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A STUDY TO EVALUATE THE *IN VITRO* ANTIMICROBIAL ACTIVITY AND ANTIANDROGENIC EFFECTS ON RATS OF Cr (III) COMPLEXES OF S^{II}N DONOR LIGANDS

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ABSTRACT: The present paper deals with synthesis and characterization of some new chromium (III) Schiff base complexes using microwave irradiation technique as well as conventional heating. The S^{II}N donor benzothiazolines, 1-(2-furanyl) ethanone benzothiazoline (Bzt₁N^{II}SH), 1-(2-thienyl) ethanone benzothiazoline (Bzt₂N^{II}SH) and 1-(2-pyridyl) ethanone benzothiazoline (Bzt₃N^{II}SH) were prepared by the condensation of ortho-aminothiophenol with respective ketones in ethanol. The chromium (III) complexes have been prepared by mixing CrCl₃.6H₂O in 1:1 and 1:2 M ratios with benzothiazolines. The structure of the ligands and their transition metal complexes were confirmed by the elemental analysis, melting point and molecular weight determinations, IR, ¹H NMR, electronic, EPR spectral studies. On the basis of these studies an octahedral environment around the chromium (III) ion has been proposed. The *in vitro* antimicrobial and *in vivo* antifertility activities of Schiff base ligands and their respective chromium (III) complexes were performed on pathogenic bacterial and fungal strains and male albino rats respectively. The results indicated that the complexes showed higher activity than the parent ligands.

INTRODUCTION: Over the past few years, pharmaceutical and chemical industry is continuously searching for technologies that make synthesis easier and faster in large scale. The present day industrialization has led to immense environmental deterioration.

The increasing environmental consciousness throughout the world has put a pressing need to develop an alternate synthetic approach for biologically and synthetically important compounds.

This requires a new approach, which will reduce the material and energy intensity of chemical processes and products, minimize or eliminate the dispersion of harmful chemicals in the environment in a way that enhances the industrially benign approach and meets the challenges of green chemistry¹. Green chemistry is defined as the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products.

Microwave-assisted synthesis is a branch of green chemistry. Microwave synthesis represents one of the important dimensions of modern chemistry attracting a considerable amount of attention². The use of microwave ovens in chemical synthesis and analysis has increasingly grown in importance, due to its ability to dramatically reduce reaction times, improve yield, and simplify procedures³.

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Schiff bases and their complexes have numerous applications, e.g., anticancer, antibacterial, antiviral, antifungal, and other biological properties⁴. Benzothiazole and their derivatives are well known biologically active compounds^{5, 6}. 2-Arylbenzothiazoles are a class of molecules which possess an interesting variety of biological activities⁷⁻⁹. They are a class of potent and selective antitumor agents which exhibit nanomolar inhibitory activity against a range of human breast, ovarian, colon and renal cell lines *in vitro*¹⁰.

Much research has been devoted¹¹⁻¹³ to study the metalloorganic and biological behavior of such derivatives containing the azomethine (>C=N) linkage. The biological activity of these compounds may be connected to their ability to form complexes with certain metal ions which may lead to a "locked geometry" via the coordination mechanism so that only certain substances are able to become attached to the framework of this interaction. The metal complexes of such type of ligand systems exhibit interesting metal–nitrogen and metal–sulfur bonding features with increased electron delocalization which may lead to improved biological activity¹⁴.

Biological roles of chromium are surrounded by controversy¹⁵. By contrast, most nutritionists regard chromium (III) as an essential micronutrient, acting as an insulin activator¹⁶⁻¹⁷. In order to understand in more detail the biological behavior of the same Schiff bases we have coordinated these

with other transition metal Cr (III). It is expected that this alteration may result in achieving new targets in synthesizing and designing new metal-chelated compounds that could fight more aggressively antibiotic resistant strains.

In this paper, we therefore wish to report the synthesis, characterization and antimicrobial properties of some new chromium (III) complexes of biologically potent S^{II}N donor azomethines.

MATERIALS AND METHODS: The CrCl₃.6H₂O was purchased from Alfa Aesar. All the reagents were dried and distilled before use. 1-(2-furanyl) ethanone, 1-(2-thienyl) ethanone, 1-(2-pyridyl) ethanone and ortho-aminothiophenol were purchased and used as such.

Preparation of the ligands: The benzothiazoline ligands, 1-(2-furanyl)ethanone benzothiazoline (Bzt₁N^{II}SH), 1-(2-thienyl)ethanone benzothiazoline (Bzt₂N^{II}SH) and 1-(2-pyridyl)ethanone benzothiazoline (Bzt₃N^{II}SH) were prepared by the condensation of 1-(2-furanyl)ethanone (0.02 mol), 1-(2-thienyl)ethanone (0.02 mol) and 1-(2-pyridyl)ethanone (0.02 mol) with 2-mercaptoaniline (0.02 mol) in 1:1 M ratio using ~100 mL alcohol as a solvent. The reaction mixture was stirred for 3–4 h, and the resulting product was filtered off, recrystallized from ethanol, and dried in vacuum. The structures of ligands are shown in Fig. 1.

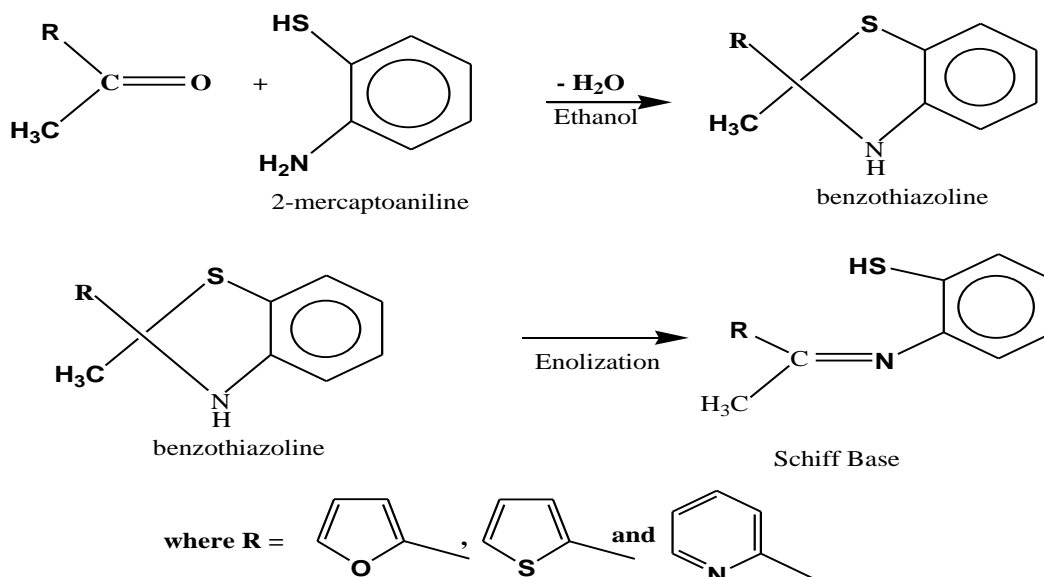


FIG. 1: STRUCTURE OF THE LIGANDS

Preparation of the complexes: The complexes were prepared by two different routes.

