RASĀYAN *J. Chem.*
Vol. 17 | No. 3 |939-944| July - September | 2024
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

ANTIBACTERIAL STUDIES OF METAL ION OF URANYL $(UO_2)^{+2}$ WITH NOVEL POLYMERICLIGANDS PL-1 TO PL-6

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ABSTRACT
In today's time, increasing infection and resistance to an antibiotic is hazardous for the community. Every year, millions of people die as a result of bacterial illnesses around the world. Evolution in resistance has reduced the effectiveness of antibacterial drugs or made these drugs ineffective. This investigation aims to evaluate the antimicrobial potential of polymeric metal chelates of PATHQ with UO_2^{+2} metal ions on some gram -ve and gram +ve microorganisms. In recent work, uranyl $(UO_2)^{+2}$ novel compounds were synthesized from polyamine-s-triazine-5-amino-8-Hydroxyquinoline (PATHQ) and anti-microbial analysis was done by a zone of inhibition method. Mueller–Hinton agar was prepared and used for analysis. Antibacterial studies have been performed with 100 ppm concentration on different types of microorganisms i.e., *B. megaterium, S. aureus, P. aeruginosa* and *E.coli.*The plates were incubated at 32.5 ± 2.5ºC for 18 to 24 hours in an incubator. The results showed that the remarkable inhibition of bacterial growth was shown against the all-tested organisms. The microbial activity of the compound was due to the presence of UO2+2 metal ions. Hence, these compounds can be leads in the development of new pharmaceutical research activities.
Keywords: Antibacterial Activity, *B.megaterium, S.aureus, P. aeruginosa and E.coli.*
RASĀYAN *J. Chem.*, Vol. 17, No.3, 2024

INTRODUCTION

Emerging contagious illnesses, such as healthcare-associated infections (HCAIs), are a major problem in today's medical system. HCAIs are often difficult to treat because of the presence of additional factors like antimicrobial resistance, chronicity, and tolerance to traditional drugs. There is a clear need for new classes of antibiotics that employ different modes of action to be found and developed (MOAs). The advent of 5-triazines, related to different natural exercises like antimicrobial[1,2], antiprotozoal[3], anticancer[4] antimalarial5, and antiviral[6] action, separately, sped up the pace of progress in orchestrating new 1,3,5-triazine subsidiaries. Bicalutamide, an antitumor medication, contains the beneficial pharmacophore 4-amino-2-trifluoromethyl-benzonitrile as a molecular unit. Because of its excellent chemical stability and low radioactive risk, uranyl ion is one of the rare earth resources drawing interest from scientists.[7,8] It created two Schiff base-UO_2^{+2} complexes that were only effective against Gram-positive bacteria and were generally more effective than their equivalent ligands (7,9). The particle uranium, and its potential medical and environmental applications in terms of structural alterations to biological molecules and DNA disintegration.[10,11,12] Gram + ve and -ve microorganism classification and antimicrobial suitability are given below.

Staphylococcus aureus

Classification

Coagulase is produced by both S. aureus and S. intermedius. Staphylococci that are still present do not produce coagulase. They often have a high tolerance for sodium and are reactive. Identification relies on biotype research.

http://doi.org/10.31788/RJC.2024.1738408

Antimicrobial Susceptibility
90% of S. aureus generate the enzyme -lactamase, which can be used to screen for penicillin G resistance. Nafcillin resistance is present in approximately 35% of Staphylococcus isolates and over 75% of Staphylococcal isolates (together with oxacillin and methicillin resistance) (Brooks *et al.,* 2007). For resistant pathogens, additional medications include gentamicin, erythromycin, and vancomycin (like MRSA).

Pseudomonas aeruginosa
Classification
P. aeruginosa is a rod-shaped, unipolar, aerobic, and occasionally facultatively anaerobic bacteria. It is known to be an opportunistic pathogen that affects both people and plants.

