyridine and the give reaction was introduced by Tudor Rosu *et al* [56].
- ***L_v*:** A new Schiff base was synthesized which was reported by Ali Asghar jarrahpour *et al* [57]by the condensation of istatin benzyisatin with 5-fluoroisatin by mixing it with amines.
- ***L_w*:** Schiff base ligand was presented by N. Raman *et al* [58]which was the synthesis of Cu complex of 4-aminoantipyrine from PhNH2 and salicylidine-4-aminoantipyrine.
- ***L_x*:** Some other complexes of different metals with mixed ligands were also formed such as [M (SB)2], M = transition metals(Cu, Ni, Mn, Co, Cd) and bis-acetophenone ethylenediamine. These complexes were characterized by using different techniques. These specific types of mixed ligands have octahedral shape. They also show antifungal, antibacterial activities in apposition to yeast, fungi, bacteria etc. The technique of synthesizing mixed ligand was reported by Patel *et al* [59].



(IX)

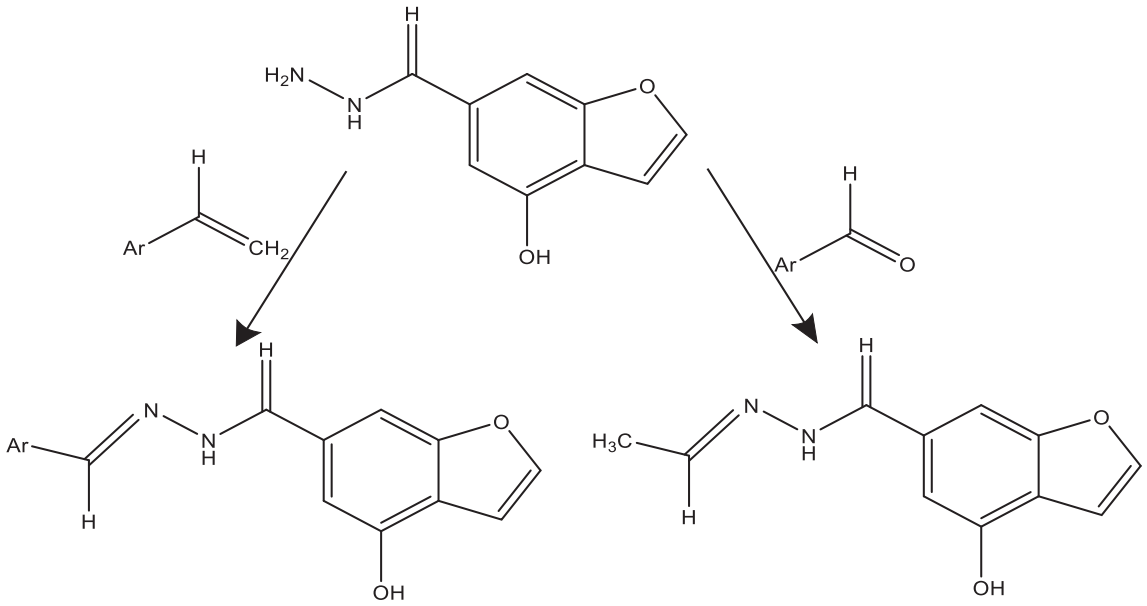
- ***L_y*:** When 2-hydroxy-benzaldehyde and 4-(2-amino-ethyl)-benzene-1,2-diol was condensed another Schiff base was formed which was named as (4-{2-[(2-hydroxy-benzylidene)-amino]-ethyl}-benzene-1,2-diol). The synthesized ligand was reacted with different metals such as Pt(IV), Ni(II) and Pd(II) to form complexes. These Schiff base metal complexes were characterized with different techniques like proton nuclear magnetic resonance, UV–vis, IR and chloride content. The anti-oxidant activities of the compounds were also evaluated [60].

