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Cytotoxicity and Antimicrobial Activity of Metal based Proxo Complexes of Uranium (VI) Synthesizing with Organic Acids and Amine Bases

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Abstract

The extensive use of the antibiotics caused in the serious medical problem of drugs resistance relating to the public health. New synthetic derivatives of antibiotics with their pathway have become an important task to mitigate the drug resistance problems. The mixed ligand complexes of U (VI) Co(II) with organic acids and amino bases and have been synthesized and characterized. The complexes were found to be moderate to strong antibacterial activity. The peroxo complexes also showed the cytotoxic effect against the brine shrimp brine shrimp *nauplii*. Results also revealed that the bacteria *S. dysenteriae* and *S. sonnei* exhibited higher resistant to all the complexes compared to other bacteria tested. the peroxo complexes were found to be less active in fungi than that of bacteria. All the fungi including *Aspergillus niger, A. fumigatus, A. flarus* exhibited more or less similar patterns of sensitivity to the complexes. Results indicate that the lethal toxicity of peroxo complexes of metal U(VI) varied significantly against brine shrimp at different exposure periods.

1. Introduction

Most of the heavy metals are generally toxic to the biosphere at very low level [1]. The mechanism of heavy metal toxicity in the environment includes the generation of free radicals to cause oxidative stress, damage of biological molecules such as enzymes, proteins, lipids, and nucleic acids, damage of DNA which is key to carcinogenesis as well as neurotoxicity [2,3]. It has been reported that some of the heavy metal toxicity are acute while others could be chronic which may cause damage of biological organs [4]. The exposure of heavy metals to the biological food chain involve in various diverse forms through food, water and air pollution, and most important by occupational exposure at workplace [5]. Recently, the researchers are interested to work on the broad-spectrum activity and action mechanisms of synthesis metal compounds against pathogenic microbes. Rocha et al. reported that there are three criterions to be followed in the interaction of metal ions for antibiotics while producing any new drugs [6]. The first one includes a reversed mechanism of microbial resistance; the second one looking for promoting the development of new drugs with an action mechanism unknown to the pathogenic bacteria; and a third one aiming at reducing the toxicity of the metal ion in the form of a complex [7]. It has been reported that the peroxo complexes metal ions with organic ligands exhibits better antimicrobial activity compared to free ligands (not coordinated), since it ensures the investigation of new drugs with unknown mechanism of action against pathogenic bacteria [8,9]. There are various laboratory techniques that can be used to measure the susceptibility of bacteria to antimicrobial agents of peroxo complexes *in vitro* [10,11].

It has been reported that the development of new therapeutic agent of peroxo complexes synthesizing with organic acids and amine bases are now drawing attention of medicinal chemist [12]. Several studies have been published relating to the biological activities peroxo complexes of metal, including their genotoxicity [13], antimicrobial, antifungal [14] and herbicidal activities [15]. Peroxo complexes of metal resulting from various organic acids and amine derivatives were repeatedly reported to have mutagenicity [16], bactericidal [17], and antifungal activities [18]. Moreover, the growing interest in transition metal complexes containing organic acids and amine base antibiotics is derived from their functions and well-established chemical in biological systems as well as their pharmaceutical and catalytic applications [19,20].In last decades, the numerous peroxo metal complexes have been synthesized and characterized by several researchers [21]. Peroxo ligands play a prime role in transition metal coordination chemistry [22, 23]. The tetra dentate Schiff base metal complexes used as metal enzymes [24], catalyst [25,26], material chemistry [27], and biomimetic chemistry [28]. The peroxo metal complexes are usually able to inhibit the growth of several animal tumors, and some metals have shown good antitumor activity against animal tumors [29,30]. It has shown that the DNA via both covalent and non-covalent interactions uses to bind by many transition metal complexes and the nitrogen base of DNA replaced the covalent binding of the labile ligand of the complexes [31]. Moreover, the non-covalent DNA interactions include intercalative, electrostatic and groove (surface) binding of cationic metal complexes outside of the DNA helix, major or minor groove. The DNA molecules are primarily damaged under various conditions like interactions with some molecules and this damage may cause various pathological alters in biological organisms, which is due to their possible application as new therapeutic agents and their photochemical properties which make them potential probes of DNA structure and conformation [32,33].

