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Antimicrobial Activity Of Thiosemicarbazone Derivatives Of Lawsone And Its Nickel Complexes

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ABSTRACT

Thiosemicarbazone derivative at 1 and 2 position of the Biologically important Lawsone (2-hydroxy-1,4-naphthalenedione) have been synthesized. This possesses a powerful chelating ability, appreciable analytical utility and significant biological activity. Metal complexes of TSCND with Ni(II) metal have been synthesized and studied with the help of spectral analysis and elemental analysis. The antimicrobial activity of the ligands and their metal complexes against bacteria and fungus has been carried out. It is found that the metal complexes have higher activities than those of free ligands.

Keywords: Lawsone, Thiosemicarbazone derivative, Nickel (II) complex and microbial Studies

INTRODUCTION

Naturally occurring quinones have several different roles in organisms, they are functional constituents of several biochemical systems (e.g. ubiquinones and vitamin K₁), they are dyes or they act as defensive compounds. Quinones are used as pharmaceuticals. The exposure of cell to quinonidal compounds may lead to several deleterious consequences. Chronic exposure to quinones may be carcinogenic; several quinones are mutagenic in the Ames test as well as to cultures of eukaryotic cells. Acute exposure to quinones may cause cell death. Several anticancer drugs contain the quinone part (figure 1) and adramycin, a synthetic quinone is useful in cancer chemotherapy .

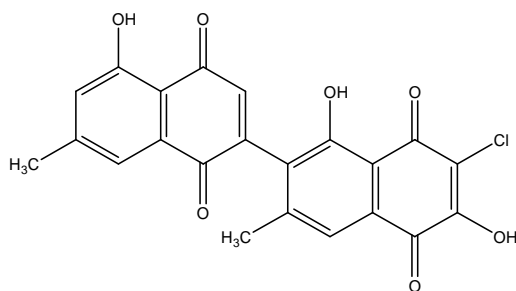


Figure 1. 1,4-naphthoquinones as a part

Quinone compounds are known for their antibacterial activity. This peculiarity is well exhibited in the compounds of our interest i.e. 1,4-naphthoquinones, which are vitamin K₃ analogs (figure 2).

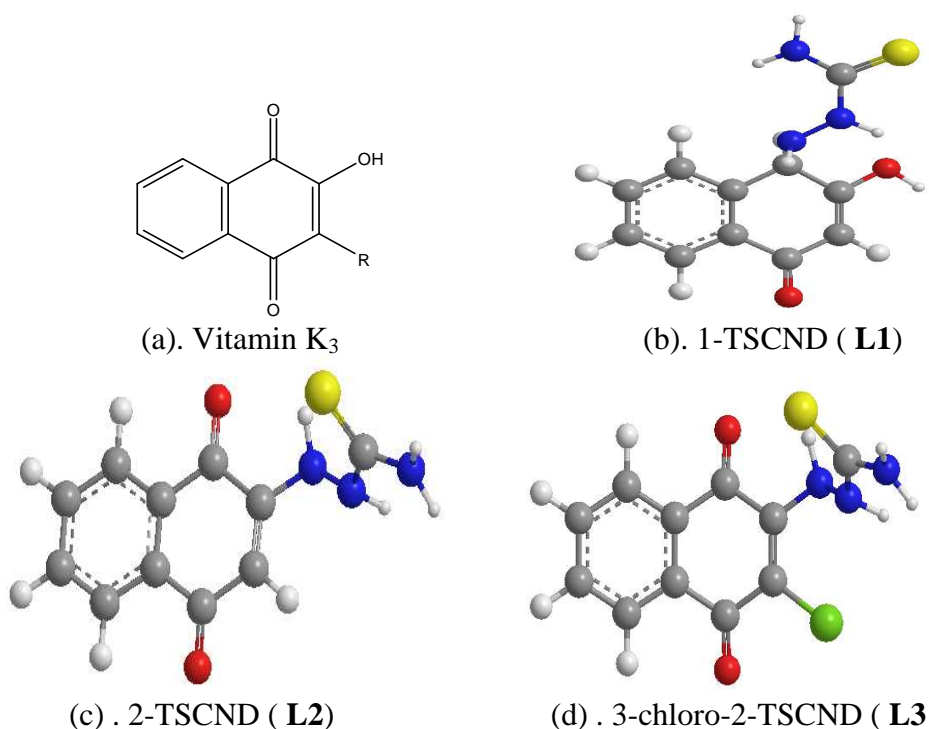


Figure 2. Vitamin K₃

In our laboratory, several derivatives of hydroxyl- naphthalenediones and their metal complexes have been studied, particularly with their antimicrobial and antifungal activity. The complexes with sulphur, nitrogen and oxygen impart special biological activity [1-4], particularly thiosemicarbazone derivatives [5-9]. The inhibitory action of these compounds is given to their chelating properties [10-16]. In the present work the antimicrobial study of thiosemicarbazone derivative of Lawsone [17] and its complexes with Ni(II), where the change of ligating system from O O , O N to O N S. is studied.

