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Biological Activity and Kinetic Study of Multidentate Schiff base Copper (II) Metal Complex of Modified Chitosan

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ABSTRACT

A novel complex of quadridentate ligand modified chitosan was synthesized by sequential attachment of Isatin (1H-indole-2, 3-Dione) copper chloride dehydrate to chitosan. Synthesized catalyst was characterized by different techniques like FTIR, ESI-MS, and Powder X-ray diffraction method. The biological activity was done using diffusion disc technique. It was found that the complex shows excellent activity towards fungi and bacteria. The catalytic activity of this catalyst was tested for the oxidation of 2-butanol by varying the temperature of system as well as concentration of substrate and catalyst. Values of activation energy have been evaluated from the kinetic data.

Keywords: Quadridentate ligand, Anti-Microbial activity, Catalyst, Oxidation, Activation energy

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INTRODUCTION

The oxidation of primary and secondary alcohols into the corresponding carbonyl compounds plays a central role in organic synthesis. Selective oxidation of aliphatic alcohols to aldehydes with molecular oxygen is presumably the most demanding transformation. A great number of new catalysts have been suggested in recent years for the "clean" oxidation of alcohols with molecular oxygen. Many of them are based on ruthenium and to a smaller extent, on palladium species in various forms. The large number of patents reflects a considerable industrial interest in the application of supported Pt-group metal catalysts, dominantly in aqueous media [1,3,4,5].

There are some reports of oxidation using molecular oxygen at ambient conditions. In a series of communications Taqui khan et al reported the catalytic oxidations of olefins, saturated hydrocarbons and amines using Ru(III) EDTA complex and molecular oxygen [6,7,8]. Mahesh Dalal et al observed that the rate of oxidation of benzyl alcohol increased linearly with increase in substrate concentration using polymer anchored Ru (III) Schiff base complex and polymer anchored Ru (III) salen complexes. [9, 10]. Anthony Theodore David reported the catalytic oxidation of Schiff base modified chitosan in the oxidation of cyclohexane [11]. Haresh G. Manyar et al reported green catalytic oxidation of alcohols in water using highly efficient manganosilicate molecular sieves. Primary alcohols are selectively oxidized to aldehydes and secondary alcohols are selectively oxidized to ketones [12] . I.R Parrey et al study the Catalytic oxidation of alcohols using polystyrene EDTA Cu(II) metal complex and Catalytic oxidation of phenols using Schiff base Cu(II) metal complex using L-histadine [13,14].

In this research article the kinetic study of 2-butanol in the oxidation reaction was reported in the presence of molecular oxygen as oxidant and Schiff base quadridentate ligand complex. The article has not been published in any journal and it is completely an original research article. Further we reported the effect of temperature, concentration on the rate of reaction.

MATERIALS AND METHOD

All the chemicals were of AR Grades and used without further purification. Medium molecular weight chitosan powder was purchased from Hi- media chemical company, Mumbai India. Isatin were purchased from Merck Mumbai India. Metal chlorides (CuCl2.2H2O) and methanol were procured from Merck, Mumbai, India.

The percentages of C, H and N were determined by a Vario EL elemental analyzer. FTIR spectra of the compounds were recorded on Perkin Elmer 1750 FTIR spectrophotometer (CT 06859 USA) using KBr pellets in the range of 4000-400 cm-1. Mass spectra were recorded using Model-Q-TOF

Micro mass ESI source. Powder X-ray diffraction was accomplished using an x-ray diffractometer (XPERT PRO PAN analytical National physical lab New Delhi) for phase identification.

Microorganisms

The target strains used for screening antibacterial and antifungal activity were procured from Jamia bioscience lab, New Delhi. The bacterial strains are Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginos, Vibrio cholerae, Escherichia coli, Staphylococcus epidermis, Eubacterium lentum, Enterococcus faecalis. The fungal strains were Candida albicans, Aspergillus flavus, Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton simii.