The microbial activity of compounds of peroxo complexes has been reported by several researchers as antibacterial [34, 35], antiradical [36,37], anticancer [38], antifungal [39], and antiviral [40]. In the past decades, amine bases and their metal complexes have been widely used as coordination compounds, which can be attributed to their increasing importance as biochemical and analytical reagents. Moreover, the amine base complexes are usually ease and flexibility in their synthesis technique, diverse properties, and use as biologically active compounds [41].The importance of transitional peroxo of metal complexes containing organic acids and amine bases antibiotics is derived from their functions and well-established chemical in biological systems has enormously been increasing. In particular, the interaction between metal ligands and antibiotics such as has recently been investigated [42]. The goal of the present study was to prepare peroxo complexes of coordination compounds of uranium (VI) derived from synthesizing with organic acids and amine basesand to investigate the antibacterial activity against gram positive and gram negative strains.

2. Material and Methods

2.1Preparation of compound

The metal complex was synthesized according to the methodology suggested by Nasrin [43]. The complexes were formed with the reaction of Uranylnitrate with organic acids and amine bases which could be reflected as follows:

$$UO_2(NO)_2 + amH + 2L + H_2O_2 \rightarrow [UO(O_2)\,(amH)_2\,L] + H_2O + HNO_3$$

Where, amH= deprotonated glycine, alanine, phenylalanine and leucine; L= quinoline, isoquinoline, pyridine, 2-picoline or 4-picoline.

Solution of amH like glycine (0.150g, 0.002 mol) or alanine (0.1782g, 0.002 mol) or phenylalanine (0.330g, 0.002mol) or leucine (0.2623g, 0.002mol) in water (20 ml) was mixed with Uranyl nitrate (1.005g,0.002 mol) and stirred. Then a solution of 'L' (0.01 mol) in ethanol was added to these mixture and stirred continuously followed by adding of 30% H_2O_2 (2 ml). The precipitate appeared which was filtered, washed with ethanol for several times. It was then dried and stored in *Vacuo* over P_4O_{10}.

2.1 Reaction of 1 and 3 complexes with triphenylphosphine

Triphenyl phosphine (1.321g, 0.005 mol) was taken and dissolved in THF (50ml) which was refluxed with an equimolar quantity of the complexes (0.005 mol) suspended in the same solvent (30 ml). Then, the solution was filtered and the residue was collected. The final product was identified as $OPPh_3$, m.p. 154-155°C (m.p. 157°C).

2.3 Reaction of the complex 2 with triphenylarsine

Triphenylarsine (0.90g, 0.005 mol) in THF (50ml) added to a suspension of above compounds in the same solvents (50ml). The mixture was refluxed for 60 hours. The reaction mixture was filtered and evaporated. The final product was yielded, m.p.(' m.p. 190-192°C).

2.4 Reaction of the complexes 4 and 5 with allyl alcohol

Complexes 4 and 5 (0.002 mol) were suspended in 30 ml of THF and a stoichiometric amount of allyl alcohol was added. The mixture was stirred under reflux at 60°C for 48 hours, but failed to produce any epoxy product, complexes were recovered unchanged. Refluxing complexes 4 and 5 with allyl alcohol in a 1:1 molar ratio in THF medium in 48 hours also failed to produce any epoxy product.

2.5 Reaction of complexes 6 and 7 with allyl alchohol

A stoichiometric amount of allyl alcohol was added to a suspension of complex 6 or 7 in THF (30ml). The mixture was stirred under reflux at 65°C for 36 hours. Micro-distillation under reduced pressure (19mm Hg) yielded glycidol (75% yield) at 145-150°C. The glycidol was identified by means of its phenylurethan derivative, m.p. 58-60°C (m.p. 60°C).

3.6 Catalytic reaction of the compounds 8 with allyl alcohol (Reaction B)

Allyl alcohol (0.30 mol) was dissolved in dioxane (25 ml) and 0.5 g of complex 8 was added followed by 30% H_2O_2 solution (25 ml). The mixture was kept under reflux at 90°C for 24 hours. The reaction mixture was then filtered and distilled at 19 mm Hg pressure. The product collected at 175-180°C was glycerol (50% yield) which was identified as its tribenzoyl ester derivative, m.p. 70°C (m.p. 69°C).

2.7 Antimicrobial sensibility testing by disk diffusion

The antimicrobial sensibility testing (antibiogram) was carried out using the disk diffusion method (Kirby-Bauer method). The sterile filter paper discs saturated with solutions was adjusted to the MIC obtained for each compound. The bacterial inocula were produced with an incubation time for 24 h, and adjusted to the standard solution of the 0.5 McFarland scale. The antimicrobial plates impregnated with the compounds were, in turn, put in each Petri plate. A disk was set in the center of the plate and the others around it, making sure that the distance from the center to another disc was no less than 20 mm, and that the disc was not close to the border.