(A) In microwave assisted synthesis, the complexes were prepared by irradiating the reaction mixture of $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ (0.002 mol) and respective ligands (0.002 and 0.004 mol) in 1:1 and 1:2 molar ratios using NaOH in appropriate stoichiometric proportions in methanol. A drastic reduction in the reaction time was observed due to the rapid heating capability of microwaves. Finally, the products were recovered from the microwave oven and dissolved in a 2-4 mL of dry methanol, where the precipitate of sodium chloride formed during the course of the reaction was removed by filtration and the filtrate was concentrated under reduced pressure. The resulting compounds were washed with cyclohexane and recrystallized in methanol.

(B) These complexes were also synthesized by the thermal method where instead of 7-9 min, reactions were completed in 12–16 h and the yield of the products was also less than that obtained by the microwave assisted synthesis. In this method the methanolic solution of $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ (0.002 mol) was added to the methanolic solution of ligands (0.002 and 0.002 mol) in 1:1 and 1:2 M ratios using NaOH in appropriate stoichiometric proportions. The resulting mixture was heated under reflux for 12-16 h, the precipitate of sodium chloride formed during the course of the reaction was removed by filtration and the solvent was concentrated under reduced pressure. The product was dried in *vacuum*.

The resulting compounds were washed with cyclohexane and recrystallized in methanol. The purity was further checked by TLC using silica gelG. A comparison between thermal method and microwave method is given in **Table 1**.

TABLE 1: COMPARISON BETWEEN CONVENTIONAL AND MICROWAVE METHODS OF SYNTHESIS

| Compounds | Yield (%) | | Solvent (mL) | | Time | |
|--|-----------|-----------|--------------|-----------|-------------|---------------------|
| | Thermal | Microwave | Thermal | Microwave | Thermal (h) | Microwave (Minutes) |
| $[\text{Cr}(\text{Bzt}_1) \cdot \text{Cl}_2 \cdot (\text{H}_2\text{O})_2]$ | 79 | 82 | 50 | 2 | 15 | 8 |
| $[\text{Cr}(\text{Bzt}_1)_2 \cdot \text{Cl} \cdot (\text{H}_2\text{O})]$ | 70 | 79 | 50 | 3 | 16 | 8 |
| $[\text{Cr}(\text{Bzt}_2) \cdot \text{Cl}_2 \cdot (\text{H}_2\text{O})_2]$ | 76 | 88 | 40 | 3 | 15 | 9 |
| $[\text{Cr}(\text{Bzt}_2)_2 \cdot \text{Cl} \cdot (\text{H}_2\text{O})]$ | 72 | 82 | 45 | 4 | 12 | 7 |
| $[\text{Cr}(\text{Bzt}_3) \cdot \text{Cl}_2 \cdot (\text{H}_2\text{O})_2]$ | 68 | 80 | 50 | 3 | 12 | 8.5 |
| $[\text{Cr}(\text{Bzt}_3)_2 \cdot \text{Cl} \cdot \text{H}_2\text{O}]$ | 76 | 89 | 40 | 4 | 15 | 7.3 |

Physical measurements and analytical method:

The molecular weights were determined by the Rast Camphor method¹⁸. The metal contents were analysed gravimetrically. Sulfur and nitrogen were determined by Messenger's¹⁹ and Kjeldahl's methods²⁰ respectively. Carbon and hydrogen analyses were performed at the Central Drug Research Institute (CDRI), Lucknow. Infrared spectra were recorded on a Nicolet Magna FTIR-550 spectrophotometer using KBr pellets. ¹H NMR spectra were recorded on a JEOL-AL-300 FT NMR spectrometer in DMSO-d₆. The electronic spectra were recorded on a Varian-Cary/5E spectrophotometer at SAIF, IIT, Madras, Chennai. EPR spectra of the complexes were monitored on Varian E-4X band spectrometer at SAIF, IIT, Madras, Chennai. Molar conductance was measured on CC601 digital conductivity meter.

Anti-microbial studies:

Anti-fungal studies: Bioefficacies of the ligands synthesized by thermal method and their metal complexes synthesized by thermal as well as microwave methods were checked *in vitro*. The *in vitro* antifungal activities of the ligands and their complexes have been evaluated against two pathogenic fungi, *Aspergillus niger* and *Fusarium oxysporum* by the agar plate technique²¹. The potato dextrose agar (PDA) medium was prepared in the laboratory to maintain the fungal growth. For PDA preparation, 20 g potato was extracted with distilled water (100 mL) at 100°C for 1 h and it was filtered off by cotton filter. The potato juice was then mixed with 2 g dextrose and 1.5 g agar and finally the pH of the prepared PDA media was adjusted at 7.

Solutions of the test compounds in methanol at 100 and 200 ppm concentrations were prepared and then were mixed with the medium. The medium then was poured into petri plates and the spores of fungi were placed on the medium with the help of inoculum's needle. These petri plates were wrapped in the polythene bags containing a few drops of alcohol and were placed in an incubator at $25\pm 2^{\circ}\text{C}$. The activity was determined after 96 h of incubation at room temperature (25°C). The controls were also run and three replicates were used in each case. The linear growth of the fungus was obtained by measuring the diameter of the fungal colony after four days and the percentage inhibition was calculated as $100 \times (C-T)/C$, where C=diameter of the fungus colony in the control plate after 96 h and T=diameter of the fungal colony in the test plates after the same period. The antifungal screening data of compounds were compared with the standard (Fluconazole).

Antibacterial screening: *In vitro* antibacterial screening is generally performed by disc diffusion method²². The antibacterial activity of the ligands and their chromium (III) complexes were evaluated against bacteria *Staphylococcus aureus* and *Escherichia coli*. The nutrient agar medium having the composition peptone 5 g, beef extract 5 g, NaCl 5g, agar-agar 20 g and distilled water 1000 mL was pipetted into the petri dish. When it solidified, 5 mL of warm seeded agar was applied. The seeded agar was prepared by cooling the molten agar to 40°C and then added the 10 mL of bacterial suspension. The compounds were dissolved in methanol in 500 and 1000 ppm concentrations. Paper discs of Whatman No.1 filter paper measuring diameter of 5 mm were soaked in these solutions of varied concentrations.

The discs were dried and placed on the medium previously seeded with organisms in petri plates at suitable distance. The petri plates were stored in an incubator at $28\pm 2^{\circ}\text{C}$ for 24 h. The diameters of the zone of inhibition produced by the compounds were compared with the standard antibiotic (Streptomycin). The zone of inhibition thus formed around each disc containing the test compounds was measured accurately in mm.

Determination of minimum inhibitory concentration (MIC): Minimum Inhibitory Concentration, MIC, is the lowest concentration of test agent that inhibited visible growth of bacteria after 18 h incubation at 37°C . The determination of the MIC involves a semi quantitative test procedure, which gives an approximation to the least concentration of an antimicrobial needed to prevent microbial growth. The minimum inhibitory concentration was determined by liquid dilution method²³. Stock solutions of chromium (III) complexes with 10-50 $\mu\text{g/mL}$ concentrations were prepared with aqueous methanol solvent. Inoculum of the overnight culture was prepared.

