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SYNTHESIS OF TRANSITION METAL ION COMPLEX OF 2-AMINOBENZOXAZOLE AND ANTIFUNGAL ACTIVITY AND ROLE IN PHARMACEUTICAL CHEMISTRY

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Abstract:
In view of the fact that a large number of derivatives of benzoxazole have been found to exhibit a wide variety of antimicrobial activities. Heterocyclic compounds play an important role in medicinal chemistry and exhibit wide range of biological activities in pharmaceutical chemistry. Complexes of 2-aminobenzoxazole (L) with chloride of iron (II), was synthesized. The molar ratio metal: ligand in the reaction of the complex formation was 1:2. It should be noticed, that the reaction of all the metal salts yielded bis (ligand) complex of the general formula M (L) 2(CL) 2. The complex was characterized by elemental analysis, melting point, FT-IR, 1H NMR, spectral data. The antifungal activity against different fungai, A.niger, A.flavus, Fusarium oxysporum, paecilomyces variotii, C.albicans.

Keywords: *2-Amino Benzoxazole; Antifungal activity; fe(II).*

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1. Introduction

The derivative of benzoxazole is 2-amino benzoxazole is present in compounds involved in research aimed at evaluating new metal ion complex that possess interesting biological activities like antimicrobial activities. Benzoxazoles derivative have been reported to show a broad range of biological activities. Notable among these are antiviral, antifungal and antibacterial activities, etc. The approach to practice medicinal chemistry has developed from an empirical one involving organic synthesis of new compound, based largely on modification of structures of known activity1. According to Manfred Wolf, present development of medicinal chemistry has resistance, stating that "underlying the new age in foundation that includes explosive development of molecular biology since 1960, the advances in physical chemistry and physical organic chemistry has made possible by high speed computers and new powerful analytical methods. Numerous heterocyclic compounds, cyclic anhydrates, cyclic imides, cyclic acetals of dihydroxy alcohols, the solvents, dioxanes and tetrahydrofuran, in all of these, the chemistry is

essentially that of their open-chain analogues. Heterocyclic intermediates are being used more and more in synthesis as protecting groups, readily generated, and readily removed2.

Benzoxazole moieties have attracted special attention in chemistry and biochemistry. These heterocycles show various pharmaceutical properties such as antiviral, antibiotic, antibacterial, antifungal, antitumor, anti-inflammatory, antiulcer, antitubarecular, and analgesic activities. Furthermore, some of them have found applications as fluorescent whitening agents, a number of methods have been reported for the preparation of these heterocycles including the condensation of carboxylic acids, orthoesters, acid chlorides, nitriles amides, aldehydes and esters with o-substituted amino aromatics derivatives from orthoesters3. Generally in the pharmaceutical field, new drugs are continuously discovered by molecular modification of lead compound of established activity. Molecular modification can possibly result in augmenting the activity4. Molecular modification involves combination of separate group having similar activity in one compound by eliminating, substituting or adding new moiety to parent lead compound. In the survey of literature, it is seen that drug design by molecular modification is a productive source of new drug; therefore the need to synthesize new molecules as potential medicinal agents is more relevant today10. Among medicinal agents, there is growing interest in the development of newer, effective antifungal and antimicrobial agents. Among the variety of compounds studied, benzoxazole derivatives form an important class5.

The prominent role of 2-amino benzoxazole in biological activity. Keeping the above facts in mind our present paper involves synthesis and antifungal activity of Fe (II) complex with ligand 2-amino benzoxazole. The prepared compounds show antifungal activity.

2. Material and Methods

All the reagents and solvents used were of sigma Aldrich or use after distillation. Preparation of complex-the complex was prepared by refluxing for two hours, the respective metal chiloride with ligand in 1:2 molar ratio in etanolic medium on concentrating, the complex so formed was suctioned, filtered, washed with alcohol and dried in vacuo on the basis of analytical data the complex was found to possess molecular formulae ml2x2 where m=fe(II),l2=2-aminobenzoxazole and x2=cl.

Table 1: Elemental analysis data

Complex	**%Found/Calcu.**						
	C	**H**	**N**	**O**	**Cl**	**M.P.**	**SOLUBILTY**
$[Fe(C_7H_6N_2O)_2]Cl_2$	42.28	4.61	13.34	16.99	15.36	120.c	Ethanol
	(42.3)	(4.59)	(13.32)	(16.96)	(15.38)	-	-

The metal complex was analysed using standard procedure 8-15. The IR Spectra of the metal complex was recorded on Spectrophotometer employing KBr pellets (“FTIR-Imaging System”). And CHNO, 1HNMR spectra recorded on (CHNO) Elemental Analyzer, Nuclear Magnetic Resonance Spectrometer 1HNMR spectra of complex were recorded in DMSO at SAIF, I. I. T Mumbai.