The plates were then kept in an incubator at a temperature of 35°C for 20 h. After that, the inhibition halos produced around the disc (including the diameter of the disc) were measured, using a digital caliper

rule. Inhibition zones higher than 7 mm in diameter were considered as positive results. Petri dish containing only the Miller-Hinton culture medium was included in each incubation phases for the negative control. Three Petri dishes containing standard antimicrobial discs were incubated for control of the bacterial inoculums. The bioassays were performed in triplicate with three repetitions. The measurements of the inhibition halos were evaluated statistically. All the complexes were tested against the pathogenic fungi *viz. Aspergillus niger*, *A. fumigatus,* and *A. flarus* as a concentration of 200 µg/disc for each. The antimicrobial activity was determined after 72 h of incubation at room temperature (30ºC). The media used in these respects were nutrient agar (DIFCO) for antibacterial assay and potato dextrose agar for antifungal assay. The experiment was performed in triplicate duplicate to minimize errors.

2.8 Cytotoxicity Bioassay

The cytotoxicity as well as efficacy of bioactive complexes against brine shrimp was determined for lethality bioassay [44]. In the present study, *in vivo* lethality test was performed against the brine shrimp nauplii eggs (*Ariemia salina* L.). The eggs were placed on one side of a small tank divided by a net containing 3.8% NaCl solution for hatching. After two days of hatching, the nauplii were ready for the experiment as described previously. 3 mg of the of each complex was taken and dissolved in 0.6 ml of DMSO to get a concentration of 5mg/ml. From stock solutions, 10, 20, 40, 80 and 160 µl were taken in 5 different vials making the volume up to 5 ml. Ten brine shrimp *nauplii* were then placed in each vial. The vial containing the same volume of DMSO plus water up to 5 ml was used as a control batch. After 24h of incubation, the number of survivors of brine shrimp *nauplii* in each vial was recorded. The percentage of mortality of the nauplii was calculated for each concentration and lethal mortality for 50 (LC_{50}) and 99 (LC_{99}) percent were determined using probit analysis.

3. Results and discussion

The detail descriptions on the aspects of syntheses and characterization of these peroxo complexes have earlier been reported by Nasrin [45] and based on the IR spectroscopic and other physical interpretations the molecular structure of peroxo complex (4) could be illustrated as shown in Figure 1.

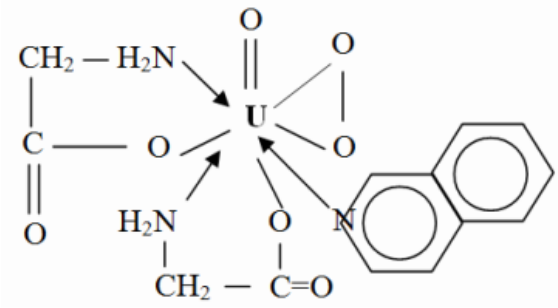

Figure 1. Proposed structure of peroxo complex (4), [UO(O2)(gly)2(Q)] (adopted from Nasrin [45]).

Results indicate that the bacteria *Shigella flexneri* and *S. shiga* showed susceptible against all the complexes tested showing the inhibition halo ranging from 18 to 23 mm compared to other bacteria (Table 1, Fig. 2). Results also revealed that the bacteria *S. dysenteriae* and *S. sonnei* exhibited higher resistant to all the complexes compared to other bacteria tested. Moreover, the complex $[UO(O_2)(gly)_2(Q)]$ was found to be least antimicrobial activity against *S. aureus* showing the inhibition halo of 8 while the complex $[UO(O_2)(ala)_2(iso\text{-}Q)]$ showed the higher antimicrobial activity having inhibition halo of 23 against *S. flexneri* (Table 1). Antibacterial activity of the peroxo complexes of

U(VI) against *Bacillus subtilis, B. megaterium, Escherichia coli* and *Sarcina lutea* are shown in Table 2. Results showed that all the complexes of U(VI) were found to be formed the inhibition halo ranging from 13 to 23 mm against *Bacillus subtilis, B. megaterium, Escherichia coli* and *Sarcina lutea.*