Antimicrobial SusceptibilityF
Pseudomonas aeruginosa is the definition of an opportunistic nosocomial pathogen. It can cause a variety of infections and significantly increase morbidity in individuals with impaired immune systems.

B.megaterium
Classification
Bacteria; Firmicutes; Bacilli; Bacillales; Bacillaceae; Bacillus; Bacillus megaterium.

Antimicrobial Susceptibility
The bacterium Bacillus megaterium can be found just about anywhere on Earth. It is an endophyte and a ubiquitous soil bacterium, and it also occurs naturally in many foods.

E. coli
Classification
Escherichia coli is the most commonly encountered member of the family Enterobacteriaceae in the normal colonic flora and the most common cause of opportunistic infections (Sherris, 1984). All members of the family Enterobacteriaceae are facultative, all ferment glucose and reduce nitrates to nitrites, and all are oxidase-negative (Sherris, 1984).

Antimicrobial Susceptibility
Strains of Escherichia coli found in the population are typically vulnerable to all drugs active against the Enterobacteriaceae. However, isolates obtained in institutions may be immune to any mix of possibly useful antimicrobics due to the prevalence of R plasmids, so treatment must be directed by resistance testing. (Sherris, 1984).

EXPERIMENTAL

Material and Method
Every one of the compounds was of unadulterated or laboratory-grade quality. A previous publication detailed a procedure for preparing polyamine (PA) and PA-triazine (PAT) resin through polymerization. The 5-amino-hydroxy quinoline used in this study was made using a technique described in the literature.

Synthesis of PAT-5-Amino-8-Hydroxyquinoline (PATHQ)
Concentrated NaOH was added to a solution of PAT polymer (0.001 moles) and 5-amino-8-hydroxyquinoline (0.02 mole) in THF (100 milliliters) at a pH of 9-10, with the primary training pH being 9-10. After stirring at ambient temperature for 8 hours, the combination was elevated to 60 over the course of 5 minutes. The resulting gel-like substance was purified, rinsed with water, and desiccated in the air. The final particle size was 100 microns of powder. The return was 90%. Water and most organic liquids couldn't dissolve it, and it remained solid up to 300 degrees Celsius.

Synthesis of Polymeric Chelates andUO_2^{+2}
For the synthesis of PATHQ's polymeric metal chelates, PATHQ was reacted with the appropriate metal acetates. Here's how the process works in depth. In order to dissolve the desiccated PATHQ polymer (0.01 mole), 200 milliliters of a 20% liquid formic acid solution was heated in a water boiler for 10 minutes. A tepid arrangement of metal acetic acid derivation (0.01 mole) in half water formic corrosive was added

drop by drop while agitating this distributed solution. To facilitate the coagulation of polymeric chelates, the reaction liquid was turned alkaline with diluted ammonia. The by-products were put into a water soak for an additional hour to aid in digestion. When the polymer chelates had completely dissolved, they were filtered off, rinsed in boiling water, acetone, and DMF, and air-dried. Copolymer chelates of PATHQ with UO_2^{+2} transition metal ions were prepared Fig.-1.