1.3. Historical studies of Schiff base

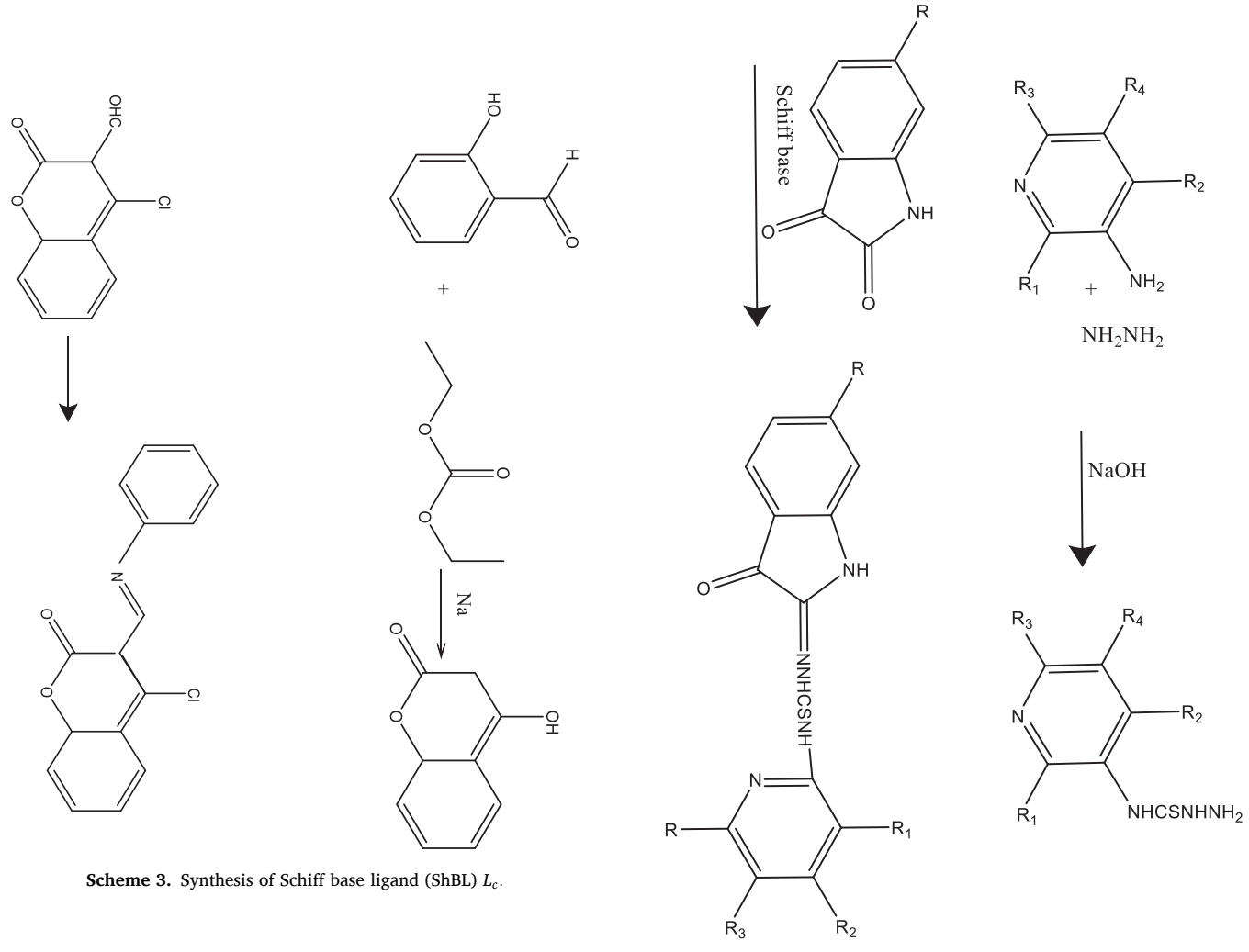
A German chemist, winner of Noble prize Hugo Schiff produced Schiff base by condensation of primary amines and carbonyl compounds [98]. If structure of Schiff is studied it shows resemblance to ketone or aldehyde where carbonyl group is exchanged by an imine group(Fig. 1) [99–101]. It contains functional group of C═N, *N*-atom connected to alkyl group. This base is apposite to azomethine. In the honor of Hugo, these compounds are named as Schiff base. By stereo chemical analysis it was indicated that Schiff bases are formed in such a way that *N*-atom of peptide group bends toward the side chain of amino group and transfer of charge occurs in between group of proteins and oxygen atom of Schiff base. When metal complexes are formed they cause an effective decrease in the metal ions polarity [102].

A newly formed Schiff base was prepared by condensing 4-dimethylaminobenzaldehyde with Benzamide. The prepared mixture was refluxed for almost 2 h. Precipitates of the product were formed by adding a small amount of base (NaOH). While doing spectral studies it was found that the ligand is coordinated with six sites [82,103,104].

