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Susceptibility Profiles of Multiple Antibiotic-Resistant Uropathogens to Eleagnine Compound Isolated from *Chryophyllum albidum* G. Don Holl (Sapotaceae) Seed Cotyledons

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Abstract

Persistent and recurrent urinary tract infections (UTIs) have been attributed to uropathogens developing resistance to multiple antibiotics. This has led to a rise in morbidity and mortality, treatment costs, hospital stays, and hospital visits, and has made the quest for more potent plant-derived antimicrobials unavoidable. The purpose of this study was to assess the susceptibility of various antibiotic-resistant uropathogens to eleagnine isolated from the seed cotyledon of *Chryophyllum albidum*. Using standard microbiological techniques, 100 uropathogens were isolated from urine samples of patients presented with UTIs at a Teaching Hospital Complex of a tertiary university in southwestern Nigeria. The isolates were identified using chromogenic agar and authenticated using conventional biochemical tests. Susceptibility profiles of the isolates to 12 selected commonly used antibiotics were determined using the Kirby-Bauer disk diffusion method. Susceptibility profiles of the multiple antibiotic-resistant uropathogens to eleagnine were determined using the broth microdilution technique. The results revealed *Staphylococcus aureus* as the predominant isolate with 72% occurrence. Susceptibility was highest for Levofloxacin (98%), and resistance was highest for meropenem. Also, the majority (81%) of the uropathogens have a multiple antibiotic resistance (MAR) index ≥ 0.2. All the multiple antibiotic-resistant uropathogens tested were susceptible to eleagnine with MIC_{50} of 0.625 mg/mL and MIC_{90} of 2.5 mg/mL. The study concluded that eleagnine exhibits antibacterial activity against multiple antibiotic-resistant uropathogens and may be effective in the management of recurrent and persistent urinary tract infections.

Keywords: Eleagnine, uropathogens, *Chryophyllum albidum,* multiple antibiotic-resistant

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Introduction

Urinary tract infection has been regarded as an important bacterial disease and contributes to significant morbidity in both outpatients and inpatients (Baral *et al*., 2012; Khan *et al*., 2014). UTIs are the second most common form of infection, accounting for nearly 25% of all infections (Foxman, 2003). It has been reported that the annual health expenditure on UTI in the United States of America amounts to 1.6 billion dollars (Vasquez and Hands, 2004; Sulham and Hammelman, 2021). UTI affects both males and females, but it is more prevalent in women (Czajkowski *et al*., 2021). Infants, pregnant women, the elderly, patients with spinal cord injuries and/or catheters, patients with diabetes or multiple sclerosis, patients with acquired immunodeficiency syndrome/human immunodeficiency virus, and patients with underlying urologic abnormalities are among the specific subpopulations at higher risk of UTI (Foxman, 2003). However, recurrent and persistent urinary tract infections have been attributed to multiple antibiotic-resistant uropathogens. This has led to an increase in the treatment cost, an increase in mortality and morbidity, an increase length of hospital stays and an increase in the number of hospital visits (Sharma *et al*., 2024).

A promising solution to uropathogens developing resistance to multiple antibiotics remains the use of more efficacious and effective antimicrobials, usually from natural source including medicinal plants. One of such promising plants is *Chryophyllum albidum.*
Chryophyllum albidum, popularly known as African star apple, is one of the medicinal plants with many ethobotanical uses. Its various uses include its use in the treatment of malaria, yellow fever, diarrhea, skin conditions, stomach aches, hypertension, and asthma. It has also been used as a cough suppressant aside from its use in the treatment of hemorrhoids, wounds and urinary-related infections. However, several pharmacological activities attributed to *C. albidum* have been reported. These include: antioxidant, antimicrobial, anti-inflammatory, antimalarial, antidiabetic, hepatoprotective, and cognitive enhancement (Ajayi *et al*., 2020; Ogunleye *et al*., 2020). Some of these activities have been attributed to the presence of phytochemical constituents such as tannins, flavonoids, saponins, terpenoids, alkaloids, reducing sugar, and cardiac glycosides (Cyril *et al*., 2023). Among these phytoconstituents, alkaloids remain the most widely and extensively studied (Heinrich *et al*., 2021), from which an active compound, eleagnine, a β-carboline alkaloid, has been isolated.
Idowu *et al.* (2016) reported the isolation of eleagnine, among other compounds, from the seed cotyledons of *C. albidum* and attributed the antimicrobial activity of the plant to eleagnine. According to Medu *et al*. (2016), eleagnine had no activity against Trichophyton but demonstrated greater bacteriostatic effect against Gram-positive organisms and *Candida* spp. than Gram-negative bacteria. Although the antimicrobial activity of eleagnine has been reported (Usifoh *et al*., 2019), there is no information about the susceptibility profiles of clinical bacterial isolates associated with urinary tract infections to this carboline compound, let alone the multiple antibiotic-resistant ones. Therefore, the purpose of this study was to assess the effectiveness of eleagnine compound isolated from the cotyledons of *C. albidum* against various antibiotic-resistant uropathogens.