In a series of tubes, 1 mL each of chromium (III) complex solutions with different concentrations were taken and 0.4 mL of the inoculum was added to each tubes. Further 3.5 mL of the sterile water was added to each of the test tubes. These test tubes were incubated for 24 h and observed for the presence of turbidity. The absorbance of the suspension of the inoculum was observed with spectrophotometer at 555 nm. The end result of the test was the minimum concentration of antimicrobial (test materials) which gave a clear solution, i.e., no visual growth.

Antifertility activity: The estimation of potency of the synthesized compounds and their antiandrogenic effects on male albino rats were studied and the emphasis has been given on the:

- Body and organ weights
- Sperm dynamics and fertility
- Biochemical parameters

MATERIAL AND METHODS:

Animals used: The sexually mature healthy male albino rats (*Ratus norvegicus*) with an average body weight between 185-208 g (80-100 days old) were used for the present study. They were housed in an air conditioned animals room at $24\pm 2^{\circ}\text{C}$ with 14 h light and water and food was given *ad libitum*. The animals were fed with food pellet procured from Ashirwad Industries, Chandigarh as well sprouted gram and wheat seeds as an alternative feed. Tap water was supplied *ad libitum*.

Preparation of Animals for the Study: The weighed rats were divided into 10 groups and each group composed of 3 rats. The first group (group A) was selected as control and treated with olive oil 0.5 mL / day, which was chosen as the vehicle to administer the synthesized compounds. In rest of the groups (groups B, C, D, E, F, G, H, I and J), ligands and the complexes were given for 55 days.

Mode of Administration of the Compound: In the group B, C and D the ligand 35 mg/kg body weight suspended in olive oil was given orally through the mouth by pearl point needle for a period of 55 days. The animals of groups E, F, G, H, I and J received same doses of respective compound for the same period. It was then administered orally through the mouth by pearl point needle.

Fertility Test: The fertility test of individual rat was done before the experiment and after 55 days of the experiment. Each rat was cohabited with progesterone female in 1:2 ratios. Vaginal smear was examined every morning for positive mating and numbers of litters delivered were recorded. The rats were sacrificed within 24h after the last administration of the compounds, i.e. on 55th days of the experiment.

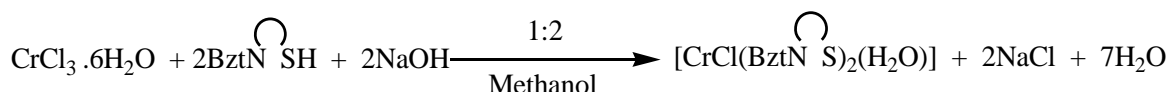
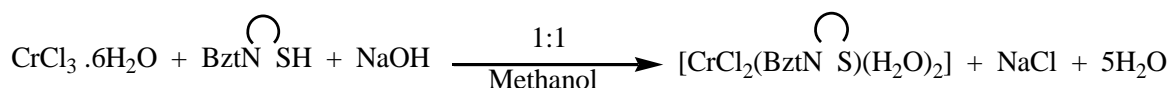
Sperm Motility: The epididymis is exposed by a scrotal incision. Then a cut is made at the distal end of the cauda epididymis and spermatozoa were expressed out by gentle pressure in a measured amount of physiological saline to make sperm suspension. Sperm suspension was then placed on a glass slide and observed for forward motility. At least 100 spermatozoa per rat were observed under microscope using pre-calibrated micrometer.

Sperm Density: The sperm suspension made as above is placed on Neubauer's chamber of haemocytometer and allowed to settle for 1 h. The number of spermatozoa in appropriate squares counted under light microscope at 100 X magnification lens. Then with the help of standard formulae counts/mL were calculated.

Biochemical Estimations: Biochemical estimations of protein, sialic acid, Fructose and cholesterol were carried out in testes and seminal vesicle by standard laboratory techniques. Student 't' test was used for the assessment of significance of variations and the data were presented as mean \pm SEM.

Body and Organ Weight Measurements: The rats were weighed weekly and change in the body weight was recorded. The animals were sacrificed under light ether anesthesia. The testes, epididymis, seminal vesicle and ventral prostate were removed, cleared off fat, blood vessels and connective tissue before weighing. Sperm motility and sperm density were assessed in cauda epididymis and testes. Liver was also dissected and separated. The weight of each organ was measured with an electronic weighing machine, which has sensitivity of 0.01 g.

RESULTS AND DISCUSSION: The reactions of $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ with the ligands, and stoichiometric amount of NaOH, were carried out in 1:1 and 1:2 M ratios in methanol. The successive replacement of chloride resulted in the formation of products $[\text{CrCl}_2(\text{BztN}^\cap\text{S})(\text{H}_2\text{O})_2]$ and $[(\text{CrCl}(\text{BztN}^\cap\text{S})_2)(\text{H}_2\text{O})]$. The overall reaction of 1:1 and 1:2 complexes are as follows:



Where, $\text{BztN}^\cap\text{SH}$ is the ligand molecule

A suggested structure for chromium complexes in molar ratio 1:1 and 1:2 is shown in **Fig. 2** and **3** respectively.

The physical properties and analytical data of the ligands and their metal complexes, synthesized by conventional method are enlisted in **Table 2**.

TABLE 2: ANALYTICAL DATA AND PHYSICAL PROPERTIES OF THE LIGANDS AND COMPLEXES SYNTHESIZED BY CONVENTIONAL HEATING

| Compounds | Color | Melting Point (°C) | Found (Calculated.) (%) | | | | | Molar mass Found (Calculated) | Magnetic Moment (B.M) (μ) |
|--|--------------|--------------------|-------------------------|----------------|------------------|------------------|------------------|-------------------------------|---------------------------------|
| | | | C | H | N | S | M | | |
| Bzt ₁ H | Yellow | 73 | 66.17 (66.33) | 4.81 (5.10) | 6.23 (6.44) | 14.61 (14.76) | - | 209.23 (217.29) | |
| Bzt ₂ H | Yellow | 88 | 61.44 (61.76) | 4.44 (4.75) | 5.72 (6.00) | 27.34 (27.48) | - | 226.30 (233.35) | - |
| Bzt ₃ H | Light yellow | 84 | 68.24 (68.39) | 5.12 (5.29) | 12.01 (12.27) | 13.79 (14.04) | - | 218.27 (228.31) | - |
| [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | Green | 148 | 38.22 (38.41) | 3.44 (3.76) | 3.42 (3.73) | 8.31 (8.54) | 13.60 (13.85) | 367.18 (375.21) | 3.75 |
| [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | Green | 154 | 53.32 (53.58) | 3.81 (4.12) | 4.88 (5.21) | 11.51 (11.92) | 9.48 (9.66) | 527.01 (538.02) | 3.70 |
| [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | Green | 103 | 36.35 (36.84) | 3.37 (3.60) | 3.43 (3.57) | 16.16 (16.39) | 13.09 (13.28) | 382.25 (391.27) | 3.79 |
| [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | Green | 119 | 50.32 (50.55) | 3.56 (3.88) | 4.49 (4.91) | 22.24 (22.49) | 9.11 (9.20) | 557.11 (570.15) | 3.80 |
| [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | Green | 114 | 39.90 (40.24) | 3.58 (3.91) | 6.15 (7.25) | 8.03 (8.28) | 13.21 (13.46) | 374.21 (386.24) | 3.70 |
| [Cr(Bzt ₃) ₂ .Cl.H ₂ O] | Green | 126 | 55.26 (55.75) | 4.02 (4.31) | 9.71 (10.00) | 11.10 (11.44) | 9.13 (9.28) | 551.01 (560.07) | 3.75 |