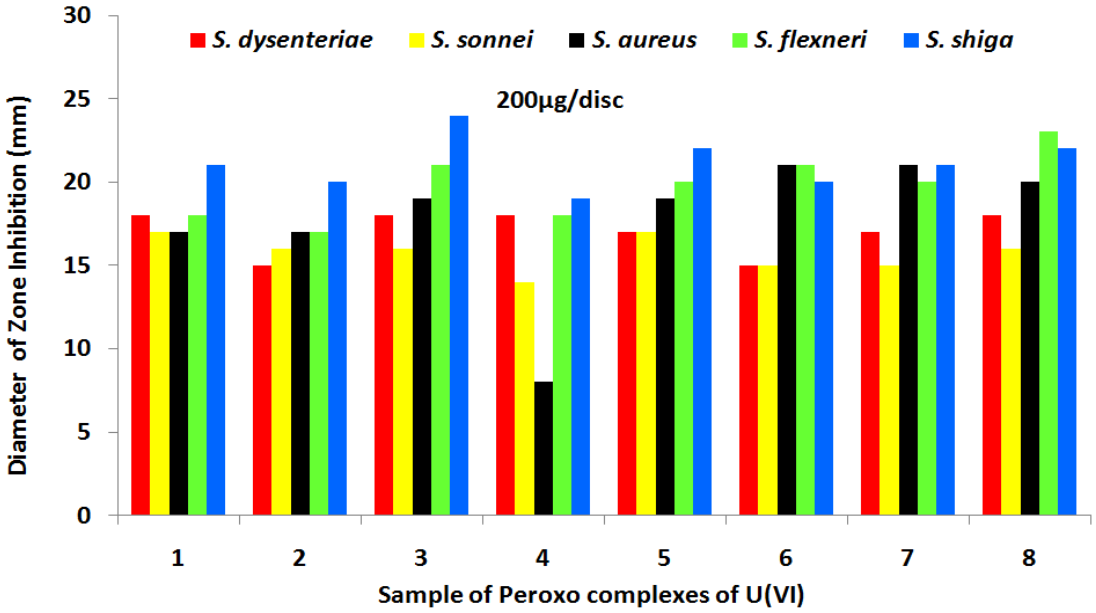

Figure 2: Antibacterial activity of the peroxo complexes of U(VI) against *Shigella dysenteriae, S. sonnei, S. aureus, S. flexneri*and *S. shiga.*

Table 1: Antibacterial activity of the peroxo complexes of U(VI) against *Shigella dysenteriae, S. sonnei, S. aureus, S. flexneri*and *S. shiga.*

No.	Peroxo complexes of U(VI)	Diameter of zone inhibition (mm)200 µg/disc				
		S. dysenteriae	*S. sonnei*	*S. aureus*	*S. flexneri*	*S. shiga*
1	$[UO(O_2)(gly)_2(py)]$	18	17	17	18	21
2	$[UO(O_2)(gly)_2(2\text{-pic})]$	15	16	17	17	20
3	$[UO(O_2)(gly)_2(4\text{-pic})]$	18	16	19	21	24
4	$[UO(O_2)(gly)_2(Q)]$	18	14	8	18	19
5	$[UO(O_2)(gly)_2(\text{iso-Q})]$	17	17	19	20	22
6	$[UO(O_2)(ala)_2(py)]$	15	15	21	21	20
7	$[UO(O_2)(ala)_2(2\text{-pic})]$	17	15	21	20	21
8	$[UO(O_2)(ala)_2(\text{iso-Q})]$	18	16	20	23	22

Furthermore, *Sarcina lutea* exhibited more susceptible against the complexes showing the higher values of inhibition halo compared to other bacteria tested (Table 2, Fig. 3). Results also clearly indicate that the complex $[UO(O_2)(ala)_2(\text{iso-Q})]$ revealed more active against all the *Bacillus subtilis, B. megaterium, Escherichia coli* and *Sarcina lutea* showing higher values of inhibition halo while the complex $[UO(O_2)(gly)_2(2\text{-pic})]$ showed less active (Table 2, Fig 3). The peroxo complexes of U(VI) also showed antibacterial activity against *Salmonella typhi, Streptococcus bodyii, S. -β-haemolyticus* and*Pseudomonas aeruginosa* (Table 3, Fig. 4). As the results indicate, *Salmonella bodyii* was found to be higher resistant towards all the complexes showing the lower values of inhibition halo compared to other bacteria. On the other hand, *S. typhi* exhibited comparatively more susceptible. Moreover, the complex $[UO(O_2)(gly)_2(2\text{-pic})]$ was not able inhibit al all against the *Salmonella bodyii*. As shown in Table 4 and Fig. 4, the peroxo complexes were found to be less active in fungi than that of bacteria.