Materials and Methods

Study area

The study was carried out at the Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria.

Ethical clearance

Ethical clearance with approval number IPH/OAU/12/2904 was sought and obtained from the Health Research Ethics Committee of the Institute of Public Health, Obafemi Awolowo University, Ile-Ife, Nigeria, prior to the commencement of the study.

Sample collections

Urine samples were collected from one hundred (100) patients presenting with urinary tract infections at the Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria. The consents of these patients were sought and obtained prior to the collection of urine samples. Volunteers were taught how to properly collect the midstream urine to avoid contamination. Sterile universal bottles were used for this purpose. The urine samples were processed within 2 h of collection.

Isolation and characterization of uropathogens

The urine samples were vortex-mixed to ensure uniform distribution of the content, and a loopful of each was plated on Cystine-Lactose-Electrolyte Deficient (CLED) agar, MacConkey agar, Manitol salt agar, and blood agar medium. The inoculated plates were incubated aerobically at 37°C for 24 h, after which they were examined for the presence of growth as exemplified by the presence of colonies. The estimated number of bacterial colonies was used to determine the UTI status of the patients. Each urine

sample with significant bacterial growth ($\geq 10^5$ cfu/mL) was sub-cultured to obtain pure isolates. The pure isolates were characterized using Chromogenic agar, and results were authenticated using conventional biochemical tests.

Antibiotic susceptibility profiles of the uropathogens

The antibiotic susceptibility profiles of the isolates were determined using the Kirby-Bauer disk diffusion method on Mueller-Hinton (MH) agar. The bacterial suspension was standardized to a 0.5 McFarland turbidity standard ($\approx 10^8$ CFU/mL) and spread on the surface of an MH agar plate with the aid of a sterile swab stick. Each antibiotic disc containing the following antibiotics: azithromycin 15 µg, Meropenem 10 µg, ceftriaxone 30 µg, erythromycin 5 µg, co-trimoxazole 25 µg, levofloxacin 5 µg, gentamicin 10 µg, ciprofloxacin 5 µg, Augmentin 30 µg, vancomycin 30 µg, chloramphenicol 10 µg, and cephalexin 30 µg was aseptically picked with a sterile forceps and firmly pressed to the MH agar surface. Inhibition zone diameters were determined in millimeters after plates were incubated for 24 hours at 37 °C.
Escherichia coli ATCC 25922 was used as a positive test strain. Results were interpreted in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2020). Isolates resistant to three or more antibiotic classes were classified as multidrug-resistant (MDR).

Susceptibility profiles of multiple antibiotic-resistant uropathogens to eleagnine

The minimum inhibitory concentration (MIC) of eleagnine against the selected multiple antibiotic-resistant uropathogens was determined. MICs were determined by the broth microdilution technique. Serial concentrations (5 – 0.0098 mg/mL) were prepared in Mueller –Hinton broth. Test organisms were appropriately diluted and inoculated to a final inoculum size of approximately 10^5 cfu/mL after being adjusted to the 0.5 McFarland standard ($\approx 10^8$ cfu/mL). After incubation at 37°C for 24 h under aerobic conditions, 10 µL of 0.2% resazurin dye was added and incubated further for another hour to assess bacterial growth. The lowest concentration with no visible growth, as exemplified by lack of change in resazurin colour, was recorded as the minimum inhibitory concentration (MIC).
Statistical analysis: The association between the minimum inhibitory concentration (MIC) and the multiple antibiotic resistance index (MARI) was determined by calculating the spearman's rank correlation coefficient using the GraphPad Prism.