UV spectra: The nature of the ligand field around the metal ion and the geometry of the metal complexes have been deduced from the electronic spectra and magnetic moment data of the complexes. The electronic spectra of the complexes were recorded in DMSO. In case of chromium (III) complexes the three transitions are expected and are also observed experimentally. Three bands at 15650-16630, 21000-23560 and 29110-32000 cm^{-1} are observed due to the ${}^4A_{2g} \rightarrow {}^4T_{2g}(v_1)$, ${}^4A_{2g} \rightarrow {}^4T_{1g}(v_2)$ and ${}^4A_{2g} \rightarrow {}^4T_{1g}(P)(v_3)$ transitions, respectively, suggesting an octahedral geometry around the Cr^{3+} ion^{24,25}. Various ligand field parameters like Dq, B and β have been calculated and given in **Table 3**. Energy of the first spin allowed transition [${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$] directly gives the value of 10Dq. Electronic repulsion parameter is expressed in terms of Racah parameter and 'B' has been evaluated during these studies. The nephelauxetic ratio β indicates that the complexes have appreciable covalent character.

All the chromium (III) complexes are solids dark green in colour, stable at ambient temperature. Molecular weight determinations indicate their monomeric nature. Measured molar conductance ($10\text{-}15 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$) of 10^{-3} M solution in DMF shows the non-electrolytic behaviour of the metal complexes.

ESR spectra and magnetic moment: The ESR spectra of 1:1 and 1:2 chromium (III) complexes synthesized by different routes were recorded at room temperature. These consist of a single broad peak in each case and from which the Lande splitting factor ('g' values) has been calculated. For the present complexes, the g values lie in the range 1.9433-1.9867 which is characteristic of octahedral geometry²⁶. The room temperature magnetic moment of the chromium (III) complexes (**Table 2**) was found in the range 3.70-3.80, indicative²⁷ of three unpaired electrons on chromium (III) ion in an ideal octahedral environment.

IR spectra The significant IR bands of the ligands and their metal complexes used for the establishment of the mode of the coordination of bidentate ligands towards the metal ion are reported in **Table 4**.

TABLE 3: ELECTRONIC SPECTRAL DATA (cm⁻¹) OF THE CHROMIUM (III) COMPLEXES

| Compounds | Transitions | Spectral bands cm ⁻¹ (nm) | Dq | B | $\beta = B/B^0$ | ν_2/ν_1 |
|--|--|--------------------------------------|------|-----|-----------------|---------------|
| [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | ⁴ A _{2g} (F)→ ⁴ T _{2g} (F) | 16630 (601) | 1663 | 703 | 0.76 | 1.41 |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (F) | 23560 (424) | | | | |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (P) | 29600 (337) | | | | |
| [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | ⁴ A _{2g} (F)→ ⁴ T _{2g} (F) | 16000 (625) | 1600 | 470 | 0.51 | 1.31 |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (F) | 21000 (476) | | | | |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (P) | 29110 (343) | | | | |
| [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | ⁴ A _{2g} (F)→ ⁴ T _{2g} (F) | 15650 (638) | 1565 | 619 | 0.67 | 1.39 |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (F) | 21856 (457) | | | | |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (P) | 32000 (312) | | | | |
| [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | ⁴ A _{2g} (F)→ ⁴ T _{2g} (F) | 16610 (602) | 1661 | 661 | 0.72 | 1.40 |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (F) | 23235 (430) | | | | |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (P) | 31997 (312) | | | | |
| Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | ⁴ A _{2g} (F)→ ⁴ T _{2g} (F) | 15995 (625) | 1599 | 662 | 0.72 | 1.41 |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (F) | 22560 (443) | | | | |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (P) | 30855 (324) | | | | |
| [Cr(Bzt ₃) ₂ .Cl.H ₂ O] | ⁴ A _{2g} (F)→ ⁴ T _{2g} (F) | 16540 (604) | 1654 | 570 | 0.62 | 1.35 |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (F) | 22440 (445) | | | | |
| | ⁴ A _{2g} (F)→ ⁴ T _{1g} (P) | 29215 (342) | | | | |

TABLE 4: IR (cm⁻¹) SPECTRAL DATA OF THE LIGANDS AND THEIR METAL COMPLEXES

| Compounds | IR spectral data (cm ⁻¹) | | | | |
|--|--------------------------------------|------------|-------------|-------------|-------------|
| | ν (NH) | ν (OH) | ν (C=N) | ν (M←N) | ν (M←S) |
| Bzt ₁ H | 3300 | - | - | - | - |
| Bzt ₂ H | 3260 | - | - | - | - |
| Bzt ₃ H | 3255 | - | - | - | - |
| [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | - | 3445 | 1600 | 450 | 345 |
| [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | - | 3450 | 1593 | 473 | 342 |
| [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | - | 3450 | 1598 | 470 | 350 |
| [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | - | 3430 | 1590 | 450 | 352 |
| [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | - | 3400 | 1606 | 465 | 355 |
| [Cr(Bzt ₃) ₂ .Cl.H ₂ O] | - | 3440 | 1610 | 475 | 358 |

In the spectrum of the free ligands absence of the ν (SH) mode at 2595–2550 cm⁻¹ and the presence of ν (NH) mode at 3300-3255 cm⁻¹ indicates the presence of the benzothiazoline ring structure²⁸ in the ligand. The ν (NH) absorption bands disappear in the spectra of the complexes, suggesting the deprotonation of the ligands on chelation. A sharp and strong band observed at 1610-1590 cm⁻¹ due to the azomethine group in the spectra of metal complexes, these bands are not observed in the spectra of ligands, is the strong evidence for the existence of benzothiazoline structure rather than the Schiff base structure in the ligands and confirming that the ligands adopt the Schiff base form in complexes.

In the spectra of chromium (III) complexes a band is observed in the range 885-840 cm⁻¹ which may be attributed to the coordinated water molecule. Further, a broad band around 3450-3400 cm⁻¹ may be due to ν (O-H) of water molecule.

The far IR spectra of these metal complexes exhibited new bands, which are not present in the spectra of the ligands. On the basis of the foregoing discussion, an octahedral environment around the metal atom has been proposed and the structures shown in **Fig. 2** and **3** have been proposed for the chromium (III).

