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ANTIMICROBIAL ACTIVITY OF NICKEL(II) COMPLEX WITH 2-AMINOBENOXAZOLE AND SALICYLIC ACID

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ABSTRACT
Heterocyclic compounds play an important role in medicinal chemistry and exhibit wide range of biological activities. Nickel(II) chloride reacts with 2-aminobenzoxazole and co-ligand salicylic acid to give mixed ligand complex of the formula $[NiL_2Cl_2]$, where L=2-aminobenzoxazole and salicylic acid. The antimicrobial activity of the complex against E.coli ATCC25922,Salmonella abony ATCC6017, Pseudomonas aeruginosa ATCC27853, Staphylococcous aureus ATCC25923, Bacillus subtilis ATCC11774. Benzoxazole derivative have been reported Antibacterial activity and antifungal activity. The minimum inhibitory concentration (MIC) was determined for the complex . It was found that tested compounds were more active against gram-positive slightly active to gram-negative bacteria and antifungal activity against different fungai A.niger ATCC16888, A.flavus MTCC9606, Fusarium oxysporum MTCC1755, paecilomyces variotii MTCC2040 C.albicans ATCC10231.

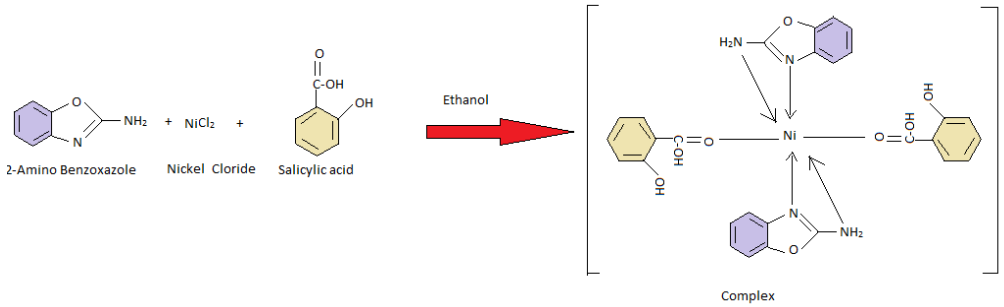
KEYWORDS: 2-amino Benzoxazole , Antibacterial activity , Antifungal activity, Ni(II).

INTRODUCTION

The approach to the study and design of medicinal agents has centered primarily on the gross chemical structure of natural and synthetic compounds having established biological action. Benzoxazole and its derivative 2-aminobenzoxazole are interesting heterocycles because of their antimicrobial activity. It has been found that they possess antibacterial(I), antifungal, antihistaminic, cytostatic, local analgesic, hypotensive(II) and anti-inflammatory activity(III). It was confirmed to have a moderate in vitro anti-HIV activity(IV). In recent years, transition metal complexes have attracted particular interest because of their potential use in several biological processes. However, in the recent time, possible therapeutic properties of the metal complexes have been examined. It was found that the complex of transition metal with 2-aminobenzoxazole showed a higher antimicrobial activitiy(V). Following our studies of the reactivity of 2-aminobenzoxazole with metallic chloride(VI), we evaluated the antimicrobial activity of this type of complex in this study. We report in vitro antimicrobial activities of 2-

aminobenzoxazole and their nickel(II) complex against three gram-positive and two gram-negative becteria(VII). Modifications of the basic structure are obtained by chemical synthesis and the effect of these change in biological response are used to compile structure activity relationship. These relationships are intended to serve as a guide in the interpretation of the structural feature essential for a given type of drug activity and also in the design of new agents of similar biological activity(VIII). A currently promising approach is the attempt to relate certain physio chemical properties of drugs to their mode of action which leads to an understanding of drug action or result in the development of more effective drug(IX).

REACTION SCHEME--



MATERIAL AND METHODS

The present investigating studies includes the chemistry and application of highly interesting and significantly useful oxygen and nitrogen molecules(X).

Reagents

All chemicals used to prepare the ligands and complex were of analytical reagent grade, commercially available from different sources. The ligands were synthesized as described in the literature(XI).

