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(RESEARCH ARTICLE)

Investigation of antimicrobial activities of bioactive compound against *Pseudomonas aeruginousa* isolated from burns infections

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Abstract

Forty-five samples in total there are just twenty isolates of *Pseudomonas aeruginousa*. Over the period of four months, from January 2025 to April 2025, a variety of clinical samples were gathered from numerous hospitals in Baghdad, including Al-Sader, Ibn Al-Balady, Fatima Al-Zahraa, and Al-Imam Ali Hospitals. The clinical samples of patients with burns infections were included. The Vitek 2 compact and a biochemical test verified that all isolates were cultivated on king A, king B, ctrmide agar, macConkey agar, and blood agar. Using the disk diffusion technique, the susceptibility of *P. aeruginousa* isolates to 16 antibiotics from various classes was determined. *P. aeruginousa* isolates exhibited strong resistance to the majority of the antibiotics under investigation, according to the findings of the sensitivity test. Numerous *Aspergillus terreus* bioactive extract compounds that were extracted from soil showed antibacterial activity. Through a number of signal transduction pathways, secondary metabolites activate the host's defenses. At varying concentrations, the bioactive molecule showed high levels of efficacy against *P. aeruginousa* isolates from burns.

Keywords: *Aspergillus terreus*; *Pseudomonas aeruginousa*; Multidrug resistance; Antimicrobial activity

1. Introduction

Pseudomonas aeruginosa, is gram-negative, a rod-shaped, aerobic, and motile bacterium, and, that may be isolated from a range of resources, including as soil, animal tissue, and plants [1]. This bacteria thrives on different surfaces, water, and medical equipment by using its essential binding components, such as pili, biofilms formation, and flagella. *P. aeruginosa* is therefore common in both artificial and natural environments, including hospitals, household sink drains, lakes [2]. *P. aeruginosa*, that causes infections in humans and is an opportunistic bacterium. It currently plays a significant role in antibiotic resistance and nosocomial infections [3]. This bacteria is associated with infections in healthcare settings, including infections in ventilator-associated pneumonia (VAP), urinary tract infections, surgical site infections, intensive care units, bloodstream infections linked to central lines, keratitis, burn wound infections, and otitis media. In contrast, *P. aeruginosa* is an organism that can produce a variety of virulence factors, rapidly develop antibiotic resistance, and adjust to environmental changes and effect on immunocompromised individuals due in part to its ability to create a range of virulence factors, that cause significant tissue damage and to evade both innate immune and acquired responses through adhesion, colonization, and biofilm formation [4]. Additionally, it causes severe burns, cancer, newborn infections, and illnesses with a high fatality rate in people with cystic fibrosis [5]. Therefore, a fresh approach to therapy is required. During the growth phase, microorganisms generate a variety of metabolites that are important to industry, including as pigments, enzymes, dyes, and antibacterial agents. Through metabolic activities, microorganisms such as bacteria, fungus, and actinomycetes create chemical compounds known as antimicrobial agents during the stationary phase of microbial development. "Antibiotics" are secondary metabolites that do not aid in the growth or development of live organisms [6]. Secondary metabolites are a class of chemicals that are primarily responsible for the chemistry of natural goods. Filamentous fungus are the source of some of the most powerful

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secondary metabolites that have been turned into medicinal medications [7]. The study objectives were to identify and isolate *P. aeruginosa* from burn patients, check for antibiotic resistance in these isolates, look for phenotypic virulence factors, screen for fungal isolates that can produce antimicrobial agents.

2. Materials and Methods

2.1. Sample Collection

Throughout the period, of four months, from January 2025 to April 2025. A total of 45 different clinical samples, including those from burn infections, were gathered from different hospitals in Baghdad including; Fatima Al-Sader, Al-Zahraa, Al-Imam Ali, Ibn Al-Balady Hospitals.

2.2. Isolation of *Pseudomonas aeruginosa*

Following collection, the clinical samples of burns infections, were straight-cultured on ctrmide, blood agar plates, and incubated for 24 hours at 37 º C. For essential identification, white colonies on blood agar, grayish and opaque, were recultured on macConkey agar plates and incubated for 24 hours at 37ºC. To get pure colonies, the chosen colonies were subcultured on another macConkey agar plates. All culture media were produced in accordance with the manufacturer instructions, and additional tests were conducted in accordance with [8].

2.3. Identification of *P. aeruginosa* by Using VITEK 2 Compact System

For the identification of clinically important microorganisms, the VITEK® 2 Compact system is advised. A computer, printer, and the VITEK® 2 Compact device are all part of the system. Programs for data administration and analysis are among the software packages that come with the VITEK® 2 Compact system. This card, which has 64 holes and contains specific culture media with substrate specifically for biochemical tests, as well as one hole that contains culture media as a negative control, fulfills a number of standard tests that have been modified to be used within the VITEK-2 Compact systems. It is an analyst automated diagnostic apparatus confirmatory used for isolates using the card ID-GNB. The card is designed for accurate and rapid diagnosis of the types of gram negative bacteria. The diagnosis of this card depends on the biochemical methods and develop new foundation materials. Results may be obtained in as little as 4 hours.