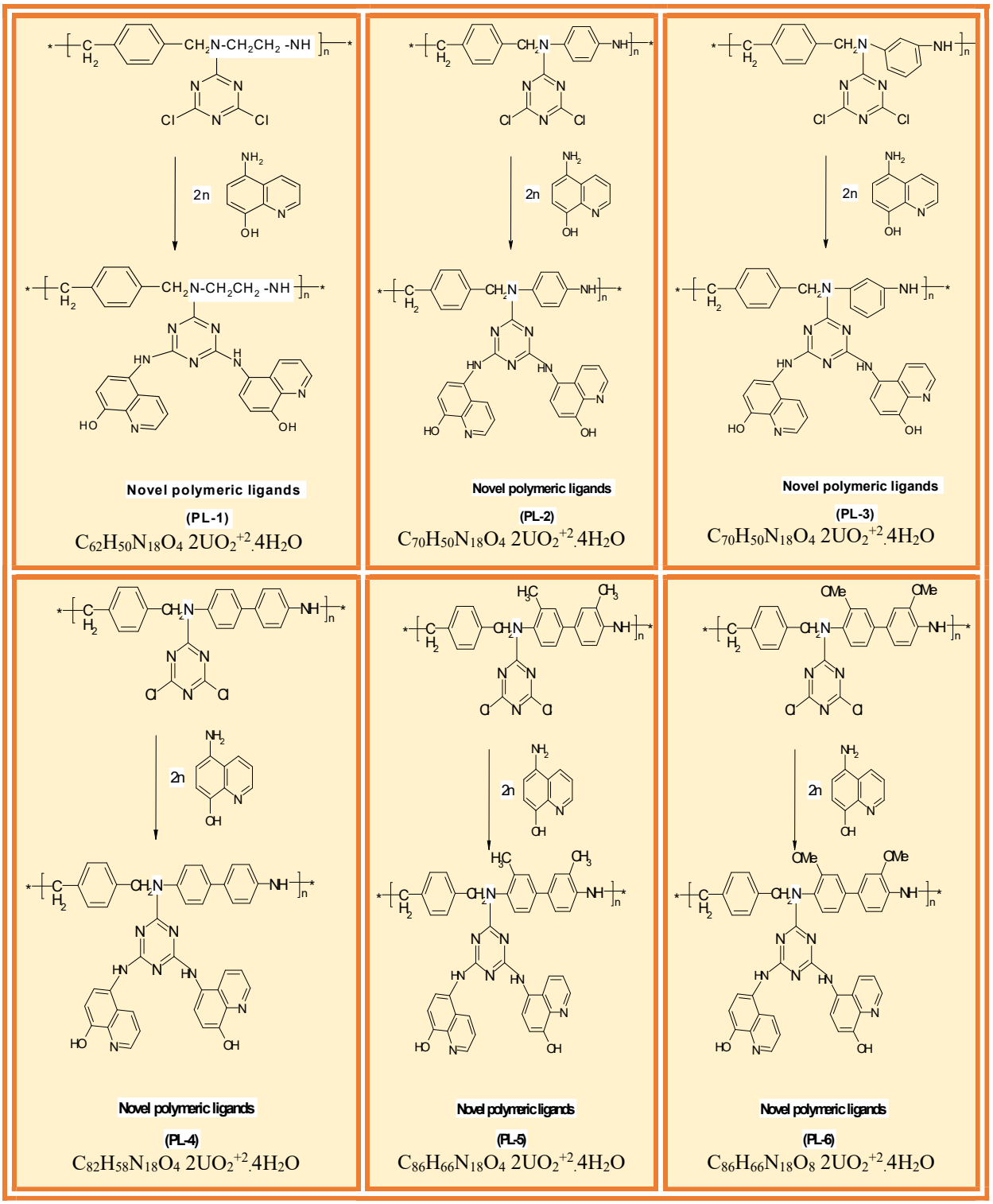


Fig.-1: (PL-1) UO_2^{+2}, (PL-2)UO_2^{+2}, (PL-3)UO_2^{+2}, (PL-4)UO_2^{+2}, (PL-5)$UO_2^{+2}$and (PL-6) UO_2^{+2}

Preparation of Mueller–Hinton Agar Media

According to microbiological limit testing, it is recommended for the cultivation of gram +ve bacteria and gram -ve bacteria from anti-bacteria tests. Weight accurately the 38.00 g of media. Slowly add media to the flask with purified water, taking care that the media does not spill. Take the pH of the media before sterilization in an autoclave. After the completion of sterilization, the media was unloaded from the autoclave. Cool to 45 degrees centigrade and pour media in under LAF. After sterilization of the media plate pH was done and a GPT test was performed. Media GPT is carried out in line with the harmonized technique of USP and bacteria grow after 5 days of incubation at 30°C-35°C. The final pH range is 7.20 to 7.40.