Preparation of test pathogens

The bacteria cultures were grown in Brain Heart Infusion liquid medium at 37 ^{0}C. After 12 h of growth, each Microorganism, at a concentration of 1 9 106 cells/mL equivalent to 0.5 McFarland Standard was spread on the Surface of Mueller–Hinton agar plates. The dilutions were made in sterile low glucose Nutrient broth. Test pathogens were spread on the test plates—Mueller Hintion agar (MHA) and 6 mm diameter well is made in the agar and test material was loaded in 500–50 lg/well concentration compared with sterile antibiotic loaded in the well in a concentration of 20 lg/well. After 24 h of incubation the zone of inhibition (mm in diameter) was measured and taken as the activity against the test pathogen.

Procedure for oxidation

The oxidation reactions were carried out at room temperature in a static reactor using molecular oxygen as the oxidant at one atmospheric pressure. The required amount of the catalyst was taken inside the reaction vessel in the set-up. The system was evacuated and the substrate along with the solvent was introduced into the system by a syringe through a rubber septum. Uniform rate of stirring was maintained. The kinetics of the reaction was followed by the uptake of oxygen using a gas burette as a function of time. Blank experiments were carried out in the absence of catalyst as well as the substrate. In both cases there was no uptake of oxygen. So in both cases reactions did not proceed.

RESULTS AND DISCUSSION

Synthesis of ligand:

Chitosan was dissolved in the dilute acetic acid in presence of base and then Stirred for 4hr.25^{0}C.It was then add to methanol solution of Isatin (5mmol) in a single necked flask and Stirred continuously in 15hrs at 30^{0}C. The Resultant red brownish suspension was filtered and was thoroughly washed with methanol and then ether. The purified product was dried under vacuum at

50^0C in 1hr.Reddish powder, yield 67%.anal calculated for $C_{14}H_{14}N_2O_5$ C ,(57.93%); H, (4.86%);N ,(9.65) ;(found (%) C, (57.00%); H ,(4.66%);N,(9.22%) [12, 14]

Synthesis of metal Complex:

5mmol of Schiff base modified chitosan was added to 5mmol of Metal salt in a flask the whole solution was magnetically stirred for 10hr. at 35^0C.The resultant green complex was washed with methanol and then dried under vacuum for 30min.Green powder yield 62% anal calculated for $C_{14}H_{14}N_2O_5CuCl_2$Exact. Mol.Wt.:424 Found(M):422.m/e: 424 [M+2H+]262.[M─Chitosan+1H+]232.[M-ChitosanCl+6H+],167.[M-ChitosanCuCl+5H+].,C,(39.59); H, (3.32); N, (6.60); Cu, (14.96); found (%) C, (39.00);H, (3.15); N ,(6.51);Cu ,(14.51);IR (K Br) cm^{-1},3200 (O-H);1620, (C═N); 1490, (C═C);1700, (C═O);M-N,M-O.(490);[23-26]. TGA:6% mass loss at 1ststage. Below100^0C, 2nd loss 50% at 400-640^0C, 3rd loss 10% at 650^0C; Crystalline index=20%.[15]

Antimicrobial activity

In vitro antimicrobial activity of the Schiff base Cu(II) metal complex on the antibacterial and antifungal activities are shown in table 1& 2 . The Schiff base metal complex was assayed by disc diffusion assay (Bauer et al. 1966). The ciprofloxacin control produced zone of inhibition was between 33.0 and 44.0 mm and fluconazole control produced zone of inhibition were between 14.0 and 18.0 mm. The prepared Schiff base were found active and gives positive results against bacterial strains viz, S. aureus, E. faecalis, E. coli, S. epidermis and B. subtilis. Further the zone of inhibition and the images of ager plates for various bacterial and fungal strains are given in fig. Staphylococcus aureus, agram positive bacteria is the most susceptible of all the bacterial strains under study. From the literature cites the mechanism for this action is due to the attachment of copper to the surface of the cell there by penetrating the external cell membrane to release copper ions, which cases death Another mechanism is the copper ions produce free radicals which the caused repturing of cell membrane. The prepared Schiff base metal complexes have been found potent against five fungal strains (C. albicans, T. simii, A. flavus, T. rubrum, T. mentagrophytes). Out of two microbial strains the Cu (II) Schiff base is found more effective in fungal strains than bacterial strain and have their zone of inhibition values very proximal to the standard values.