Results

Distribution of the bacterial isolates

Among the bacterial isolates, *Staphylococcus aureus* (72%) exhibited the highest occurrence, while *Enterobacter cloacae* (1%) had the least occurrence. Others include: *Proteus mirabilis, Pseudomonas aeruginosa, Enterococcus feacalis, Escherichia coli, Klebsiella pneumoniae, Staphylococcus saprophyticus* and *Serratia marcescens* in varying proportions (Table 1).

Susceptibility profiles of the uropathogens

Susceptibility profiles of the isolated uropathogens to 12 commonly used antibiotics as well as their multiple antibiotic resistance index, calculated as the ratio of the antibiotics to which the isolate is resistant to the number of antibiotics tested are shown in Table 2. Susceptibility was highest for Levofloxacin (98%), and resistance was highest for meropenem. Also, the majority (81%) of the uropathogens have multiple antibiotic resistance (MAR) index ≥ 0.2, an indication that they originated from environments where the use of multiple antibiotics is endemic (Table 2).

Table 1: Percentage distribution of the isolates associated with urine samples of symptomatic urinary tract infection patients

Bacteria Isolates	Number of Organisms	Percentage Distribution (%)
Staphylococcus aureus	72	72
Proteus mirabilis	6	6
Pseudomonas aeruginosa	6	6
Enterococcus faecalis	4	4
Escherichia coli	3	3
Klebsiella pneumoniae	3	3
Staphylococcus saprophyticus	3	3
Serratia marcescens	2	2
Enterobacter cloacae	1	1
Total	100	100

Table 2: Susceptibility profiles of isolated uropathogens to commonly used antibiotics

CODE	Isolate	NIT	COT	GEN	AUG	LBC	CTR	CPM	CIP	AMK	VAN	AT	MEM	MAR Index
U5	*Enterobacter cloacae*	R	S	S	S	S	S	I	S	S	S	R	R	0.25
U13	*Enterococcus faecalis*	S	S	S	S	S	S	S	S	S	S	S	S	0
U18	*Enterococcus faecalis*	R	S	S	I	S	I	R	S	S	R	R	R	0.42
U28	*Enterococcus faecalis*	R	I	S	S	S	S	R	S	S	R	R	R	0.45
U98	*Enterococcus faecalis*	S	S	S	S	S	S	R	S	S	S	S	I	0.08
U20	*Escherichia coli*	R	S	S	R	S	S	R	S	S	R	R	R	0.5
U30	*Escherichia coli*	R	R	S	I	S	I	I	S	S	S	I	R	0.25
U33	*Escherichia coli*	R	S	S	R	S	S	R	S	S	R	I	R	0.42
U2	*Klebsiella pneumoniae*	S	S	S	S	S	S	R	S	S	S	S	R	0.17
U24	*Klebsiella pneumoniae*	R	I	S	I	S	S	R	S	S	R	R	R	0.42
U37	*Klebsiella pneumoniae*	R	S	S	R	S	S	R	S	S	R	R	R	0.5
U1	*Proteus mirabilis*	R	S	S	S	S	S	S	S	S	R	R	R	0.33
U11	*Proteus mirabilis*	R	S	S	I	I	S	I	S	R	R	S	R	0.33
U22	*Proteus mirabilis*	S	S	S	S	S	S	S	S	S	R	S	R	0.17
U40	*Proteus mirabilis*	S	S	I	S	S	S	I	S	S	R	S	R	0.17
U41	*Proteus mirabilis*	I	S	S	S	S	S	R	S	S	S	I	R	0.17
U51	*Proteus mirabilis*	R	S	S	S	S	S	R	S	S	R	R	R	0.42
U7	*Pseudomonas aeruginosa*	R	I	S	S	S	S	R	S	S	R	R	R	0.42
U62	*Pseudomonas aeruginosa*	S	S	S	S	S	S	R	S	S	S	R	R	0.25
U87	*Pseudomonas aeruginosa*	R	S	S	I	S	S	R	S	S	R	R	R	0.42
U89	*Pseudomonas aeruginosa*	R	R	S	I	S	S	R	R	S	R	R	R	0.58
U91	*Pseudomonas aeruginosa*	R	I	S	I	S	S	R	R	S	R	S	R	0.42
U95	*Pseudomonas aeruginosa*	R	R	S	R	S	R	R	S	S	R	R	R	0.67
U4	*Serratia marcescens*	R	S	S	S	S	S	R	S	S	R	S	R	0.33
U23	*Serratia marcescens*	R	S	R	S	S	S	R	S	S	R	S	R	0.42
U3	*Staphylococcus aureus*	I	R	S	S	S	S	R	S	S	R	R	R	0.42
U6	*Staphylococcus aureus*	R	S	S	S	S	S	S	S	S	S	R	R	0.25
U8	*Staphylococcus aureus*	R	I	R	I	S	S	I	S	S	R	S	R	0.33