The synthesis of two bi-dentate Schiff base ligands was done by using 2-Amino-5-nitrobenzaldehyde. It was dissolved in the acetonitrile and dichloromethane mixture but amine was mixed clearly in the solution of ethanol. Nearly 8 h was given to this mixture for refluxing.

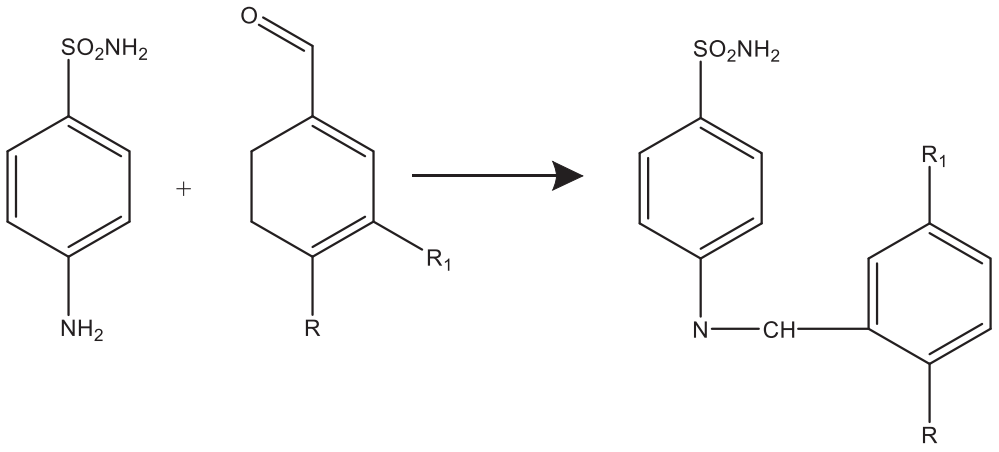


Scheme 2. Synthesis of Schiff base ligand ShBL(L_b).

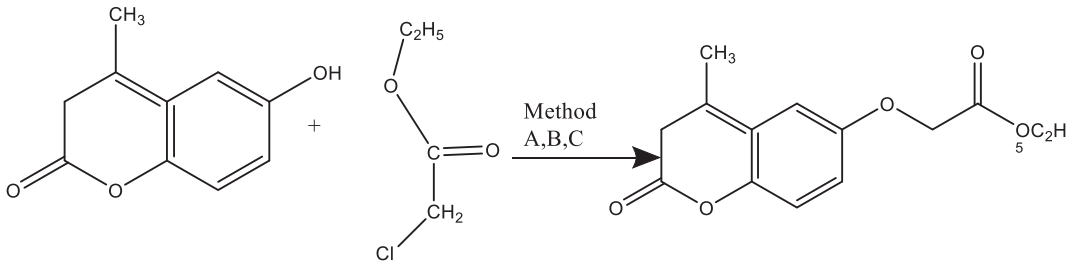


Scheme 3. Synthesis of Schiff base ligand (ShBL) L_c.

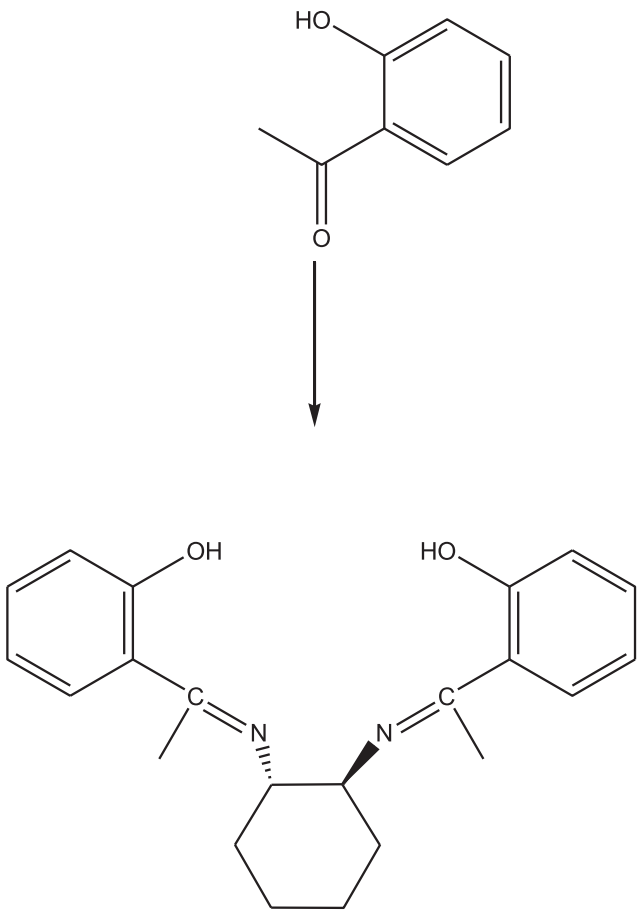
Scheme 4. Synthesis of Schiff base ligand (ShBL) L_d.