Table 2: Antibacterial activity of the peroxo complexes of U(VI) against *Bacillus subtilis, B. megaterium, Escherichia coli* and *Sarcina lutea.*

No.	Peroxo complexes of U(VI)	Diameter of zone inhibition (mm)200 µg/disc			
		B. subtilis	*B. megatrium*	*E. coli*	*S. lutea*
1	$[UO(O_2)(gly)_2(py)]$	18	18	20	20
2	$[UO(O_2)(gly)_2(2\text{-pic})]$	17	17	19	19
3	$[UO(O_2)(gly)_2(4\text{-pic})]$	20	22	14	23
4	$[UO(O_2)(gly)_2(Q)]$	19	23	14	21
5	$[UO(O_2)(gly)_2(iso\text{-}Q)]$	20	19	15	21
6	$[UO(O_2)(ala)_2(py)]$	21	19	13	22
7	$[UO(O_2)(ala)_2(2\text{-pic})]$	20	18	15	23
8	$[UO(O_2)(ala)_2(iso\text{-}Q)]$	21	18	20	20

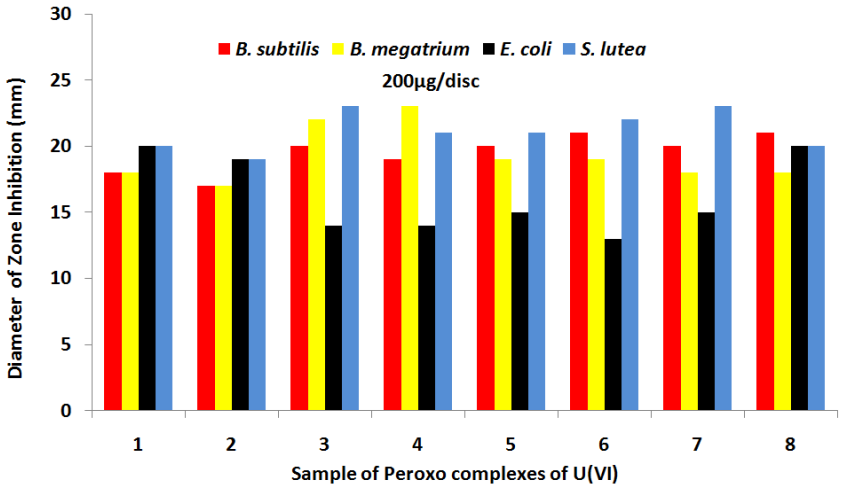

Figure 3: Antibacterial activity of the peroxo complexes of U(VI) against *Bacillus subtilis, B. megaterium, Escherichia coli* and *Sarcina lutea.*

All the fungi including *Aspergillus niger, A. fumigatus, A. flarus* exhibited more or less similar patterns of sensitivity to the complexes. Although, the fungi *A. flarus* exhibits more resistant to all the peroxo complexes than other fungi tested indicating the lower of values of inhibition halo (Table 4 and Fig. 5). Furthermore, the peroxo complexes $[UO(O_2)(ala)_2(py)]$ and $[UO(O_2)(gly)_2(py)]$ were found to be less active against the *A. flarus* showing the minimum values (11mm) of inhibition halo while the complexes $[UO(O_2)(ala)_2(py)]$ and $[UO(O_2)(ala)_2(iso\text{-}Q)]$ exhibited more active the *A. fumigates* having higher values (18 mm) of inhibition halo.

Table 3: Antibacterial activity of the peroxo complexes of U(VI) against *Salmonella typhi, Streptococcus bodyii, S. -β-haemolyticus* and*Pseudomonas aeruginosa*

No.	Peroxo complexes of U(VI)	Diameter of zone inhibition (mm)200 µg/disc			
		S. typhi	*S. bodyii*	*S.-β-haemolyticus*	*P. auriginosa*
1	$[UO(O_2)(gly)_2(py)]$	17	10	14	17
2	$[UO(O_2)(gly)_2(2\text{-pic})]$	17	0	13	16
3	$[UO(O_2)(gly)_2(4\text{-pic})]$	19	11	15	21
4	$[UO(O_2)(gly)_2(Q)]$	11	12	21	22
5	$[UO(O_2)(gly)_2(iso\text{-}Q)]$	18	10	16	17
6	$[UO(O_2)(ala)_2(py)]$	20	10	15	19
7	$[UO(O_2)(ala)_2(2\text{-pic})]$	19	10	14	19
8	$[UO(O_2)(ala)_2(iso\text{-}Q)]$	20	10	16	20