U9	*Staphylococcus aureus*	R	S	S	I	S	S	R	S	S	R	I	R	0.33
U10	*Staphylococcus aureus*	R	R	S	R	S	R	R	S	S	R	R	R	0.67
U12	*Staphylococcus aureus*	R	R	S	R	S	I	R	S	S	R	I	R	0.5
U14	*Staphylococcus aureus*	I	I	S	R	S	S	R	R	S	R	R	R	0.5
U15	*Staphylococcus aureus*	R	S	S	I	S	S	R	S	S	R	I	R	0.33
U16	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	R	R	0.42
U17	*Staphylococcus aureus*	R	R	S	R	S	R	R	S	R	R	I	R	0.67
U19	*Staphylococcus aureus*	I	S	S	I	S	S	R	S	S	R	R	R	0.33
U21	*Staphylococcus aureus*	R	S	S	I	S	S	S	R	S	R	I	R	0.33
U25	*Staphylococcus aureus*	S	S	S	S	S	S	S	S	S	S	S	R	0.08
U26	*Staphylococcus aureus*	I	R	S	R	S	S	R	S	S	R	R	R	0.5
U27	*Staphylococcus aureus*	R	S	S	I	S	S	R	S	S	R	S	R	0.33
U29	*Staphylococcus aureus*	R	R	S	I	S	S	R	S	S	R	R	R	0.5
U31	*Staphylococcus aureus*	R	R	S	R	S	S	R	S	S	S	I	R	0.42
U32	*Staphylococcus aureus*	R	R	S	I	S	S	R	S	S	R	S	R	0.42
U34	*Staphylococcus aureus*	R	S	S	I	S	S	S	S	S	S	S	R	0.17
U35	*Staphylococcus aureus*	R	R	S	R	S	S	S	S	S	R	S	R	0.42
U38	*Staphylococcus aureus*	R	S	S	I	S	S	S	S	S	R	S	R	0.25
U39	*Staphylococcus aureus*	S	S	S	S	S	S	S	S	S	S	S	S	0
U42	*Staphylococcus aureus*	R	I	S	S	S	S	R	S	S	R	R	R	0.42
U43	*Staphylococcus aureus*	R	R	S	I	S	S	R	S	S	S	S	R	0.33
U44	*Staphylococcus aureus*	S	S	S	R	S	S	R	S	S	R	R	R	0.42
U45	*staphylococcus aureus*	S	S	S	I	S	S	R	S	S	R	S	R	0.25
U46	*staphylococcus aureus*	I	R	S	I	S	S	R	S	S	R	R	R	0.42
U47	*staphylococcus aureus*	S	S	S	S	S	S	S	S	S	S	S	R	0.08
U48	*staphylococcus aureus*	S	S	S	S	S	S	S	S	S	S	I	R	0.08
U49	*staphylococcus aureus*	S	S	S	S	S	I	S	S	S	S	R	R	0.17
U50	*staphylococcus aureus*	S	S	S	R	S	S	S	S	S	S	S	R	0.17
U52	*Staphylococcus aureus*	R	S	I	S	S	R	R	R	S	R	R	R	0.58
U53	*Staphylococcus aureus*	R	R	S	R	S	I	R	S	S	R	R	R	0.58
U54	*Staphylococcus aureus*	R	R	R	R	S	I	R	S	R	R	R	R	0.75