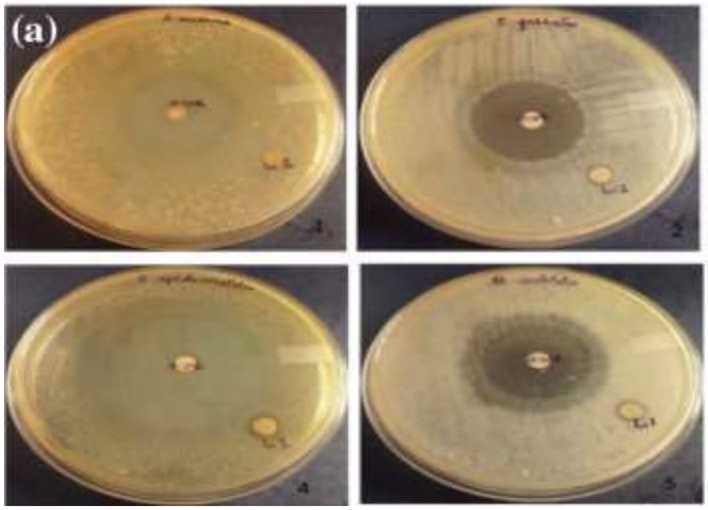

Figure 1: Images of ager plants containing synthesized Cu (II) Schiff base metal complex-bacterial strains

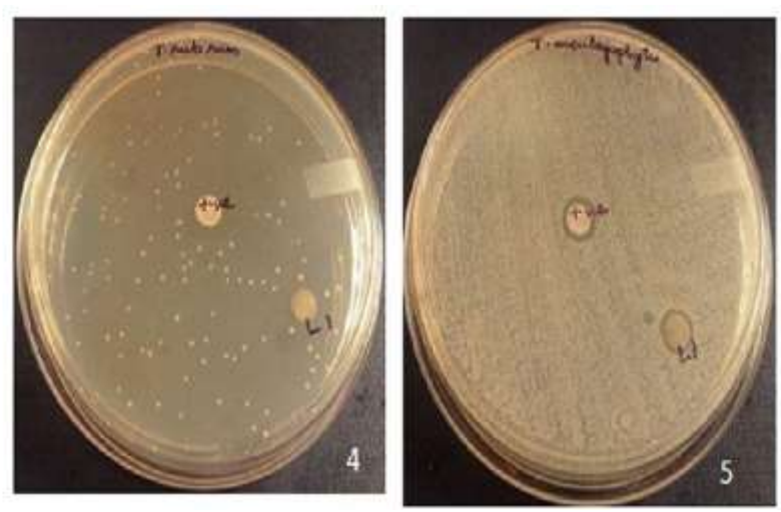

Figure 2: Images of ager plants containing synthesized Cu (II) Schiff base metal complex-fungal strains

Table 1 Antibacterial activity of synthesized Schiff base Cu (II) metal

Bacteria	**Zone of inhibition in mm Cu(II) 500µg/disc**	**positive control ciprofloxacin 5µg/disc**
Staphylococcus	22	44
Enterococcus faecalis	9	28
Escherichia coli	9	30
Staphylococcus epidermis	9	35
Bacillus subtilis	7	23
Eubacterium lentum	not active	not active
Pseudomonas aeruginos	not active	not active
Vibrio cholera	not active	not active

Table 2: Antifungal activity of synthesized Schiff base Cu (II) metal

Bacteria	**Zone of inhibition in mm Cu(II) 500µg/disc**	**positive control ciprofloxacin 5µg/disc**
Candida albicans	17	44
Tricophyton simii	12	33
Aspergellus flavus	9	32
Trichophyton rubrum	11	37
Trichophyton mentagrophytes	13	29

Catalytic Oxidation Reactions:

To evaluate the catalytic activity of the Schiff base modified Chitosan Cu (II) catalyst, the oxidation of 2-butanol was conducted using molecular oxygen as oxidant. The oxidation was studied by varying the reaction conditions. This includes the type of solvent, the temperature (35-45^{0}C) reaction time and the amount of catalyst (3.5× 10^{-5} to 14.2× 10^{-5}moll^{-1}).The Procedure of oxidation reaction was described in [16]. In the first step the catalyst was allowed to swell in the solvent for 15min. in round bottom flask to this was added 5mmol of butanol fallowed by 1atm.O2.the reaction mixture was stirred at desired temperature. A control experiment in the absence of catalyst was also conducted.