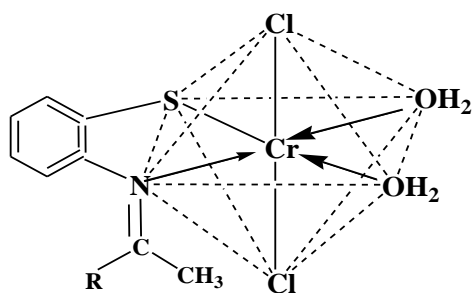


FIG. 2: SUGGESTED STRUCTURES FOR CHROMIUM 1:1 COMPLEXES

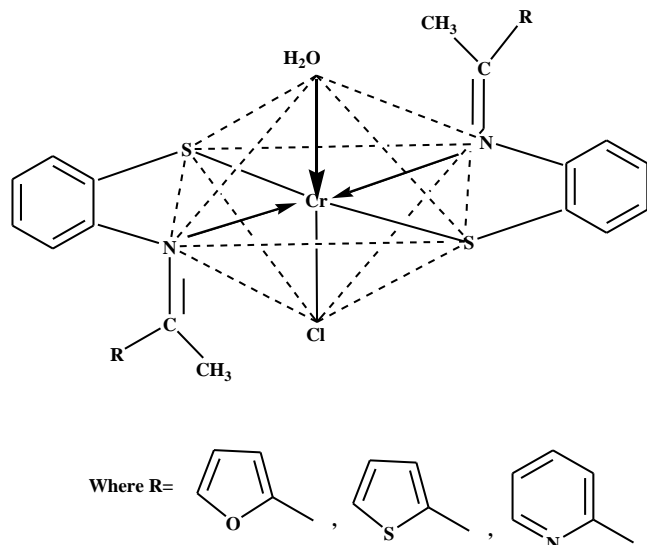


FIG. 3 SUGGESTED STRUCTURES FOR CHROMIUM 1:2 COMPLEXES

¹H- NMR spectra: The ¹H NMR spectral data of the ligands Bzt₁N⁰SH, Bzt₂N⁰SH, Bzt₃N⁰SH were recorded in DMSO-d₆ taking TMS as an internal standard (Table 5).

TABLE 5: ¹H NMR SPECTRAL DATA (δ, PPM) OF THE BENZOTHAZOLINES

| Ligands | N—H (bs) | N=C—CH ₃ (s) | Aromatic protons (m) |
|------------------------------------|-------------|----------------------------|----------------------|
| Bzt ₁ N ⁰ SH | 5.44 | 3.40 | 6.40 – 7.24 |
| Bzt ₂ N ⁰ SH | 4.32 | a | 6.44 - 7.36 |
| Bzt ₃ N ⁰ SH | 5.40 | 1.80 | 6.36 - 7.28 |

^a Merged with –NH proton.

Antimicrobial assay: The ligands and their chromium (III) complexes synthesized through thermal as well as microwave methods were evaluated for their antimicrobial activity against bacteria, *Staphylococcus aureus* and *Escherichia*

coli, and fungi, *Aspergillus niger* and *Fusarium oxysporum*. The results are summarized in Tables 6 and 7.

The results were compared with those of the standard drug Streptomycin for bacteria and Fluconazole for fungi. All the ligands and their respective chromium (III) complexes were found to be sensitive against all the fungal and bacterial strains.

The MIC values calculated for the ligands and their chromium (III) complexes as shown in Table 8 indicated that the ligands and their metal complexes were the most active in inhibiting the growth of the tested organisms between 18-37 minimum inhibitory concentration (μg/mL) against selected bacteria and fungi.

The results reveal that there is a considerable increase in the toxicity of the complexes as compared to the ligands. On giving a closer look at these results, a common feature, which appears is that the bioactivity enhances due to the following points.

1. The chelation reduces the polarity²⁹ and increase the lipophilic nature of the metal complex, which subsequently favors its permeation through the lipid layer of the cell membrane. This can be well ascribed to Tweedy's chelation theory³⁰.
2. Solubility and concentration of the compounds also play an important role in biological activity. It is seen that lower concentration of compounds can check the sporulation in fungi, and a higher concentration inhibits the growth of organisms almost completely.
3. The toxicity of antibacterial compounds against different species of bacteria depends either on the difference in ribosomes, or the impermeability of the cell to the antimicrobial agent³¹.

TABLE 6: ANTIBACTERIAL SCREENING DATA FOR THE LIGAND AND THEIR COMPLEXES

| Compounds | Antibacterial activity {Diameter (mm) of inhibition zone after 24h (conc. in ppm)} | | | |
|--|--|-----------|------------------------------|-----------|
| | <i>E. coli</i> | | <i>Staphylococcus aureus</i> | |
| | 500 | 1000 | 500 | 1000 |
| Bzt ₁ H | 6.3±0.01 | 8.0±0.03 | 7.6±0.10 | 8.9±0.06 |
| Bzt ₂ H | 6.7±0.02 | 9.0±0.01 | 8.1±0.05 | 9.6±0.07 |
| Bzt ₃ H | 7.0±0.01 | 8.4±0.06 | 9.0±0.01 | 10.1±0.04 |
| [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | 13.0±0.02 | 15.0±0.07 | 13.6±0.06 | 15.2±0.12 |
| [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | 13.1±0.02 | 17.0±0.05 | 14.0±0.05 | 16.6±0.03 |
| [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | 12.5±0.02 | 14.9±0.01 | 13.0±0.08 | 17.3±0.03 |
| [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | 13.8±0.01 | 16.8±0.11 | 13.7±0.05 | 18.2±0.04 |
| [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | 12.7±0.03 | 18.0±0.12 | 15.6±0.10 | 18.0±0.04 |
| [Cr(Bzt ₃) ₂ .Cl.H ₂ O] | 14.0±0.03 | 19.0±0.03 | 15.7±0.03 | 19.5±0.03 |
| Streptomycin | 18.4±0.10 | 20.5±0.11 | 21.9±0.10 | 22.0±0.06 |

TABLE 7: ANTIFUNGAL SCREENING DATA FOR THE LIGANDS AND THEIR COMPLEXES

| Compounds | (Antifungal activity) | | | |
|--|---|----------|---------------------------|----------|
| | Percentage inhibition after 96 h (conc. in ppm) | | | |
| | <i>Aspergillus niger</i> | | <i>Fusarium oxysporum</i> | |
| | 100 | 200 | 100 | 200 |
| Bzt ₁ H | 41.0±0.3 | 47.2±0.9 | 40.0±0.4 | 46.3±0.7 |
| Bzt ₂ H | 50.0±0.2 | 55.6±0.1 | 53.5±0.8 | 57.6±0.6 |
| Bzt ₃ H | 37.5±0.2 | 42.3±0.2 | 40.2±0.1 | 47.8±0.7 |
| [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | 63.1±0.1 | 67.1±0.3 | 55.3±0.9 | 69.8±0.7 |
| [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | 63.6±0.5 | 71.4±0.3 | 57.0±0.4 | 65.3±0.1 |
| [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | 66.0±0.8 | 74.3±0.6 | 61.1±0.1 | 70.8±0.3 |
| [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | 66.7±0.5 | 81.4±0.7 | 70.0±0.6 | 78.0±0.3 |
| [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | 58.5±0.2 | 66.0±0.6 | 62.7±0.1 | 65.3±0.2 |
| [Cr(Bzt ₃) ₂ .Cl.H ₂ O] | 61.0±0.6 | 67.2±0.3 | 64.4±0.2 | 70.9±0.9 |
| Fluconazole | 90.0±0.8 | 96.2±1.1 | 93.7±0.1 | 99.0±0.2 |