Table 2: I.R. spectral data of Ligand and its Metal Complex

Ligand	Fe(II)	Tentative assignment
3050	3153	V C-H
3336	3336	vN-H
1618	1618	vC=C
1661	1661	vC-O
1251	1251	vC-N
-	261	vM-Cl
-	360	vM-N

Table 3: Physical data of compound

Compound	M.P.(oC)	Yield (%)	Molecular Formula
1.	120 oC	90%	$[Fe(C_7H_6N_2O)_2]Cl_2$

Table 4: 1HNMR Spectral data of compound

Protons	NMR Spectra (DMSO)
ArH	6.8-8.0
NH2	3.5-6.0

2.1. Antimicrobial Investigations

Disc-diffusion technique

Antimicrobial activity of the synthesized compound was tested by the disc-diffusion technique. Disc-diffusion technique- It is type of quantitative analysis and is done by using Kirby-Bauer method to determine the antimicrobial activity of a compound at a fixed concentration6.

Media

The potato dextrose broth and potato dextrose agar media employed in fungal studies were prepared dissolving the required amount of individual component of the subjective media in distilled water and then autoclaved at 115-121^{o}c for 20 mnts7.

Preparation of discs

The discs were prepared by cutting the Whatman's filter paper through the sterilized paper punch machine in order to get the same diameter and then autoclaved and dried 60^{o}c for one hour.

Test

For the growth of microorganism pour plate method was used. In this method 1ml of defined density of microbial pure culture suspension was poured into 90 mm glass Petri plates (Borosil, India) and spread by L-spreader after that add autoclaved media poured, and left to solidify under laminar air flow. After solidification of media was the sterile filter paper disc, impregnated with fixed dose viz.10mg/ml,1mg/ml,100µg/ml,10µg/ml,1µg/ml. Of the compound were placed on the plate keeping equal distance between them with the help of sterilized forceps.The plates were incubated for 24hr at 37^{o}c for the fungal strains.

Measurement zone of inhibition

The diameter of the clearing zone appeared encircling the discs were measured as zone of inhibition in mm. The diameter of zone of inhibition is directly proportional to the degree of sensitivity of the fungal strains and concentration of compound under test. The data of antifungal activity reveals that, with the increase in concentration of drug, increase in zone of inhibition occur in petridish8.

2.2. Biological Activity

The synthesized compounds were screened for antimicrobial activity by zone of inhibition method. Antifungal activity was observed for the complex using five strains of fungai A.niger, A.flavus, Fusarium oxysporum, paecilomyces variotii, C.albicans9.

Table 5: Antimicrobial activity data 10 mg/ml solution in DMSO, serially diluted, used 50 µl for test

Test Fungai	10 mg/ml	1 mg/ml	100 µg/ml	10 µg/ml	1 µg/ml	NC
Fe Compound	Zone of inhibition in mm					
A.niger	18	15	13	11	8	0
A.flavus	18	16	10	8	6	0
Fusarium oxysporum	16	14	12	10	8	0
paecilomyces variotii	20	18	16	12	8	0
C.albicans	22	18	16	10	6	0

3. Results and Discussion

The IR spectrum of metal complex has been recorded in table 2. It is the spectra of metal complex. The band appearing in the region 3153 and 1618 cm^{-1} are assigned to v(C-H) and v(C=C) vibration, respectively and are suggestive aromatic character of the complex .The band appearing in the region 1251, 3336, 260-265 cm^{-1} due to the presence of v(C-N), v (N-H) and v (M-Cl) vibrational mode respectively, band at region 1661 cm^{-1} assignable to v(C-O) frequency. In the metal complex amino group shows shift suggesting the coordination of nitrogen with metal ion. Chloro complex of Fe (II) in possess characteristic band of v (M-Cl) and v (M-N) which is observed at 280 and 260-370 cm^{-1} respectively. The purity of the synthesized compounds were confirmed by their sharp melting point Also some 1H NMR spectra were useful for some protons in the compounds such as δ 6.80-8.0 ppm indicates the presence of phenyl ring protons and $ArNH_2$ δ 3.5-6.0 ppm occasionally raised lines usually broadened.

4. Conclusions and Recommendations

In view of eradicating microbial infections and the present research work shows that the synthesized compound have a significant role, the research work are important extension of the existing knowledge in the field of mixed ligand complexes. This heterocyclic compound active against different fungai A.niger, A.flavus, Fusarium oxysporum, paecilomyces variotii, C.albicans. The synthesized compounds were screened for antimicrobial activity by zone of inhibition method.

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