Scheme 5. Synthesis of Schiff base ligand (ShBL) L_e.



Scheme 6. Synthesis of Schiff base ligand (ShBL) L_h.



Scheme 7. Synthesis of Schiff base ligand (ShBL) L_o.

2. Importance of Schiff base in biological activities

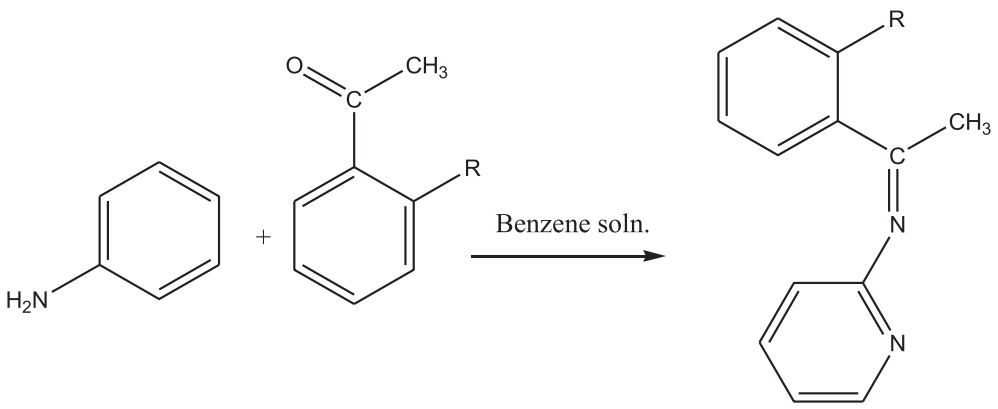
The importance of Schiff base has increased in the field of bio-inorganic studies. The transition metals are showing extraordinary reactivity towards a lot of diseases. These metal complexes are being used in the treatment of many dangerous diseases such as cancer [105]. The strength of metal complexes has an effect on chelation of the ligands. If the metal complexes are unstable, there would be no chance for them to be applied on biological mechanisms [100]. The ligands of salicylaldehyde have greater ability against antibacterial species.

It dominance has been realized in the field of biological activities. Some of them are reported as follows.

a. Antimicrobial activities

In the polar (DMSO, DMF) and non-polar (chloroform), the antimicrobial activities of the metal complexes against *N. asteroids* were studied. It is clearly shown in the given graph that all complexes of metal that were synthesized showed more activity in polar solvents than that of non-polar solvents. It was observed that when DMSO which is a polar solvent was used to study the antibacterial activity of the metal complexes it was greater in some metals such as Cu that showed greater response in the DMSO. On the other hand, in non-polar solvents Ni showed a little bit of the activity but all others were not that active.

The antibacterial activities of complexes were studied in polar and non-polar solvents against pseudomonas bacteria. Different theories (Overtone's concept and Tweedy's Chelation Theory) were used to explain about antimicrobial activities of all the complexes of metals. The concept of Overtone is that the surroundings of the cell which are lipid membranes are helpful for the lipid solubility so, it plays vital role to control antimicrobial activities. When chelated compounds are formed, metal ions reduce their polarity because of the overlapping of ligands with half-filled sharing of positive metal ions along with their donor groups. Further, π-electrons delocalization over the ring is enhanced.