U55	*Staphylococcus aureus*	S	R	R	R	R	I	R	S	R	S	S	R	0.58
U57	*Staphylococcus aureus*	S	S	R	S	S	S	S	S	S	S	S	R	0.17
U58	*Staphylococcus aureus*	S	S	S	S	S	S	S	S	S	S	S	R	0.08
U59	*Staphylococcus aureus*	S	S	S	I	S	I	R	R	S	S	R	R	0.33
U60	*Staphylococcus aureus*	S	S	S	S	S	S	R	S	S	S	S	R	0.17
U61	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	R	S	0.33
U63	*Staphylococcus aureus*	S	R	S	R	S	S	R	S	S	S	R	R	0.42
U64	*Staphylococcus aureus*	R	R	S	S	S	I	S	S	S	R	R	S	0.33
U65	*Staphylococcus aureus*	R	R	S	R	S	R	R	S	S	R	R	R	0.67
U66	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	I	R	0.33
U67	*Staphylococcus aureus*	R	I	S	I	S	S	R	S	S	R	R	R	0.42
U68	*Staphylococcus aureus*	R	S	S	I	S	S	R	S	S	R	R	R	0.42
U69	*Staphylococcus aureus*	S	S	R	S	S	S	R	S	S	S	R	R	0.33
U70	*Staphylococcus aureus*	R	R	S	S	S	S	R	S	S	R	I	R	0.42
U71	*Staphylococcus aureus*	S	S	S	S	S	S	R	S	S	R	R	R	0.33
U72	*Staphylococcus aureus*	R	R	S	R	S	I	R	S	S	R	R	R	0.58
U73	*Staphylococcus aureus*	R	R	S	R	S	R	R	S	S	R	R	R	0.67
U74	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	R	R	0.42
U75	*Staphylococcus aureus*	R	S	S	I	S	S	R	S	S	R	R	R	0.42
U76	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	S	R	0.33
U77	*Staphylococcus aureus*	R	S	S	S	S	S	S	S	S	R	R	R	0.33
U78	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	R	R	0.42
U79	*Staphylococcus aureus*	R	R	S	I	S	S	R	S	S	R	R	R	0.5
U80	*Staphylococcus aureus*	R	R	S	S	S	S	R	S	S	R	R	R	0.5
U81	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	R	R	0.42
U82	*Staphylococcus aureus*	R	S	S	I	S	S	R	S	S	R	R	R	0.42
U83	*Staphylococcus aureus*	R	R	S	R	S	S	R	S	S	R	I	R	0.5
U84	*Staphylococcus aureus*	S	S	S	S	S	S	S	S	S	S	I	S	0
U85	*Staphylococcus aureus*	S	S	R	I	S	S	R	S	S	S	R	R	0.33
U86	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	R	R	0.42
U88	*Staphylococcus aureus*	R	R	S	R	S	I	R	R	S	R	R	R	0.67

U90	*Staphylococcus aureus*	R	I	S	S	S	S	R	S	S	R	S	I	0.25
U92	*Staphylococcus aureus*	S	R	S	S	S	S	S	S	S	S	S	S	0.08
U94	*Staphylococcus aureus*	R	I	S	I	S	S	R	S	S	R	R	R	0.42
U96	*Staphylococcus aureus*	R	I	S	I	S	S	R	S	S	R	R	R	0.42
U97	*Staphylococcus aureus*	R	S	S	S	S	S	R	S	S	R	S	R	0.42
U99	*Staphylococcus aureus*	R	R	S	I	S	S	R	S	S	R	I	R	0.42
U100	*Staphylococcus aureus*	R	S	R	I	S	I	R	I	S	R	R	R	0.5
U36	*Staphylococcus saprophyticus*	R	S	S	S	S	S	S	S	S	R	R	R	0.33
U56	*Staphylococcus saprophyticus*	S	S	S	S	S	S	S	S	S	S	S	S	0
U93	*Staphylococcus saprophyticus*	S	I	R	S	S	R	R	S	S	S	I	R	0.33
	E. coli ATCC 25922	S	S	S	S	S	S	S	S	S	S	S	S	0