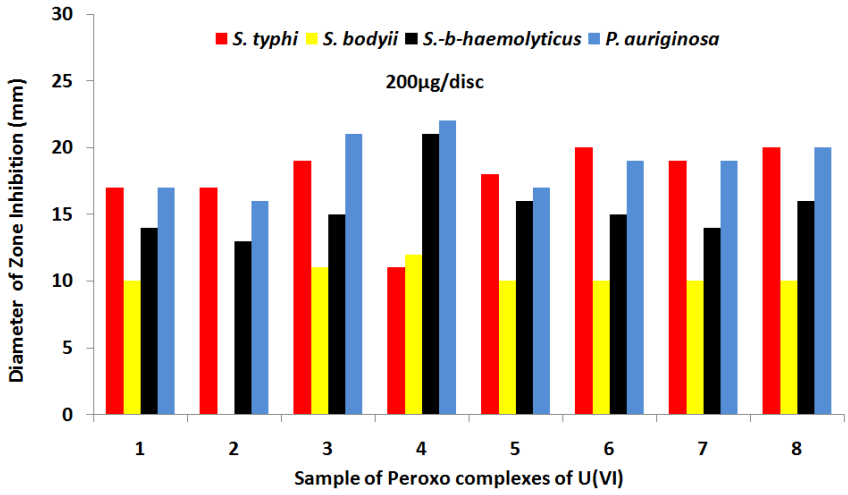

Figure 4: Antibacterial activity of the peroxo complexes of U(VI) against *Salmonella typhi, Streptococcus bodyii, S. -β-haemolyticus* and*Pseudomonas aeruginosa*

Table 4: Antifungal activity of the peroxo complexes of U(VI) against *Aspergillus niger, A. fumigatus, A. flarus.*

No.	Peroxo complexes of U(VI)	Diameter of zone inhibition (mm)200 µg/disc		
		A. niger	*A. fumigatus*	*A. flarus*
1	$[UO(O_2)(gly)_2(py)]$	17	13	11
2	$[UO(O_2)(gly)_2(2\text{-pic})]$	16	14	13
3	$[UO(O_2)(gly)_2(4\text{-pic})]$	13	14	15
4	$[UO(O_2)(gly)_2(Q)]$	13	13	14
5	$[UO(O_2)(gly)_2(\text{iso-Q})]$	14	13	14
6	$[UO(O_2)(ala)_2(py)]$	15	18	11
7	$[UO(O_2)(ala)_2(2\text{-pic})]$	16	15	13
8	$[UO(O_2)(ala)_2(\text{iso-Q})]$	15	18	14

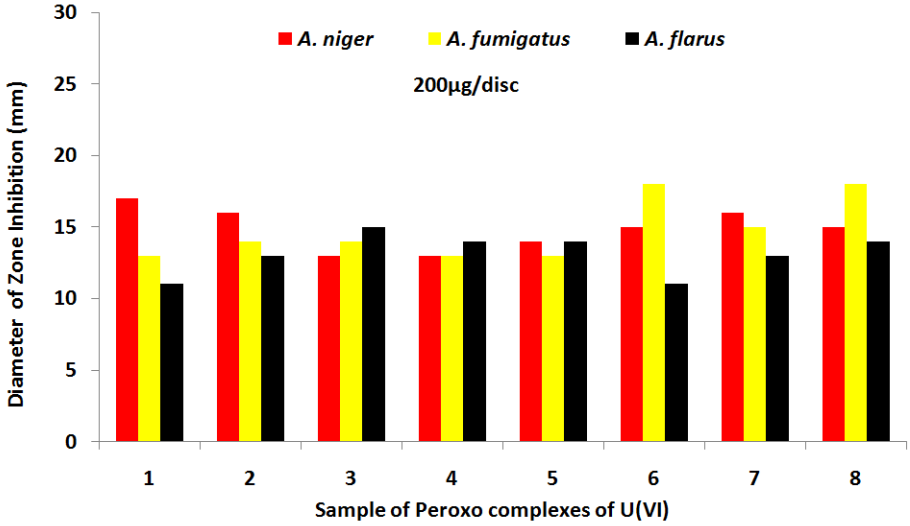

Figure 5: Antifungal activity of the peroxo complexes of U(VI) against *Aspergillus niger, A. fumigates* and *A. flarus.*