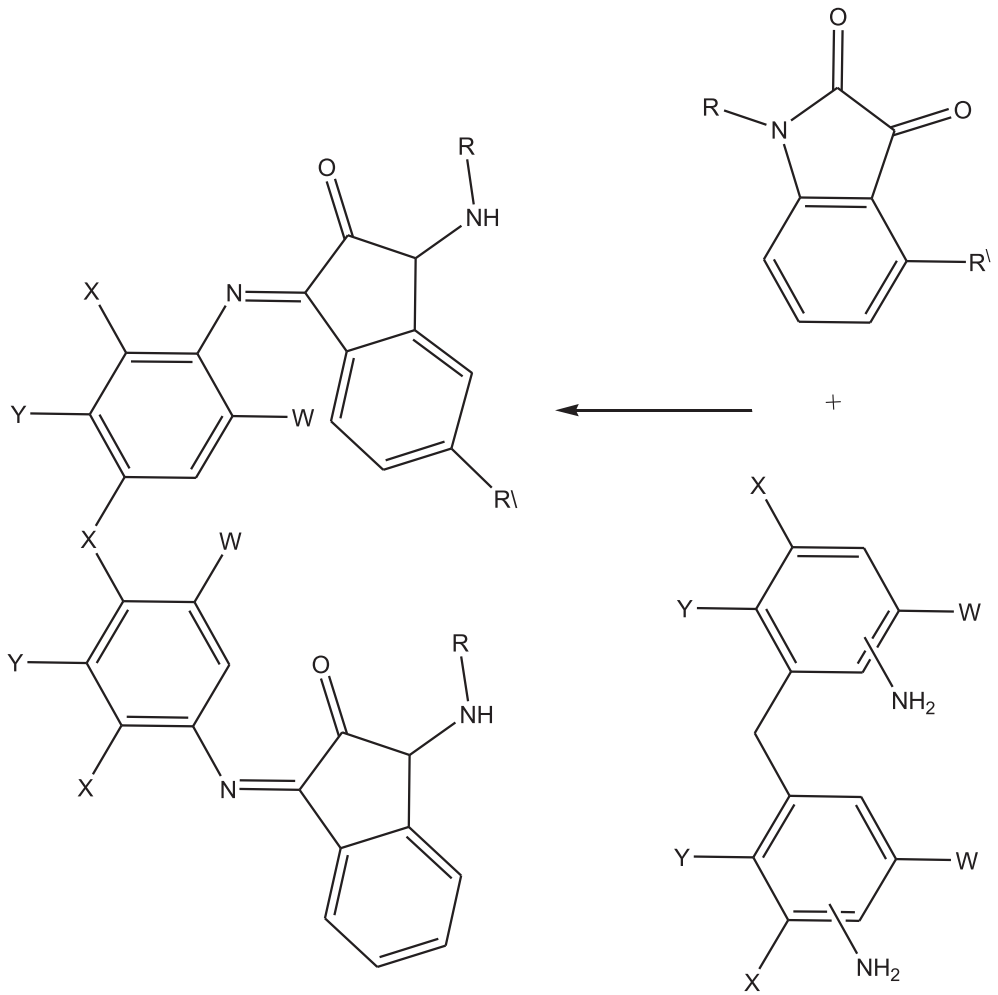
Scheme 8. Synthesis of Schiff base ligand (ShBL) L_q.

Due to this enhanced character penetration of complexes in lipid membranes is also enhanced binding sites of metal are blocked in the microorganism's enzyme. Due to all this blockage, the respiration process is also disturbed which affect the protein synthesis and further growth of organism is restricted.

b. Anti-bacterial activities

The complexes of 2-thiophene carboxaldehyde and 2-aminobenzoic acid along with metals Fe, Cu, Ni etc. shows antibacterial in oppose of bacteria like *Escherichia coli, S. pyogenes or pseudomonas aeruginosa*. It was also found that these complexes are used for the treatment of many bacterial diseases that are caused by bacteria *Escherichia Coli*. Moreover, some metals like Fe, Co, Cu were used to stop the growth of *gram-positive bacteria*. So, from all the discussion it was proved that by using any of these metal complexes of Schiff base bacterial treatment can be done in a safe way [106].

Some other metal complexes like Platinum with salicylaldehyde and 2-furaldehyde along with o- and p- phenyl anediamine were also studied against *E. coli, Bascillus subtilis staphylococcus* etc. It was confirmed by



Scheme 9. Synthesis of Schiff base ligand (ShBL) L_v.

Table 1
Particulates of ligands along with metal complexes.