Culture Preparation of *B. megaterium, S. aureus, P. aeruginosa and E. coli.*

Carefully handle microbial cultures to prevent contamination of the area. Clean the Biosafety cabinet working bench with a disinfectant solution of 70 % IPA. Remove stock culture from the freezer. Use these subcultures as a working culture.

Detection Method

Zone of Inhibition Method

Take a media plate of Mueller–Hinton agar (M173- Hi media) and transfer it to the biosafety cabinet. Take a culture tube of ***B. megaterium*** and the spared plate method proceeds. Use 01MHA media plate for testing and make 01 cup 8.0-millimeter diameter through stopper proceeding induvial dish. In each petri dish, pour 100 µL, of each of the sample solutions. Keep the plates as such for 1-2 hours for the diffusion of the solution. Transfer the plates carefully into an incubator set at 30-35 °C so that there is no spill of dilution filled into each cup. Incubate the Petri dishes at 30-35 degrees for 05 days. Measure the area of the white zone-produced ligand complexes after incubation on a suitable antibiotic zone reader or Vernier caliper. The same procedure is applied for *S. aureus, P. aeruginosa and E. coli.*

Analytical Discussion

The same procedure is applied for *S. aureus, P. aeruginosa and E. coli.*

RESULTS AND DISCUSSION

Evaluation of Antimicrobial Result

The compounds (PL-1, PL-2, PL-3, PL-4, PL-5 and PL-6) and UO_2^{+2} ions were tested for antibacterial efficacy against four distinct bacteria strains including *B. megaterium, S. aureus, P. aeruginosa and E. coli* the same concentration (100%) as the compounds. These strains have been chosen based on their potential for use in further formulation research. The compounds PL-1 to PL-6 and UO_2^{+2} have anti-bacterial activity compared to other organisms.

Results of *B. megaterium*

It appears that polymeric metal chelates of PATHQ with UO_2^{+2} metal ions inhibited the growth of all (100%) the gram +ve bacteria (Table no.01 and Graph 01). Their anti-bacterial activities were recorded on(PL-1) UO_2^{+2} (ZOI in mm 15), (PL-2) UO_2^{+2} (ZOI in mm 17), (PL-3) UO_2^{+2} (ZOI in mm 15), (PL-4) UO_2^{+2} (ZOI in mm 14), (PL-5) UO_2^{+2} (ZOI in mm 16) and (PL-6) UO_2^{+2} (ZOI in mm 17).

Results of S. *aureus*

It appears that polymeric metal chelates of PATHQ with $UO2^{+2}$ metal ions inhibited the growth of all (100%) the gram +ve bacteria (Table no.01 and Graph 01). Their anti-bacterial activities were recorded on (PL-1) UO_2^{+2} (ZOI in mm 18), (PL-2) UO_2^{+2} (ZOI in mm 14), (PL-3) UO_2^{+2} (ZOI in mm 18), (PL-4) UO_2^{+2} (ZOI in mm 16), (PL-5) UO_2^{+2} (ZOI in mm 15) and (PL-6) UO_2^{+2} (ZOI in mm 17).

Results of *P. aeruginosa*

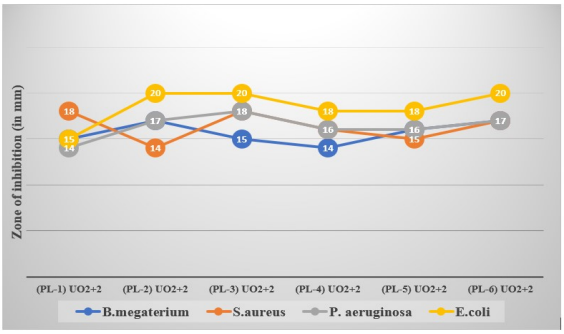
It appears that polymeric metal chelates of PATHQ with $UO2^{+2}$ metal ions inhibited the growth of all (100%) the gram +ve bacteria (Table no.01 and Graph 01). Their anti-bacterial activities were recorded on (PL-1) UO_2^{+2} (ZOI in mm 14), (PL-2) UO_2^{+2} (ZOI in mm 17), (PL-3) UO_2^{+2} (ZOI in mm 18), (PL-4) UO_2^{+2} (ZOI in mm 16), (PL-5) UO_2^{+2} (ZOI in mm 16) and (PL-6) UO_2^{+2} (ZOI in mm 17).