S: Sensitive; R: Resistant; I: Intermediate

Key: MEM: Meropenem; VAN: Vancomycin; AUG: Augmentin; CPM: Cefepime; AT: Aztreonam; NIT: Nitrofurantoin; AMK: Amikacin; COT: Cotrimoxazole; CTR: Ceftriaxone; CIP: Ciprofloxacin; GEN: Gentamicin; LBC: Levofloxacin

Minimum Inhibitory Concentration (MIC) of eleagnine

Eleagnine displayed antibacterial activity against the isolated uropathogens irrespective of their MAR index. However, the MIC of eleagnine against all *Serratia marcescens* species was 2.5 mg/mL, all *Escherichia coli* species, 2.5 mg/mL, and *Klebsiella pneumoniae* species, 1.25 mg/mL. Other species displayed varying susceptibility to eleagnine, with *Staphylococcus aureus* having a range of MIC between 5 and 0.15625 mg/mL (Table 3). Statistical analysis revealed a weak association between the MIC and MARI with Spearman's coefficient of -0.06988, an indication that MARI has no effect on the antibacterial activity displayed by eleagnine.

Table 3: Minimum Inhibitory Concentration (MIC) of eleagnine against isolated uropathogens

CODE	Isolate	MIC (mg/mL)	MAR Index
U5	*Enterobacter cloacae*	2.5	0.25
U13	*Enterococcus faecalis*	1.25	0
U18	*Enterococcus faecalis*	1.25	0.42
U28	*Enterococcus faecalis*	2.5	0.45
U98	*Enterococcus faecalis*	1.25	0.08
U20	*Escherichia coli*	2.5	0.5
U30	*Escherichia coli*	2.5	0.25
U33	*Escherichia coli*	2.5	0.42
U2	*Klebsiella pneumoniae*	1.25	0.17
U24	*Klebsiella pneumoniae*	1.25	0.42
U37	*Klebsiella pneumoniae*	1.25	0.5
U1	*Proteus mirabilis*	2.5	0.33
U11	*Proteus mirabilis*	2.5	0.33
U22	*Proteus mirabilis*	0.625	0.17
U40	*Proteus mirabilis*	2.5	0.17
U41	*Proteus mirabilis*	2.5	0.17
U51	*Proteus mirabilis*	0.625	0.42
U7	*Pseudomonas aeruginosa*	1.25	0.42
U62	*Pseudomonas aeruginosa*	0.15625	0.25
U87	*Pseudomonas aeruginosa*	0.625	0.42
U89	*Pseudomonas aeruginosa*	0.625	0.58
U91	*Pseudomonas aeruginosa*	0.625	0.42
U95	*Pseudomonas aeruginosa*	1.25	0.67
U4	*Serratia marcescens*	2.5	0.33
U23	*Serratia marcescens*	2.5	0.42

U3	*Staphylococcus aureus*	1.25	0.42
U6	*Staphylococcus aureus*	0.625	0.25
U8	*Staphylococcus aureus*	2.5	0.33
U9	*Staphylococcus aureus*	2.5	0.33
U10	*Staphylococcus aureus*	0.625	0.67
U12	*Staphylococcus aureus*	0.3125	0.5
U14	*Staphylococcus aureus*	0.625	0.5
U15	*Staphylococcus aureus*	0.625	0.33
U16	*Staphylococcus aureus*	0.625	0.42
U17	*Staphylococcus aureus*	0.3125	0.67
U19	*Staphylococcus aureus*	0.15625	0.33
U21	*Staphylococcus aureus*	2.5	0.33
U25	*Staphylococcus aureus*	0.625	0.08
U26	*Staphylococcus aureus*	0.625	0.5
U27	*Staphylococcus aureus*	0.3125	0.33
U29	*Staphylococcus aureus*	1.25	0.5
U31	*Staphylococcus aureus*	1.25	0.42
U32	*Staphylococcus aureus*	0.625	0.42
U34	*Staphylococcus aureus*	1.25	0.17
U35	*Staphylococcus aureus*	0.15625	0.42
U38	*Staphylococcus aureus*	0.3125	0.25
U39	*Staphylococcus aureus*	1.25	0
U42	*Staphylococcus aureus*	0.15625	0.42
U43	*Staphylococcus aureus*	0.3125	0.33
U44	*Staphylococcus aureus*	0.3125	0.42
U45	*Staphylococcus aureus*	0.625	0.25
U46	*Staphylococcus aureus*	0.3125	0.42
U47	*Staphylococcus aureus*	0.625	0.08
U48	*Staphylococcus aureus*	0.15625	0.08
U49	*Staphylococcus aureus*	0.625	0.17
U50	*Staphylococcus aureus*	0.15625	0.17
U52	*Staphylococcus aureus*	0.625	0.58
U53	*Staphylococcus aureus*	0.3125	0.58
U54	*Staphylococcus aureus*	0.625	0.75