Results revealed that the lethal toxicity of peroxo complexes of metal U(VI) varied significantly against brine shrimp at different exposure periods (Table 5, Fig. 6 & 7). The complex $[UO(O_2)(gly)_2(4\text{-pic})]$ was found to more toxic against the brine shrimp showing the lower values of lethal concentration for 50 (LC_{99}) and 99% (LC_{99}) mortality at both exposures of 16- and 36-h except the LC_{99} mortality level at 36-h (Table 5). Furthermore, the complex $[UO(O_2)(ala)_2(2\text{-pic})]$ exhibits less toxic against the brine

shrimp particularly for 50% mortality indicating higher values of lethal concentration at 16h exposure. In addition, this complex was found to be more efficient for both the lethal concentration at 36-h of exposure. Results also showed that the concentrations 63.74, 74.59, 327.46, 44.18, 69.62, 44.18, 51.32, 360.96 µg/ml for $[UO(O_2)(gly)_2(py)]$, $[UO(O_2)(gly)_2(2\text{-pic})]$, $[UO(O_2)(gly)_2(4\text{-pic})]$, $[UO(O_2)(gly)_2(Q)]$, $[UO(O_2)(gly)_2(iso\text{-}Q)]$, $[UO(O_2)(ala)_2(py)]$, $[UO(O_2)(ala)_2(2\text{-pic})]$, $[UO(O_2)(ala)_2(iso\text{-}Q)]$ are required respectively for the 99% level mortality of brine shrimp at 36h exposure.

Table 5: Lethal toxicity of peroxo complexes of metal U(VI) against brine shrimp at different exposure periods.

No.	Peroxo complexes of **U (VI)**	Exposure 16 h		Exposure 36 h	
		LC_{50} µg/ml	LC_{99} µg/ml	LC_{50} µg/ml	LC_{99} µg/ml
1	$[UO(O_2)(gly)_2(py)]$	37.06	1038.6	18.68	63.74
2	$[UO(O_2)(gly)_2(2\text{-pic})]$	202.66	2592.6	14.26	74.59
3	$[UO(O_2)(gly)_2(4\text{-pic})]$	25.18	787.98	3.91	327.46
4	$[UO(O_2)(gly)_2(Q)]$	340.91	19923.0	4.77	44.18
5	$[UO(O_2)(gly)_2(iso\text{-}Q)]$	111.81	1071.5	9.22	69.62
6	$[UO(O_2)(ala)_2(py)]$	104.66	1936.2	4.77	44.18
7	$[UO(O_2)(ala)_2(2\text{-pic})]$	666.50	39796.0	8.83	51.32
8	$[UO(O_2)(ala)_2(iso\text{-}Q)]$	284.86	6401.0	11.00	360.96

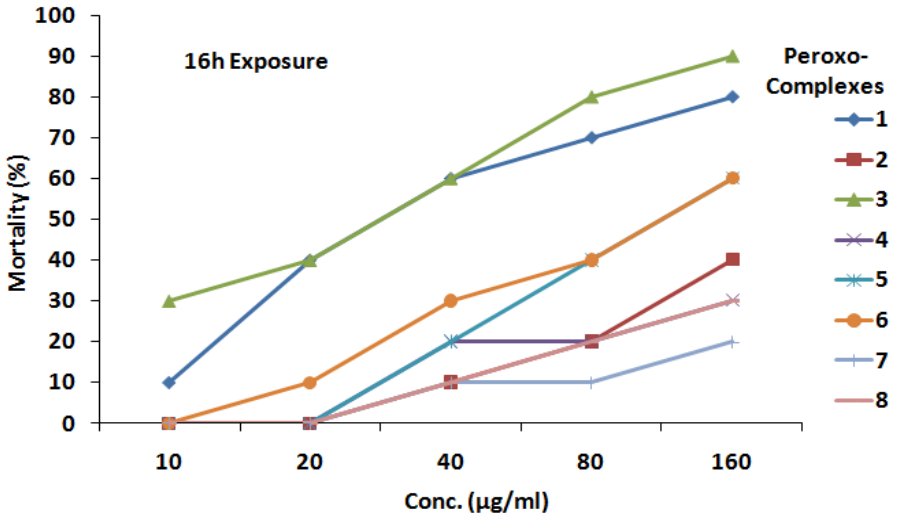

Figure 6: Lethal toxicity of peroxo complexes of metal U(VI) against brine shrimp at 16h exposure period.