Results of *E. coli*

It appears that polymeric metal chelates of PATHQ with $UO2^{+2}$ metal ions inhibited the growth of all (100%) the gram +ve bacteria (Table-1 and Graph-1). Their anti-bacterial activities were recorded on (PL-1) UO_2^{+2} (ZOI in mm 15), (PL-2) UO_2^{+2} (ZOI in mm 20), (PL-3) UO_2^{+2} (ZOI in mm 20*),* (PL-4) UO_2^{+2} (ZOI in mm 18), (PL-5) UO_2^{+2} (ZOI in mm 18) *and* (PL-6) UO_2^{+2} (ZOI in mm 20). Figure-1 displays the sample images used for testing. Complexes and metal ions that were created were able to block *E. coli*, and (PL-2) $UO_2^{+2,}$ (PL-3) $UO_2^{+2}$and(PL-6) UO_2^{+2}showed the highest effective inhibition (20 mm), even more than (PL-1) UO_2^{+2} (15mm). In addition, the metal compound demonstrated an identical degree of suppression (17-18 millimeters) against E. coli. On the other hand, the(PL-3) UO_2^{+2} complex showed substantial antibacterial activity against *P. aeruginosa (18 mm)* and the (PL-1) UO_2^{+2} complex is 14 mm. (PL-1) UO_2^{+2} and (PL-3) UO_2^{+2} complex showed substantial antibacterial activity against *S.aureus (18mm) and* (PL-2) UO_2^{+2} complex is 14mm. PL-2) UO_2^{+2} and (PL-6) UO_2^{+2} showed substantial antibacterial activity against *B.megaterium*(17) *and* (PL-4) UO_2^{+2} *complex is 14mm.* Uranyl compounds were highly effective against Escherichia coli and have a modest effect against Bacteroides megaterium, Staphylococcus aureus, and Pseudomonas aeruginosa.

Table-1: Antibacterial Effect Show of PL-1 UO_2^{+2}, PL-2 UO_2^{+2}, PL-3 UO_2^{+2}, PL-4 UO_2^{+2}, PL-5 UO_2^{+2} and PL-6 UO_2^{+2} Metal Chelates

Sample	Zone of Inhibition (In mm)			
	Gram Positive		Gram Negative	
	B.megaterium	*S.auresus*	*P.aeruginosa*	*E. coli*
(PL-2) UO_2^{+2}	15	18	14	15
(PL-2) UO_2^{+2}	17	14	17	20
(PL-3) UO_2^{+2}	15	18	18	20
(PL-4) UO_2^{+2}	14	16	16	18
(PL-5) UO_2^{+2}	16	15	16	18
(PL-6) UO_2^{+2}	17	17	17	20



Graph-1: Antibacterial Effect Show of PL-1 UO_2^{+2} , PL-2 UO_2^{+2} , PL-3 sUO_2^{+2} , PL-4 UO_2^{+2} , PL-5 UO_2^{+2} and PL-6 UO_2^{+2} Metal Chelates

CONCLUSION

The synthetic compounds derived exhibited anti-bacterial activities. Therefore, a new family of metal-based bactericidal drugs was introduced as the UO_2^{+2} metal complexes of these compounds showed greater action against Gram-positive and negative microorganisms. There is a wide variety of potential uses for synthetic antibacterial polymers in many different industries, including but not limited to those listed above.

ACKNOWLEDGEMENTS

The author thanks to Dr. Bharti Jain Head of the department Department of Chemistry and all other members of the Department of Chemistry Government MLB Girls PG Autonomas Collage Bhopal for providing research facility and encouragement.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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[RJC- 8408/2024]