TABLE 8: MINIMUM INHIBITORY CONCENTRATION (µG/ML) OF THE LIGANDS AND THEIR COMPLEXES

| Compounds | <i>E. coli</i> | <i>S. aureus</i> | <i>A. niger</i> | <i>F. oxysporum</i> |
|--|----------------|------------------|-----------------|---------------------|
| Bzt ₁ H | 32.0±0.3 | 30.0±0.2 | 34.0±0.1 | 31.0±0.2 |
| Bzt ₂ H | 36.0±0.1 | 37.0±0.2 | 37.0±0.2 | 34.0±0.1 |
| Bzt ₃ H | 29.0±0.3 | 31.0±0.2 | 33.0±0.4 | 30.0±0.3 |
| [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | 19.0±0.1 | 21.0±0.3 | 20.0±0.2 | 21.0±0.2 |
| [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | 20.0±0.4 | 23.0±0.3 | 22.0±0.3 | 22.0±0.2 |
| [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | 24.0±0.1 | 26.0±0.2 | 25.0±0.1 | 23.0±0.1 |
| [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | 27.0±0.1 | 29.0±0.1 | 30.0±0.1 | 26.0±0.1 |
| [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | 18.0±0.2 | 19.0±0.2 | 21.0±0.2 | 18.0±0.1 |
| [Cr(Bzt ₃) ₂ .Cl.H ₂ O] | 19.0±0.2 | 20.0±0.3 | 22.0±0.3 | 22.0±0.3 |

Antifertility test results: The treatment with ligands (Bzt₁N[∩]SH, Bzt₂N[∩]SH, Bzt₃N[∩]SH) and their chromium (III), complexes at the dose level of 35 mg/kg b.wt for a period of 55 days showed following variation in the different end point.

Body and Organ Weight Administration of ligands and their corresponding chromium (III) complexes did not bring about any significant change in the body weight of the treated rats. The weights of testes, epididymis, seminal vesicle and

ventral prostate were decreased significantly in all experimental groups when compared with vehicle treated controls (**Tables 9**).

Sperm Motility and Sperm Density: A significant (P ≤ 0.001) decrease in sperm motility in cauda epididymis was observed in rats treated with ligands and corresponding chromium (III) complexes. Sperm density in testes and cauda epididymis were also reduced significantly in treated rats (**Table 10**).

TABLE 9: EFFECT OF LIGANDS AND ITS CORRESPONDING METAL COMPLEXES ON REPRODUCTIVE ORGANS WEIGHT OF MALE RATs

| Group | Treatment | Body Weight (g) | | Organ Weight (mg/100g b. weight) | | | |
|-------|--|-----------------|--------------------------|----------------------------------|-------------------------|--------------------------|--------------------------|
| | | Initial | Final | Testes | Epididymis | Seminal vesicle | Ventral prostate |
| A | Control | 185.0± 7.5 | 205.0± 6.7 ^c | 1395.0±28.5 | 470.0± 7.8 | 440.0± 9.4 | 418.0± 8.5 |
| B | Bzt ₁ H | 208.0± 8.7 | 218.0± 9.5 | 1150.0±15.0 ^a | 400.0±5.40 ^a | 370.0± 10.7 ^a | 345.0± 9.5 ^a |
| C | Bzt ₂ H | 194.0± 6.50 | 209.0± 5.0 ^c | 1200.0± 12.5 ^b | 410.0±6.9 ^b | 385.0± 9.9 ^b | 365.0± 11.4 ^b |
| D | Bzt ₃ H | 200.0± 9.5 | 212.0± 9.6 ^c | 1250.0±20.6 ^b | 390.0±6.3 ^b | 380.0± 10.4 ^a | 360.0± 7.7 ^b |
| E | [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | 210.0± 9.7 | 225.0±6.7 ^c | 850.0±19.7 ^b | 240.0±7.1 ^b | 248.0±7.4 ^b | 220.5±9.7 ^b |
| F | [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | 198.8±10.6 | 228.0±9.8 ^c | 860.0±28.6 ^b | 235.0±9.8 ^b | 242.0±6.2 ^b | 225.0±7.9 ^b |
| G | [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | 190.0±10.5 | 212.0±9.0 ^b | 700.0±20.0 ^a | 285.0±9.0 ^b | 210.0±7.8 ^a | 170.0±6.4 ^c |
| H | [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | 192.0±9.5 | 202.0±10.3 ^b | 850.0±15.6 ^b | 380.0±8.6 ^b | 265.0±5.4 ^b | 210.0±6.0 ^c |
| I | [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | 195.0±8.3 | 215.0± 10.2 ^c | 905.0±17.4 ^b | 285.0±6.8 ^b | 269.0±6.9 ^b | 275.0±7.8 ^b |
| J | [Cr(Bzt ₃) ₂ .Cl.(H ₂ O)] | 188.0±8.8 | 199.0±9.3 ^c | 890.0±16.5 ^b | 260.0±8.1 ^b | 238.0±5.7 ^b | 247.0±7.9 ^b |

TABLE 10: SPERM DYNAMICS AND FERTILITY AFTER THE ADMINISTRATION OF LIGANDS ITS CORRESPONDING METAL COMPLEXES

| Group | Treatment | Sperm motility % (Cauda epididymis) | Sperm density (million/mL) | | Fertility % |
|-------|--|--|----------------------------|--------------------------|-------------|
| | | | Testes | Epididymis | |
| A | Control | 75.1 ± 2.0 | 4.7 ± 0.9 | 54.0 ± 3.9 | 100 (+ve) |
| B | Bzt ₁ H | 45.9 ± 2.8 ^b | 3.86 ± 0.48 ^b | 48.1 ± 3.1 ^b | 75.0 (+ve) |
| C | Bzt ₂ H | 58.0 ± 1.5 ^b | 3.70 ± 0.5 ^b | 47.0 ± 3.2 ^b | 78.0 (-ve) |
| D | Bzt ₃ H | 53.7 ± 1.75 ^b | 2.78 ± 0.28 ^b | 28.0 ± 1.7 ^b | 78.0 (-ve) |
| E | [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | 38.6 ± 1.35 ^b | 1.87 ± 0.15 ^b | 10.0 ± 1.1 ^b | 95.0 (-ve) |
| F | [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | 40.2 ± 1.10 ^b | 1.82 ± 0.13 ^b | 12.0 ± 1.6 ^b | 92.8 (-ve) |
| G | [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | 30.0 ± 1.15 ^b | 1.30 ± 0.12 ^b | 9.40 ± 1.1 ^b | 98.2 (-ve) |
| H | [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | 34.7 ± 1.19 ^b | 1.38 ± 0.17 ^b | 9.70 ± 1.2 ^b | 97.0 (-ve) |
| I | [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | 39.0 ± 1.7 ^b | 2.0 ± 0.19 ^b | 9.80 ± 1.1 ^b | 88.0 (-ve) |
| J | [Cr(Bzt ₃) ₂ .Cl.(H ₂ O)] | 38.6 ± 2.4 ^b | 1.78 ± 0.24 ^b | 27.91 ± 2.1 ^b | 87.8 (-ve) |

Biochemical Changes (Table 11):

Protein: Protein contents of testes, epididymis, seminal vesicle and ventral prostate were reduced significantly (P < 0.01 to 0.001) in all experimental groups.