Synthesized Ligand	Reaction context	Transition Metals	Structural conditions	Techniques for Characterization	Biological studies	Refs.
L_1	8 h reflux at 50° C	Ni, Cu	square planner shape	XRD, NMR, IR	Antibacterial studies	[61]
L_2L_3	5 h reflux	Co, Cr, Fe	Octahedral shape	ESR, NMR, XRD	Antimicrobial, antifungal activities	
	6 h reflux at 50° C	Fe	Distorted shape	EPR, FT-IR	Antifungal activities	[62]
L_4	8 h reflux	Cu	Square pyramidal with distortion	XRD, FT-IR	Antifungal, antimicrobial activities	[63]
L_5	3 h reflux	Co, Ni, Cu, Zn, Fe	Octahedral	XRD, UV/Vis, IR	Antibacterial activities	[64]
L_6	2 h reflux at 70° C	Zn	Distorted shape	IR, UV/Vis, XRD	Antibacterial activity	[65]
L_7	3 h reflux at 50° C	Ni	Tetrahedral shape	UV/Vis, IR	Antifungal activities	[44]
L_8	7 h reflux	Co, Cu, Mn, Zn	Square pyramidal with distorted form	NMR, XRD, MS	Antifungal, Antibacterial activities	[66]
L_9	$1\frac{1}{2}$ hour reflux	Ag	Pentagonal bi-pyramidal	UV–vis, IR,NMR	Antibacterial activities	[67]
L_{10}	Heating for 5 min.	Mo	Octahedral geometry in distorted form	ESR, XRD	Antibacterial studies	[68]
L_{11}	6 h reflux at 50–55 °C	Ni, Pd, V	Square pyramidal shape	NMR, FT-IR	Antibacterial and antifungal activities	[69]
L_{12}	Reflux for 4 h	Mn, Cu, Ni, Hg	Octahedral shape	UV–vis, FT-IR	Antibacterial studies	[70]
L_{13}	Reflux for $1\frac{1}{2}$ Hour	Sn	Pentagonal Bi-pyramidal with distortion	XRD	Antibacterial studies	[71]
L_{14}	7 h reflux	V, Cr, Ni, Cu	Octahedral geometry	FTIR	Antibacterial activities	[72]
L_{15}	Reflux for 6 h	Co, Cu, Zn	Octahedral, Square planner geometry	UV-IR, FT-IR,M.M	Antibacterial activities	[73]
L_{16}	Stirring for 16 h	Ni	Square planner shape	UV–vis, IR	Antifungal and antibacterial activities	[74]
L_{17}	Reflux for 2–2.5 h	Ni, Co, Cu, Mn	Distorted geometry	UV–vis, XRD	Cytotoxic activities	[75]
L_{18}	Reflux for 1 h	Os, Cu	Tetrahedral shape	XRD	Antifungal activities	[76]
L_{19}	Heat for 5 min.	Sn	Penta-coordinated shape	IR, NMR, UV–vis	Antimicrobial activities	[77]
L_{20}	Reflux for 8 h	W	Distorted pyramidal	XRD, IR	Antibacterial, Antifungal	[78]
L_{21}	Reflux for 4 h	Co	Distorted Square pyramid	UV–vis,IR, NMR	Antimicrobial, Antifungal	[63]
L_{22}	Reflux for 2 h	Ru	Octahedral shape	XRD, UV–vis	Antibacterial activities	[79]
L_{23}	Reflux for 1–2 h	Mo	Octahedral shape	UV,IR, NMR	Antifungal, Antibacterial activities	[80]
L_{24}						

(*continued on next page*)

Table 1 (*continued*)