U55	*Staphylococcus aureus*	0.3125	0.58
U57	*Staphylococcus aureus*	0.15625	0.17
U58	*Staphylococcus aureus*	0.625	0.08
U59	*Staphylococcus aureus*	0.625	0.33
U60	*Staphylococcus aureus*	0.15625	0.17
U61	*Staphylococcus aureus*	0.625	0.33
U63	*Staphylococcus aureus*	0.3125	0.42
U64	*Staphylococcus aureus*	0.3125	0.33
U65	*Staphylococcus aureus*	0.3125	0.67
U66	*Staphylococcus aureus*	0.625	0.33
U67	*Staphylococcus aureus*	0.3125	0.42
U68	*Staphylococcus aureus*	0.3125	0.42
U69	*Staphylococcus aureus*	0.625	0.33
U70	*Staphylococcus aureus*	0.3125	0.42
U71	*Staphylococcus aureus*	0.625	0.33
U72	*Staphylococcus aureus*	0.3125	0.58
U73	*Staphylococcus aureus*	0.625	0.67
U74	*Staphylococcus aureus*	0.625	0.42
U75	*Staphylococcus aureus*	0.3125	0.42
U76	*Staphylococcus aureus*	0.3125	0.33
U77	*Staphylococcus aureus*	5.00	0.33
U78	*Staphylococcus aureus*	0.15625	0.42
U79	*Staphylococcus aureus*	0.625	0.5
U80	*Staphylococcus aureus*	0.625	0.5
U81	*Staphylococcus aureus*	0.15625	0.42
U82	*Staphylococcus aureus*	0.3125	0.42
U83	*Staphylococcus aureus*	0.625	0.5
U84	*Staphylococcus aureus*	0.3125	0
U85	*Staphylococcus aureus*	0.15625	0.33
U86	*Staphylococcus aureus*	1.25	0.42
U88	*Staphylococcus aureus*	1.25	0.67
U90	*Staphylococcus aureus*	0.15625	0.25
U92	*Staphylococcus aureus*	0.625	0.08
U94	*Staphylococcus aureus*	1.25	0.42

U96	*Staphylococcus aureus*	0.15625	0.42
U97	*Staphylococcus aureus*	0.625	0.42
U99	*Staphylococcus aureus*	0.625	0.42
U100	*Staphylococcus aureus*	0.625	0.5
U36	*Staphylococcus saprophyticus*	2.5	0.33
U56	*Staphylococcus saprophyticus*	1.25	0
U93	*Staphylococcus saprophyticus*	2.5	0.33

Spearman, r = -0.06988; 95% confidence interval = -0.2682 to 0.1341; P value (two-tailed) = 0.4896
Quantitative analysis

Discussion

The contribution of urinary tract infections (UTIs) to the worldwide increase in morbidity and mortality cannot be underestimated (Bavanandan *et al*., 2023). Globally, UTIs have been associated with a significant number of deaths and a reduced quality of life of affected patients (Ozturk and Murt, 2020; Yang *et al*., 2022). Urinary tract infections (UTIs) can be caused by various pathogens, with bacteria being the primary culprits in approximately 95% of instances (Farajnia *et al*., 2009). Within the group of bacterial pathogens, the Enterobacteriaceae family plays a significant role in UTIs, particularly *Escherichia coli*, which is responsible for 70-80% of cases (Farajnia *et al*., 2009; Khan *et al*., 2014). Other bacterial organisms that can lead to UTIs include *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus* species, and *Enterococcus* species (Hooton *et al*., 2004; Khan *et al*., 2014; Shahzad *et al*., 2013).