The antimicrobial activity study of all the compounds can be studied from following microorganisms.

<i>Bacteria</i>	<i>Microorganisms</i>
Gram Positive Bacteria	Bacillus Subtilis, S. Aureus
Gram Negative Bacteria	Escherichia Coli
Fungal Strain	Aspergillus Niger
Fungal Strain	Penicillin

Media

Nutrient Agar :-

It is prepared by weighing exactly 28.0 gm of Nutrient Agar, which is purchased from HIMEDRA and get dissolved to 1000 ml of distilled water. The pH of the solution is adjusted to 7.0 with the help of dil. HCl or NaOH solution. Then the solution is heated to boil. After boiling this solution, it is sterilize by using Autoclave at 121°C for *ca.* 20 min.

Nutrient Broth :-

It is prepared by weighing separately (10.0 gm of Beef extract, 10.0 gm of Peptone and 5.0 gm of Sodium Chloride) ingredients and dissolving to 1000 ml of distilled water. The pH of the solution is adjusted to 7.0 with the help of dil. HCl or NaOH solution. . Then the solution is heated to boil. After boiling this solution, it is sterilize by using Autoclave at 121°C for *ca.* 20 min.

The stock culture of these microorganisms were maintained at 20°C in 15% glycerol. The inoculums were prepared from stock culture by streaking into the plate count agar for bacteria and on Sabourauds dextrose agar for fungi. After an overnight incubation single colony was used to inoculate sterile liquid media. The 5 ml broth was dispensed in test tube and sterilized in the autoclave at 120°C for 15 min. The broths were then inoculated with respective culture and incubated on an orbital shaker (150 rpm) overnight at 30°C

Well Diffusion Method

The wells of 5 mm diameter were made in the agar set in Petri dish previously spread with 50 µl of test compounds. The plates were pre-incubated for 2 hours at 4°C and then incubated for 18 hours at 37°C. For Aspergillus Niger, the incubation was done for 72 hours at room temperature. The zone of inhibition was then measured. The control experiments were performed using equivalent volume of the solvent itself loaded in to the wells. All the values of inhibition zone are average of three replicate experiments. The standard deviation of all values was within 5 % of arithmetic mean.

RESULTS AND DISCUSSIONS

The antimicrobial activity of thiosemicarbazone derivatives of Lawsone at 1 and 2 position and their Nickel (II) complexes with 1:1 and 1:2 ratio were evaluated against

<i>Bacteria</i>	<i>Microorganisms</i>
Gram Positive Bacteria	S. Aureus
Gram Negative Bacteria	Escherichia Coli
Fungal Strain	Penicillin

Dichlone was used as a standard, while DMF, Nickel (II) acetate were used as control. Some representative photographs showing inhibition zones.

The ligand thiosemicarbazone derivatives synthesized for present work shows the activity against all the bacteria and fungi strains studied. This observation tend to suggest that the thiosemicarbazone derivative at 2 position (L2 and L3) shows more prone for binding with target molecules of organisms thus retarding the growth. Another reason may be intermolecular hydrogen bonding probably promoting the proper binding with growth promoting biomolecules. The ligand (L1) and their Ni complex show very law activity.

Compounds:

1. 1-TSCND (L1), 2. 2-TSCND (L2). 3. 3-Cl-2-TSCND (L3)
4. Lawsone, 5. Dichlone 6. Ni(II) complex with 1-TSCND [ML₁]Ac
- 7 Ni(II) complex with 1-TSCND [M(L₁)₂]
8. Ni(II) complex with 2-TSCND [ML₂]Ac
9. Ni(II) complex with 2-TSCND [M(L₂)₂]
10. Ni(II) complex with 3-Cl-2-TSCND [ML₃]Ac
11. Ni(II) complex with 3-Cl-2-TSCND [M(L₃)₂]

Microorganisms

1. Gram +ve A-SA, B-SA, C-SA and D-SA
2. Gram -ve A-EC, B-EC, C-EC and D-EC
3. Fungal A-F, B-F, C-F and D-F

The compounds were kept in the medium as A, B, C and D for the comparison. The observed zones are as given in photographs.