The results clearly showed that the peroxo complexes of metal U(VI) exhibited the antimicrobial activity which was performed using the susceptibility test by disk diffusion for determining the MIC. The antimicrobial activity for peroxo complexes of metal U(VI) against different bacterial and fungal strains varied significantly for the MIC. In general, the peroxo complexes ofmetal U(VI) showed significant bactericidal and fungicidal activity. Biological activity of the ligand and a series of its metal complexes of U(VI) were screened for anti-bacterial and anti-fungal activity against several bacteria and fungi by using disc-agar diffusion method. The remarkable activity of ligands may arise from the organic and amine based groups which impart in elucidating the mechanism of transformation reaction in biological systems. The results reveal that the some of the complexes exhibit more activity while some of them have less activity against same microorganisms under identical experimental conditions. This would suggest that the ligands could facilitate the ability of a complex to cross a cell membrane and can be

explained by Tweedy's theory [46]. The some of the peroxo complexes shows higher anti-microbial activity than other complexes. The variation in the effectiveness of different compounds against bacteria and fungi depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells [47,48].

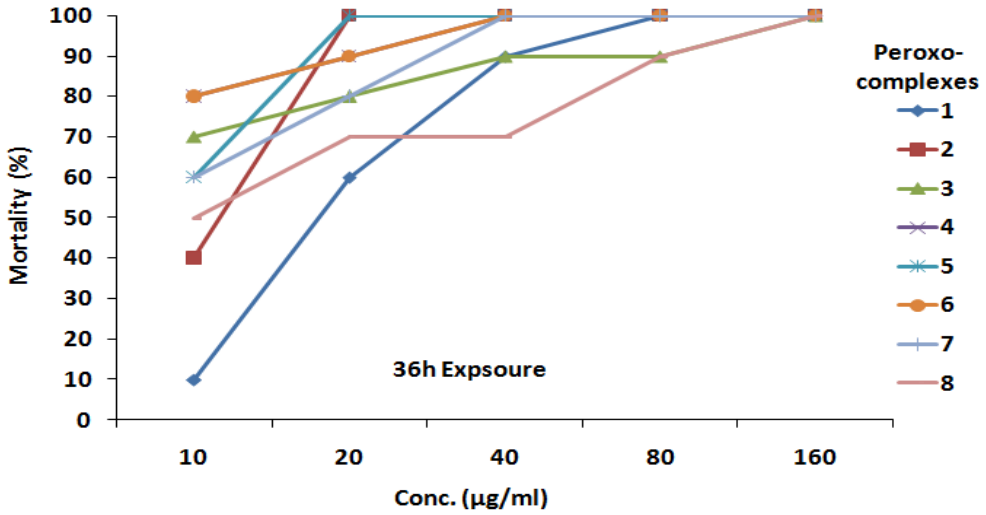

Figure 7: Lethal toxicity of peroxo complexes of metal U(VI) against brine shrimp at 36h exposure period

Interestingly, U(VI) peroxo systems interact with a variety of biologically important ligands, including organic acids and amino based. Moreover, the peroxo heteroligand complexes of this metal exhibit many analagous properties, both in their structural characteristics, and in their reactivity. It has been reported that the targets for lactam carbonyl antibiotics and related derivatives, are cell wall-synthesizing enzymes which are found as both cytoplasmic and membrane−bound enzymes and are present in almost all bacteria. They vary from one bacterium to another differing in molecular weight, amount, affinity for antibiotic derivatives and enzymatic function (e.g., carboxypeptidase, transpeptidase, or endopeptidase) [49]. Ghammamy et al. [50] synthesized some of the inorganic complexes of uranyl with N- donor ligands and The antitumor activity of some of ligand and their complexes against a panel of human tumor cell lines (HT29: Haman colon adenocarcinoma cell line T47D: human breast adenocarcinoma cell line) were determined by MTT(3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl-tetrazolium bromide) assay. They concluded that some of these compounds provide good models for the further design of potent antitumor compounds. Moreover, Reddy et al. [51] reported that dioxouranium complex has a better inhibition than the free ligand against bacteria and fungi. The present results revealed that the microbial activity of U(VI) metal complexes compared to other metal complex reflect a different mechanistic pathway by which they react with the penicillin-binding proteins (PBP) active sites to obtain formation of a stable PBP-inhibitor adduct. The level of affinity to metal-based antibiotics is determined by the nature and kinetic properties of the PBPs [49].

Conclusion

In the present activity, the effects of various synthetic ligand-containing metallic complexes on the biological function of bacteria such as antibacterial, antifungal and cytotoxicity have been studied. The practical implementation of biochemical chemistry is important in enhancing the design of compounds to reduce toxic side-effects and to understand their mechanisms along the way. Moreover, these investigations clearly indicate that peroxo compounds would be effective in establishing an appropriate strategy for the development of metal-based drugs in the pharmacological industry.

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