Sialic acid: Sialic acid contents of testes, epididymis, seminal vesicle and ventral prostate were depleted in ligands and their chromium (III) complexes.

Cholesterol: Testicular cholesterol content was increased significantly in rats treated with ligands and their chromium (III) complexes.

Glycogen: A significant decrease in testicular glycogen content was observed in all experimental groups.

DISCUSSION:

a) The administration of the ligands and their corresponding chromium (III) complexes brought about marked reduction in weight of testes and other sex accessories. Testes, epididymis and other accessory sex organs are androgen dependent for their growth and function. Thus reduction in weights of these sex accessories may reflect that the synthesis of androgen has been decreased³².

TABLE: 11 BIOCHEMICAL CHANGES IN THE TESTES OF MALE RATS AFTER TREATMENT WITH THE LIGANDS WITH THEIR CORRESPONDING METAL COMPLEXES

| Group | Treatment | Testicular Sialic acid (mg/g) | Testicular Protein (mg/g) | Testicular cholesterol (mg/g) | Seminal vesicle Glycogen (mg/g) |
|-------|--|-------------------------------|---------------------------|-------------------------------|---------------------------------|
| A | Control | 7.8 ± 0.6 | 250 ± 20 | 8.6 ± 0.7 | 440 ± 16 |
| B | Bzt ₁ H | 4.2 ± 0.6 ^b | 134 ± 18 ^b | 4.8 ± 0.5 ^b | 320 ± 15 ^b |
| C | Bzt ₂ H | 6.5 ± 0.5 ^b | 160 ± 25 ^b | 5.8 ± 0.5 ^b | 356 ± 12 ^b |
| D | Bzt ₃ H | 5.0 ± 0.6 ^b | 144 ± 20 ^b | 6.0 ± 0.5 ^b | 346 ± 13 ^b |
| E | [Cr(Bzt ₁).Cl ₂ (H ₂ O) ₂] | 2.8 ± 0.6 ^c | 100 ± 12 ^b | 3.6 ± 0.6 ^c | 204 ± 12 ^b |
| F | [Cr(Bzt ₁) ₂ .Cl.(H ₂ O)] | 2.1 ± 0.3 ^c | 102 ± 10 ^c | 2.7 ± 0.7 ^c | 196 ± 17 ^b |
| G | [Cr(Bzt ₂).Cl ₂ (H ₂ O) ₂] | 4.9 ± 0.4 ^b | 122 ± 18 ^b | 4.6 ± 0.4 ^b | 220 ± 18 ^b |
| H | [Cr(Bzt ₂) ₂ .Cl.(H ₂ O)] | 4.5 ± 0.8 ^b | 115 ± 15 ^c | 4.0 ± 0.6 ^b | 207 ± 14 ^b |
| I | [Cr(Bzt ₃).Cl ₂ (H ₂ O) ₂] | 3.4 ± 0.6 ^c | 109 ± 19 ^b | 4.1 ± 0.2 ^c | 210 ± 12 ^b |
| J | [Cr(Bzt ₃) ₂ .Cl.(H ₂ O)] | 3.2 ± 0.8 ^c | 108 ± 16 ^b | 3.9 ± 0.8 ^c | 208 ± 16 ^b |

b) The decreased sperm density in testes and cauda epididymis is an indicator of reduced spermatogenesis and reduced sperm motility may be due to altered enzymatic activity of oxidative phosphorylation process³³. Thus decrease in sperm motility and density after oral administration of ligands and their corresponding chromium (III) complexes may be due to androgen deficiency which caused impairment in testicular function by altering the enzymatic activities responsible for the spermatogenesis, suggesting thereby an antiandrogenic effect of these compounds. The decrease in male fertility could be explained by the fact that the ligands and their metal complexes acted directly on the testes and influenced the androgen biosynthesis pathway³⁴. Ligands and their chromium (III) complexes also induce biochemical changes in testes and sex accessory organs.

c) Sialic acids are concerned with changing the membrane surface of maturing spermatozoa and with the development of their fertilizing capacity. Thus decreased sialic acid in testes and sex accessory organs may inhibit the fertilizing capacity of sperm.

d) Increased testicular cholesterol is attributed to decreased concentration of androgen which resulted in impaired spermatogenesis³⁵.

Similarly, the elevation in the testicular protein contents after treatment with ligands and their metal complexes may be due to the hepatic detoxification activities caused by these compounds which results in the inhibitory effect on the activities of enzymes involved in the androgen biotransformation.

e) Marked reduction in testosterone content in association with highly reduced circulating level of this hormone confirmed alteration in the reproductive physiology of rat.

These results suggested that the ligands and their chromium (III) complexes exert inhibitory effects on testicular function and lead to infertility in male rats. Further, addition of metal ion to the ligands enhances their activity.

CONCLUSIONS: Biologically relevant ligands and their Cr (III) metal complexes have been synthesized and characterised. Based on various physicochemical and spectroscopic investigations, a hexacoordinated environment around the metal ion has been proposed.

Antimicrobial and antifertility activities of the ligands and complexes showed that the Cr (III) complexes are more active than the parent ligands.

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REFERENCES:

- Kidwai M and Mothsra P: Neat reaction technology: a green tool. *Ind. J. Chemistry*. 2006; 45B: 2330-2336.
- Ravichandran S and Karthikeyan E: Microwave synthesis – A potential tool for green chemistry. *Int. J. Chem. Tech. Res.* 2011; 3: 466-470.
- Nerkar AG, Pawale D, Ghante MR and Sawant SD: Microwave assisted organic synthesis of some traditional and named reactions: A practical approach of green chemistry. *Int. J. Pharmacy and Pharmaceutical Sciences*. 2013; 5: 564-566.
- Refat MS, EL-Deen IM, Anwer ZM and EL-Ghol SJ: Spectroscopic studies and biological evaluation of some transition metal complexes of Schiff-base ligands derived from 5-aryloxy-salicylaldehyde and thiosemicarbazide. *J. Coord. Chem.* 2009; 62: 1709-1718.
- Yadav PS, Devprakash and Senthilkumar GP: Benzothiazole: Different methods of synthesis and diverse biological activities. *Int. J. Pharmaceutical Sciences and Drug Res.* 2011; 3: 1-7.
- Mahajan DP, Bhosale JD and Bendre RS: Synthesis, Characterization and plant growth regulator activity of some substituted 2-amino benzothiazole derivatives. *J. Applicable Chemistry*. 2013; 2: 765-771.
- Xie Y, Deng S, Chen Z, Yan S and Landry DW: Identification of small-molecule inhibitors of the AB-ABAD interaction. *Med. Chem. Lett.* 2006; 16: 4657-4660.
- Sadek KU, Mekheimer RH, Hameed AFA, Elnahas F and Mohamed Hilmy Elnagdi MH: Green and highly efficient synthesis of 2-arylbenzothiazoles using glycerol without catalyst at ambient temperature. *Molecules*. 2012; 17: 6011-6019.
- Tasler S, Muller O, Wieber T, Herz T, Peyoraro WS, Lang M, Krauss R, Totzke F, Zirrgiebel U and Ehlert JE: Substituted 2-arylbenzothiazoles as kinase inhibitors: Hit-to-lead optimization. *Bioorg. Med. Chem.* 2009; 19: 6728-6737.
- Mortimer CG, Wells G, Crochard JP, Stone EL, Bradshaw TD, Stevens MFG and Westwell AD: Antitumor Benzothiazoles. 26.1 2-(3,4-Dimethoxyphenyl)-5-fluorobenzothiazole (GW 610, NSC 721648), a Simple Fluorinated 2-Arylbenzothiazole, Shows Potent and Selective Inhibitory Activity against Lung, Colon, and Breast Cancer Cell Lines. *J. Med. Chem.* 2006; 49: 179-185.
- Soni B, Bhandari A, Ranawat MS, Sharma P, Singh R, Sharma S and Prajapat RP: Synthesis and antimicrobial activity of some 2-substituted benzothiazoles containing linkage, *Pharmacophore*. 2011; 2: 36-45.
- Raafat M, Issa RM, Khedr AM and Rizk H: ¹H NMR, IR and UV/VIS Spectroscopic Studies of Some Schiff Bases Derived From 2-Aminobenzothiazole and 2-Amino-3-hydroxypyridine. *J. Chinese Chem. Society*. 2008; 55: 875-884.
- Deshpande VG, Shah SNN, Deshpande MM, Habib SI and Kulkarni PA: Synthesis and Antimicrobial Evaluation of Schiff Bases Derived from 2-amino-4, 6-dimethyl benzothiazole with 2-Hydroxy-naphthalene-1-carbaldehyde, 3-Methyl-thiophene-2-carbaldehyde and their Metal Complexes. *Int. J. Pharmaceutical and Chem. Sciences*. 2013; 2: 801-807.
- Kanwar SS, Lumba K, Gupta SK, Katoch VM, Singh P, Mishra AK and SB Kalita: Synthesis and in vitro studies of metal complexes of isonicotinoyldithiocarbamic acid. *Biotechnol. Lett.* 2008; 30: 67-680.
- Pechova A and Pavlata L: Chromium as an essential nutrient: a review. *Veterinarni Medicina*, 2007; 52: 1-18.
- Pawel Mackowiak P, Zbigniew Krejpcio Z, Maciej Sassek M, Przemyslaw Kaczmarek P, Hertig I, Chmielewska J, Wojciechowicz T, Szczepankiewicz D, Wieczorek D, Szymusiak H and Krzysztof W: Evaluation of insulin binding and signaling activity of newly synthesized chromium(III) complexes *in vitro*. *Molecular Medicine Reports*. 2010; 3: 347-353.
- Abdel-Khalek AA and Abdel-Hafeez MM: Two step one-electron transfer reaction of chromium (III) complex containing carbidopa and inosine with N-bromosuccinimide. *Ind. J. Chemistry*. 2012; 51A: 1073-1079.
- K.G. Bothara: *Text Book of Pharmaceutical Chemistry*, Nirali Publisher, Eighth Edition 2008.
- Vogel AI: *A Textbook of Quantitative Chemical Analysis*, Sixth Edition 2006.
- Vogel AI: *A Textbook of Quantitative Chemical Analysis*, Sixth Edition 2006.
- Fahmi N, Saxena C and Singh RV: Spectroscopic characterization and biological potential of palladium(II) complexes of benzylidenehydrazine carboxamide or carbothioamide. *Bull. Chem. Soc. Jpn.* 1996; 69: 963-969.
- Hendi NKK, Naher HS and Al-Charrakh AH: In vitro antibacterial and antifungal activity of Iraqipropolis. *J. Medicinal Plants Res.* 2011; 5: 5058-5066.
- Mazzola PG, Jozala AF, Lencastre Novaes LCD, Moriell P and Penna TCV: Minimal inhibitory concentration (MIC) determination of disinfectant of/ or sterilizing agents. *Brazilian J. Pharmaceutical Sciences*. 2009; 45: 241-248.
- Abou-Melha KS and Faruk H: Bimetallic complexes of Schiff base bis-[4-hydroxycoumarin-3-yl]-¹N, 5N-thiocarbohydrazone as a potentially dibasic pentadentate ligand. Synthesis, spectral, and antimicrobial properties. *J. Iran. Chem. Soc.* 2008; 5(1): 122-134.
- Dubey RK, Dubey UK and Mishra CM: Synthesis and Physicochemical Characterization of Some Schiff Base Complexes of Chromium(III). *Ind. J. Chem.* 2008; 47A: 1208-1212.
- El-ajaily MM, Maihub AA, Hudere SS and Ben saber SM: Nickle (II) chelate of Schiff base derived from 4-dimethyl-amino-benzaldehyde with cysteine. *Asian. J. Chem.* 2006; 18(4): 2427-2430.
- Cotton FA, Wilkinson G, Murillo CA and Bochmann M: *Advanced inorganic chemistry*, John Wiley & Sons Inc, New York, Sixth Edition 2003.
- Sharma K, Swami M, Fahmi N and Singh RV: Sulfur-Bonded Coordination Compounds Of Palladium(II) and Platinum(II) and Their Antimicrobial Activity. *Phosphorus, Sulfur and Silicon*. 2010; 184: 1964.
- Srivastava RS: Pseudotetrahedral Co(II), Ni(II) and Cu(II) complexes of N¹-(O-chlorophenyl)-2-(2',4'-dihydroxyphenyl)-2-benzylazomethine their fungicidal and herbicidal activity, *Inorg. Chim. Acta.* 1981; 56:165.
- Tweedy BG: Plant extracts with metal ions as potential antimicrobial agents, *Phytopathology*. 1964; 55: 910.
- Lawrence PG, Harold PL and Francis OG: *Antibiot. Chemother.* 1980; 5: 1597.
- Joshi SC, Tibrewal P, Sharma A and Sharma P: *Journal of Advanced Scientific Research*. 2012; 3(1): 45-50.
- Pereira C, Mapuskar K and Rao CV: Effect of diethyl phthalate on rat testicular antioxidant system: A dose-

- dependent toxicity study. Pesticide Biochemistry and Physiology. 2008; 90: 52-57.
34. Chaudhary N, Joshi SC and Goyal R: Effect of malathion on testicular cell population dynamics and fertility on male rat. National J Life Sciences. 2005; 2(1-2): 17-21.
35. Varki A and Gagneux P: Multifarious roles of sialic acids in immunity. Ann. N. Y. Acad. Sci. 2012; 1253: 16-36.
36. Ngoula F, Watcho P, Bousekob TS, Kenfack A, Tchoumbouéa J and Kamtchouing P: Effects of propoxur on the reproductive system of male rats. Technombone J. Afr. Health Science. 2007; 11(1):125-32.

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