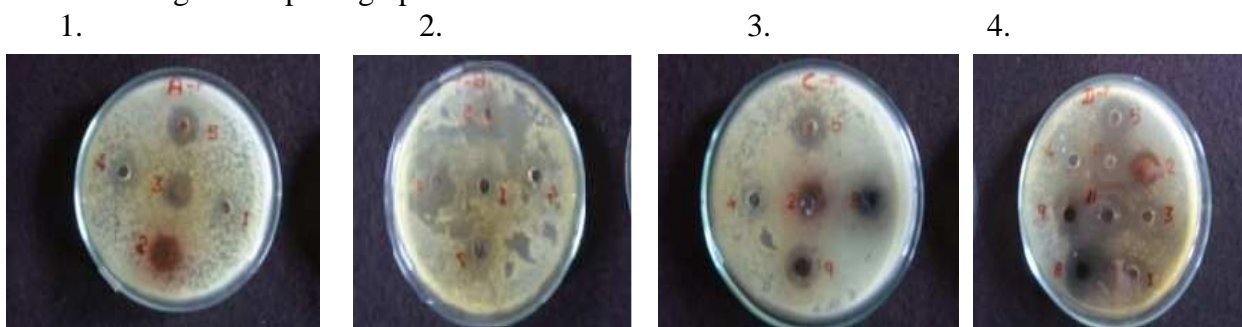


Figure 5.2. Fungal Strain - Penicillin

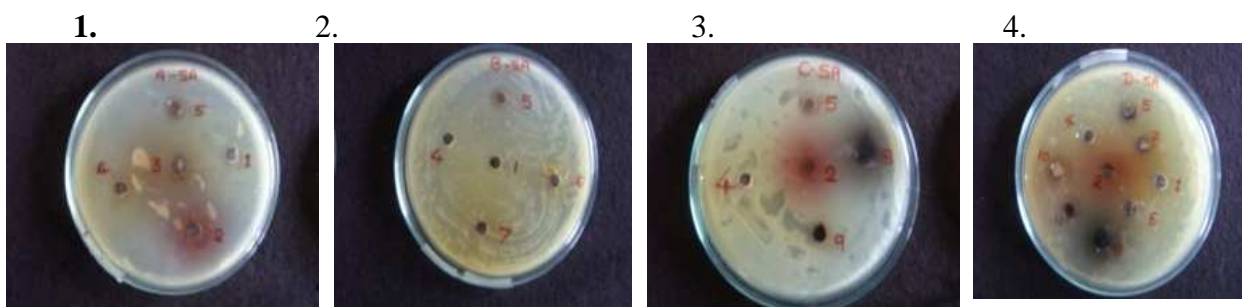
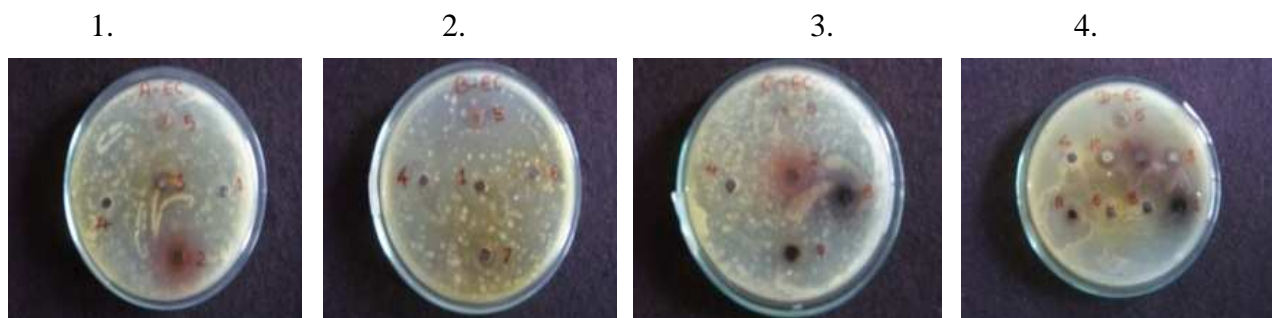


Figure 5.3. Against Gram Positive Bacteria - S. Aureus

**Table 5.2 Inhibition zones measured after 24 hours**

Sr. No.	Compound	Antibacterial		Antifungal
		Gram +ve	Gram – ve	
1	1-TSCND	6	08	12
2	2-TSCND	20	12	20
3	3-Cl-2-TSCND	10	09	15
4	Lawsone	08	06	12
5	Dichlone	08	10	15
6	Ni(1-TSCND)Ac	07	09	12
7	Ni(1-TSCND) ₂	06	08	10
8	Ni(2-TSCND)Ac	15	12	18
9	Ni(2-TSCND) ₂	08	09	18
10	Ni(3-Cl-2-TSCND)Ac	10	15	15
11	Ni(3-Cl-2-TSCND) ₂	09	12	20
12	DMF (control)	06	06	06
13	Ni(II) acetate	06	06	06

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