In this study, nine different bacterial species were found, with *S. aureus* as the most prevalent. All the bacterial species found in this study have been previously reported (Anjum *et al*., 2016; Thangavelu *et al*., 2022; Alain *et al*., 2024). The finding of *S. aureus* as the most prevalent in this study agrees with the reports of other researchers (Priyadharsini *et al*., 2014; Alshomrani *et al*., 2023; Ehiagbe and Osaro, 2025). However, other researchers have reported *E. coli* (Kibret and Abera, 2014; Anjum *et al*., 2016; Abdullahi and Oranekwulu, 2025), and *Klebsiella pneumoniae* (Omonigho *et al*., 2001; Osazuwa *et al*., 2010; Otajevwo, 2013) as the most prevalent isolates.

Uropathogens differ in their pathogenesis, virulence and antibiotic susceptibilities. It has been reported that uropathogens are developing resistance to commonly prescribed antibiotics at alarming rates (Gupta, 2002). This can be attributed to wrong diagnosis or self-medication as a result of a lack of routine diagnostic and culture facilities (Hammer *et al*., 2007; Baral *et al*., 2012). In this study, the majority of the uropathogens isolated were susceptible to levofloxacin, a fluoroquinolone antibiotic, and highly resistant to imipenem, a broad-spectrum carbapenem antibiotic.

Resistance to carbapenem antibiotics, such as imipenem, can be through decreased permeability, over-expression of efflux pumps, modification of antibiotic target sites, and enzymatic inactivation (Aurilio *et al*., 2022). The evolution of carbapenem-resistant uropathogens as found in this study poses a threat to public health as they are difficult to treat and their association with high mortality (WHO, 2017).

The presence of multiple antibiotic resistance among uropathogens has been reported (Dasgupta *et al*., 2020; Khan *et al*., 2024; Tuhamize *et al*., 2025). The association of multiple antibiotic resistance with uropathogens has been responsible for most therapeutic failures in the treatment of urinary tract infections. The multiple antibiotic resistance (MAR) index, which is defined as the ratio of the number of antibiotics to which a bacterium is resistant to the total number of antibiotics tested, is frequently used to quantify multiple antibiotic resistance. The MAR Index can be low (≤0.2), moderate (0.21–0.59), or high (≥0.6) (Puspita *et al*., 2021). Multiple antibiotic resistance has been attributed to the presence of genes that code for multiple resistance, such as plasmids, transposons, and/or integron (Nustrat *et al*., 2025).

In this study, the majority of the isolated uropathogens had between high and moderate MAR with index ≥ 0.2. This implies that they originated from sources where the use of multiple antibiotics is indiscriminate and endemic.

The search for more potent and effective antimicrobials from natural sources, including medicinal plants, has become necessary due to uropathogens' multiple antibiotic resistance. Screening of various medicinal plants has led to the discovery of many potent bioactive compounds (El-Saadony *et al*., 2025), including eleagnine, which was reportedly present in the seed cotyledons of *C. albidum* and is responsible for the antimicrobial activity of the plant's part (Idowu *et al*., 2016).

Notwithstanding the paucity of information about the mechanisms of antibacterial activity of eleagnine, Medu *et al.* (2016) reported its bactericidal activity with minimum cytotoxicity. Susceptibility of multiple antibiotic-resistant uropathogens (irrespective of their MARI) to eleagnine, as

found in this study, suggests that the mechanism of its antibacterial activity differs from those of antibiotics used for the study or that eleagnine possesses the capacity to antagonize some of the mechanisms through which uropathogens develop resistance to antibiotics. Wei *et al*. (2026) attributed the antibacterial activity of C-6 aminated β-Carboline derivatives against methicillin-resistant *Staphylococcus aureus* (MRSA) to their ability to disrupt bacterial cell walls and membranes. Other possible mechanisms of antibacterial activity of eleagnine which remain to be explored in future studies may include inhibition of efflux pumps, or inhibition of enzymes responsible for inactivation of some antibiotics.

Conclusion

The study concluded that eleagnine has antibacterial activity against multiple antibiotic-resistant uropathogens and may be useful in the management of recurrent and persistent urinary tract infections.

Declaration of Conflict of Interest

The authors affirm that they have no conflicts of interest related to this study.

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