Synthesized Ligand	Reaction context	Transition Metals	Structural conditions	Techniques for Characterization	Biological studies	Refs.
	Reflux for 4 h at 5 °C	Cu	Octahedral shape	CHNS, UV–vis	Antibacterial activities	[81]
L_{25}	Reflux for 40 h	Zn	Square planner shape	XRD, UV–vis, NMR	Antibacterial activities	[65]
L_{26}	Reflux for 2 h	Pb, Cu, Zn	Octahedral shape	UV/Vis, IR	Antifungal, Antimicrobial activities	[82]
L_{27}	Reflux for 5 h	Sn	Octahedral shape with distortion	NMR, FT-IR	Antifungal activities	[83]
L_{28}	Reflux for 4 h	Mn	Square planner shape	XRD, NMR	Antifungal, Antibacterial studies	[84]
L_{29}	Reflux for 3 h with continuous stirring	Zn, Co, Ni	Tetrahedral	FT-IR, NMR, UV–vis	Antibacterial, antifungal activities	[85]
L_{30}	Reflux for 3 h	Fe, Co, Cu	Octahedral shape	UV–vis, IR, RD	Antifungal, antimicrobial activities	[86]
L_{31}	Reflux for 6–7 h at 50 °C	Ni, Cu	Octahedral shape	IR, EPR, MS	Antibacterial activities	[87]
L_{32}	Reflux for 6–7 h at 50 °C	Fe	Octahedral shape	FT-IR, NMR, MS	Antifungal, Antibacterial activities	[88]
L_{33}	Reflux for 7 h	Mn, Co, Zn	Square pyramid with distortion	UV–vis, IR, EPR	Antimicrobial activities	[89]
L_{34}	Reflux for 3 h	Zn	Octahedral geometry	IR, UV–vis	Antifungal, Antibacterial	[90]
L_{35}	Stirring for 3 h	Ni	Octahedral shape	FTIR, UV–vis	Antifungal	[91]
L_{36}	Reflux for 3 h	Au	Square planner shape	UV–vis, IR, FTIR	Anticancer, Antifungal	[92]
L_{37}	Stirring for 2 h	Cr	Octahedral shape	IR, UV–vis, NMR	Antifungal, Anticancer	[93,94]
L_{38}	Reflux for 4 h	Cu	Square planner shape	NMR, IR	Antibacterial activities	[95]
L_{39}	Continuous stirring at room temperature	Ag	Linear shape	UV–vis, IR	Antibacterial, Antifungal	[96]
L_{40}	Stirring at room temperature	Fe(III)	Octahedral shape	UV–vis, H NMR	Antifungal, Antimicrobial activities	[97]

this experiment that when platinum was used as a Schiff base metal complex, it showed potential activities against microorganisms than their parent ligands [106,107]. Another complex of sulphametrole and veraldehydde was made by their condensation. It was also used against many bacterial activities such as *E. coli* [108]. This type of Schiff base and its metal complexes showed much better result against bacteria's. It was also found that outer membrane of *gram negative bacteria* contains lipopolysaccharides. The newly formed base along with its metal complexes increases the membrane permeability in the gram-negative bacteria from their lipophilic layer. Due to the presence of lipid membrane, only lipid-soluble materials can be passed and separate it. Thus, to control the antimicrobial activities lipophilicity is one of the enhanced factors. More is lipophilicity, more is the Schiff base and its complex penetration in the lipid membrane and vice versa. Due to this activity, the organism could not grow further.

A Schiff base was formed by condensation of dark orange colored ligand of potassium 2-N(4-N,*N*-dimethylaminobenzaldehyde)-4-trithiocarbonate 1,3,4-thiadiazole and complexes of Co, Ni, and Cu metal and they showed biological activities. This ligand did not show any antibacterial activity against Gram-positive and Gram-negative. The copper complex showed a little effect while using both bacteria (*Staphylococcus aureus* and *Pseudomonas aeruginosa*). A minor effect was observed with cobalt complex against gram positive but no activity was observed against gram negative bacteria. Maximum activity was observed by both the bacteria while using Ni (II) complexes [97].

c. Anti-fungal activities

With the advancement and development of science, there have been a lot of treatments revolving to treat incurable illness. One of these

Table 2
Antifungal activities of metal complexes and Schiff base ligands.

Compounds with concentrations(mm)	*A. niger*	*A. flavus*	*A. alternata*	*R. stolonifer*
Control				
25	6	7	6	*
50	5	6	5	*
100	7	9	5	5
FeCl3·6H2O				
25	*	*	*	10
50	*	9	14	11
100	*	12	14	12.5
CoCl2·6H2O				
25	12	8	24.5	10
50	15	10	26.5	12
100	17	24.5	27	15
CuCl2·2H2O				
25	*	*	*	9
50	8.5	*	*	15
100	8.5	*	*	17
NiCl2·6H2O				
25	19.5	*	*	12
50	25	10	16	19.5
100	25.5	11.5	16.5	21.5
ZnCl2				
25	12.5	*	*	10
50	20	*	*	10
100	24.5	*	*	12

* means there is no reactivity with the given fungi.

illnesses is cancer. A new technique to get rid of this danger is chemotherapy. But every treatment shows some side effects, the chemo is one of them. As broad sense of antimicrobial drugs are used, so there is a susceptibility of attaining fungal infection in patients [109,110]. In the same way a fungal disease HIV also prevailed in the same way and took away the lives of millions of innocents.