Preparation of complex

The complex was prepared by refluxing for two hours, the respective metal chloride with ligand in 1:2:2 molar ratio in ethanolic medium on concentrating, the complex so formed was suctioned, filtered, washed with alcohol and dried in vacuum over $CaCl_2$ (XII) On the basis of analytical data the complex was found to possess molecular formulae ml_2x_2 where m=Ni(II),l_2=2-aminobenzoxazole and salicylic acid x_2=cl(XIII).

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 determined the antimicrobial activity of a compound at a fixed concentration(XIV).

Media

The media employed in bacteriological studies were prepared dissolving the required amount of component of the subjective media .media for bacteria is Nutrient Broth and Nutrient Agar(XV).

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 discs, 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 bacterial 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 bacterial strains and concentration of compound under test. The data of antibacterial activity reveals that, with the increase in concentration of drug, increase in zone of inhibition occur in petridish(XVI).

RESULTS AND DISCUSSION

The antimicrobial activity of the Ni(II) mixed ligand complex of 2-aminobenzoxazole and salicylic acid was tested first by the agar disc-diffusion method against gram-positive and gram-negative bacteria and also fungai. The results of these studies are summarized in Table 1 and Table 2.

Table 1
Antibacterial activity

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10 mg/ml solution in DMSO, serially diluted, used 50 µl for test						
Test Bacteria	10 mg/ml	1 mg/ml	100 µg/ml	10 µg/ml	1 µg/ml	NC
Ni Compound	**Zone of inhibition in mm**					
E.coli ATCC25922	20	15	11	10	8	0
Salmonella abony ATCC6017	18	10	10	8	0	0
Pseudomonas aeruginosa ATCC27853	28	20	13	10	8	0
Staphylococcous aureus ATCC25923	22	20	15	11	10	0
Bacillus subtilis ATCC11774	20	15	14	10	8	0

Table 2
Antifungal activity

Organism	serial dilution 10 mg/ml solution in DMSO, serially diluted, used 50 µl for test					
Ni Compound	10mg/ml	1mg/ml	100µg/ml	10µg/ml	1µg/ml	NC
Fungai	**Zone of inhibition (in mm)**					
A.niger ATCC16888	14	12	10	8	6	0
A.flavus MTCC9606	18	12	10	8	6	0

Fusarium oxysporum MTCC1755	20	12	10	8	8	0
paecilomyces variotii MTCC2040	12	10	8	8	0	0
C.albicans ATCC10231	12	10	8	6	0	0

From the data given in Table, it is clear that the tested compounds were more active against gram-positive bacteria than against gram-negative Pseudomonas aeruginosa. It may be concluded that the antimicrobial activity of the compounds is related to cell wall structure of the bacteria.The zone of inhibition of Fusarium oxysporum higher than the zone of inhibition of A.flavus in the same concentration. Considering of the structural formula of the compounds that exhibited antimicrobial activity, it can be concluded that nickel (II) complex of 2-aminobenzoxazole and salicylic acid may play a role in the antimicrobial activity(XVII).

CONCLUSIONS

Nickel(II) chloride reacts with 2-aminobenzoxazole and salicylic acid to give mixed ligand complex of the formula $[NiL_2Cl_2]$, where the nickel(II) complex were evaluated for their in vitro antimicrobial activity against E.coli ATCC25922, Salmonella abony ATCC6017, Pseudomonas aeruginosa ATCC27853, Staphylococcous aureus ATCC25923, Bacillus subtilis ATCC11774. It was found that the tested compounds were more active against gram positive than gram-negative bacteria. nickel (II) complex of 2-aminobenzoxazole and salicylic acid are play important role in antimircrobial activity in the different type of bacteria. This compound shown that it is highly active against bacillus subtilis than other on the 10mg/ml concentration , at the same concentration E.coli and Pseudomonas aeruginosa , are similarly active. The zone of inhibition of Fusarium oxysporum higher than the zone of inhibition of A.flavus in the same concentration 10mg/ml. On considering the structural formula of the compound that exhibited antimicrobial activity, it can be concluded that nickel (II) complex of 2-aminobenzoxazole may play a role in the antimicrobial activity.

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