Effect of 2-butanol concentration:

The effect of substrate concentration on the rate of oxidation was determined in the Range of 4.82 × 10^{-3} to 19.3× 10^{-3}moll^{-1}at 35^{0}C and 1atm.pressure at constant catalyst concentration of 7× 10^{-5} It was found that the rate of oxidation increases linearly with increase in substrate concentration. The order of reaction was calculated from the linear plot of log (initial) rate vs. log [2-butanol] and was found fractional.Table.3

Table 3: Effect of Substrate Concentration on oxidation of 2-butanol

Cu-II Catalyst (mol lit^{-1})10^{-5}	**2-butanol (mol lit^{-1})10^{-3}**	**Rate of Reaction (ml min^{-1})**	**order**
7.12	4.83	0.35	
	9.66	0.50	0.58
	14.66	0.67	
	19.32	0.80	

At 35^{0}C,1 atmospheric pressure,20ml methanol

Effect of catalyst concentration:

The effect of catalyst concentration on the rate of reaction was studied in the range of 3.5× 10^{-5} to 14.2× 10^{-5}moll^{-1} at 35^{0}C and 1atm. Pressure at constant substrate concentration of 9.6× 10^{-3}moll^{-1}.The rate of oxidation increases with the increase in the concentration of catalyst which indicates there is no dimerisation of metal complex in the range studied and mass transfer effect could be neglected. The order of the reaction was calculated from the linear plot of log (intial) rate vs.log [catalyst]. The order was found was found fractional. Table 4

Table 4: Effect of Catalyst Concentration on oxidation of 2-butanol

2-butanol (mol lit^{-1})10^{-3}	**Cu-II(Catalyst) (mol lit^{-1})10^{-5}**	**Rate of Reaction ml min^{-1}**	**Order**
9.65	3.56	0.4	
	7.12	0.5	0.49
	10.68	0.6	
	14.24	0.7	

At 35^{0}C, 1atmospheric pressure, 20ml methanol

Effect of Temperature:

Catalytic oxidation of 2-butanol was studied in the range of 35to 45^{0}C at a fixed catalyst concentration 7× 10^{-5}moll^{-1}and substrate concentration 9.6× 10^{-3}moll^{-3} at 1atm pressure. The rate of reaction increased with increase in the temperature. The energy of activation was calculated from the plot of log (initial) × 1/T. The activation energy was found to be 32.39kj/mol. Table 5.

Table 5: Effect of Temperature on oxidation of 2-butanol

Temp.(C^o)	**Rate of Reaction(ml min^{-1})**	**Energy of Activation(KJmol^{-1})**
25	0.31	
30	0.40	32.39
35	0.50	
40	0.62	

At 35^{0}C, 1atmospheric pressure, 20ml methanol

CONCLUSION

1. Novel synthesis of quadridentate ligand of copper metal complex was successfully synthesized. The complex was characterized by different spectrochemical techniques like FT-IR,ESI-MS, Powder XRD.
2. The catalytic reaction of complex were done in the oxidation of 2-butanol.The effect of various parameters like effect of temperature, effect of catalyst, effect of substrate was also reported.
3. It was found that the complex is a suitable source in caring out oxidation of 2-butanol.
4. The oxidant used in the oxidation is molecular oxygen. The kinetic data suggested that rate of reaction is fractional order with respect to catalyst and fractional order with respect to substrate . Activation energy were also calculated from kinetic data.
5. The catalyst can be used up to four times in the same reaction without significant loss of yield but after fourth run significant loss in the yield occurs.

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