There were different types of metal complexes that were studied against fungus. A drug named cisplatin in relation with metal complexes, has the ability to treat cancerous cells [111]. Some of metals like Cu, Co, Mn were used to prepare Schiff bases that were formed from amino acids and o-pthalaldehyde. The complex was studied against three fungi. Towards all the microorganisms Cu complexes do not show any kind of activity. Co and Mn complexes show a little activity [112].

The complex of metals like Co, Cu, Zn, Ni, and Fe were studied against some fungus to find their anti-fungal activities. Four organisms were studies for anti-fungal activities such as *A. niger, A. flavus, A. alternata and R. stolonifer*. They were incubated for three days at 27 °C in the agar of potato Dextrose petri dish. The Schiff bases of tri and bidentate ligands are used to study the anti-fungal activities because they form much stable complexes. To study the anti-fungal activities DMF was used as negative control.

The complex of Fe showed greater antifungal activities in different type of fungus. But *A. niger* did not showed any activity at all. The significant activities were shown by CoCl2.6H2O against different fungus like *A. alternata*. But it showed lesser activeness towards *A. flavus, R. stolonifer* and *A. alternata* but it was inactive towards *A. niger*. It was cleared from the fact that activity of each fungi depends on its impermeability towards its cell membrane. And lipo solubility is one of the significant factor to determine the activity of fungi [113].

d. Anti-cancer activities

Any kind of bulge in the body especially on the skin belongs to the group of diseases where intemperate development of cells occur [114,115]. This is a hazardous health issue noted as a stewed condition in the whole world. Even its mild attack can cause the death of the person in every country [116]. With the development of scientific studies, the cure of this danger was created by using surgical treatments even now chemotherapy is also kept under consideration. But both of these are painful processes and can lead to death of patient with their side effects.

From last few decades, a great attempt is being made to overcome this disease by using different drugs. But nowadays, Schiff bases are considered as a powerful agent to treat cancerous patients. Scientists tried to make Schiff base complex by using rare earth metal ions and make their complexes which showed anti-cancerous effect. The anticancer effect was overcooked by using flow cytometry along with methyl thiazole tetrazolium colorimetry. They were tested against K562 bump. Later, it was proved by testing that complexes are best as anticancer agents because they can destroy the tumor's growth [117].

Some other transition metal complexes were also prepared which showed good anticancer activities especially for breast cancer. They were formed from 2-acetylpyridine along with L-tryptophan. The result was quite clear because they were best inhibitors for cell growth. The complex formed with Cd showed highest activity among the three complexes [118]. The effect of HT-29 colon cancerous cell was studied by using complexes of copper [119]. These complexes show their importance in field of drug and medicines. They are beneficial against fungi, bacteria or any other lumps in the body. Moreover, they also show their significance in bioinorganic activities [30,120,121].

Efimov et al. worked on the complex formation between Fe(III) and Co(III) and the result showed that at 30 μg mL^{-1} metal-iodide bond was the only one that prevailed the activation against phytotoxic fungi. So, it is impossible to observe this activity at lower concentration[122].

e. Anti-viral activities

Gossypol [123] Schiff base shows antiviral effect. The complexes of Ag [124] with oxidation 1 shows repression for many viruses like *cucumber mosaic virus*.

f. Anti-oxidant activities

The oxidation process is inhibited with the help of anti-oxidants. Even only small amount is effective. These materials are used to convert highly reactive species to less reactive ones. These free radicals are found in bio-compounds such as fruits [125]. anti-oxidants are considered as one of the live saving materials because all the damaged organs of human beings generate free radicals in the body. The free radicals are one of the dangerous species which can destroy living cells easily. In case of Schiff base complexes hydrogen ions can be replaced easily because they have azomethine(C═N) functional group, which alternates with OH group of aromatic ring. 4-dimethylaminobenzaldehyde is one of the key compounds that show reliable geometry for the complexes.

3. Conclusion

The most flexible and reliable ligand that has been discovered till yet is Schiff base ligand. It is considered as one of the potential fields that had increased the quest of scientist to study it with more passion and work more closely on Schiff base metal complexes. It had helped the world in the chemotherapeutic research. The variation of configuration around azomethine has uplifted the importance of coordination compounds. It was found that the metal complexes have more encouraging effect against antibacterial and antifungal activities in contrast to their parent compounds. Furthermore, due to fixed and stout geometry of the complexes had played an enormous effect on the cell membrane of the bacteria in between the lipid membranes. In fact, simulated advancements and varied structural studies of Schiff bases and its derivatives have increased the scope of coordination complexes.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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