2.4. Antibiotics Sensitivity Test

Antibiotics sensitivity test towards 16 antibiotics: AK: Amikacin. AM: Ampicillin. AZT: Aztreonam. CZ: Cefazolin. CPM: Cefepime. CTX: Cefotaxime. CIP: Ciprofloxacin. IMI: Imipenem, DXT: Doxycycline. GM: Gentamicin, LEV: Levofloxacin, NIT: Nitrofurantoin, MEM: Meropenem, PTZ: Piperacillin/ tazobactam, TIM: Ticarcillin/clavulanate, T: Tetracycline, TS: Trimethoprime/ sulphamethoxazole, was prepared by Kirby- Bauer method (diffusion discs). Three milliliters of regular saline were added to a tube containing colonies after an overnight nutrient plate agar culture. The turbidity was set at 1.5×108 CFU/ml, or 0.5 McFarland tube. After sinking a sterile cotton swab, into the bacterial solution, the swab was pressed against the tube wall to eliminate any extra fluid. Mueller-Hinton agar plates were infected with the bacterial suspension, and the plates were then allowable to dry for 10 min. The antibiotic discs were positioned on the medium surface by using sterile forceps, and the plates were then incubated for 24 hours at 37 °C [8]. A metric ruler was used to measure the zones of inhibition surrounding the discs in millimeters (mm) after the incubation was finished. These zones were then compared based on (CLSI, 2023).

2.5. Fungal Culture and Isolation of *Aspergillus terreus*

The serial dilution agar plate method was used to separate the fungus from a soil sample, which was carried out in a sterile environment. Potato dextrose agar (PDA) medium was used to isolate fungus. Five test tubes were filled with nine milliliters of distilled water that had been sterilized. 1g of the soil sample was placed in the first test tube, 10-1 [12]. 0.1 ml from each test tube was put onto PDA plates that had been treated with 0.2 g/L of streptomycin in order to stop the growth of bacteria. For six to seven days, the PDA plates containing the inoculum were incubated at 30 degrees Celsius. On PDA plates, physically different fungal colonies formed after 5 days of incubation; they were subcultured independently to create a pure culture. Pure colonies of fungal were culture onto PDA slants and kept at 4 °C for further use [9].

2.6. Extraction of Bioactive Compounds of *Aspergillus terreus*

The implantation natural components were removed by collecting the cells and centrifuging them for five minutes at 3000 PRM. After that, ethanol was used to dissolve the precipitate at a g/10 ml. An ultrasonic instrument operating at 24,000 frequencies/second broke up the flow. Additionally, the product was centrifuged for 10 minutes at 3000 RPM.

Next, leachate was collected. In order to extract the extract, ethanol detergents were then removed from the supernatant using an evaporator set to a temperature lower than 40 CO. The bioproducts were then dissolved in 70 Attents of Ammonium Sulfate after the extract had been diluted in a little quantity of distilled water. After 30 minutes of cooling at 3000, the product was separated from the precipitate. The proteins including the natural products as dry matter are obtained by dialysis by removing the Ammonium Sulfate swab from the protein-containing precipitate and then pouring the contents of the bag into the remove, an empty air-filled container at unstable pressure [10].

3. Results and Discussion

3.1. Identification of *P. aeruginosa* Isolates

Blood agar, macConkey agar, and ctrmide agar were used to cultivate forty-five burn specimens from burn infections. suspected of not digesting lactose and of being both hemolytic and non-hemolytic. The VITEK 2 GN ID Card remained used to approve the identification of suspected *P. aeruginosa* isolates after they had been further identified by the catalase and oxidase tests. Twenty isolates that were gathered were determined to be *P. aeruginosa*. In addition to King A and B, morphological analysis was conducted on various medium using MacConkey agar and Nutrient agar. The isolates' colonies ranged from mucoidal to smooth, with flat borders and a raised core. They were white or creamy in color and had a fruity smell. These findings were consistent with [11]. After being replated on differential media for pigment synthesis (King A and King B), isolates that could grow on cetrimide agar plates produced yellowish-green fluorescent pigments in King B medium and pyocyanin pigment in King A medium. MacCkonky agar, a differential medium that distinguishes between lactose-fermented and non-fermented bacteria, was used to cultivate bacterial colonies. Since MacConkey agar does not ferment lactose, pale, transparent colonies were produced [12]. According to Mbajiuka et al. (2014) [13], *P. aeruginosa* colonies on MacConkey agar displayed uneven, flat, creamy-colored colonies. Blood agar was used to cultivate specific bacterial colonies for the purpose of assessing blood hemolysis. Colonies exhibit beta hemolysis on blood agar following incubation [12], (Figure 1) shows different forms of growth of isolates of *P. aeruginosa* in different media. All these media were incubated for 24 hours at 37 °C after streaking according to [14].

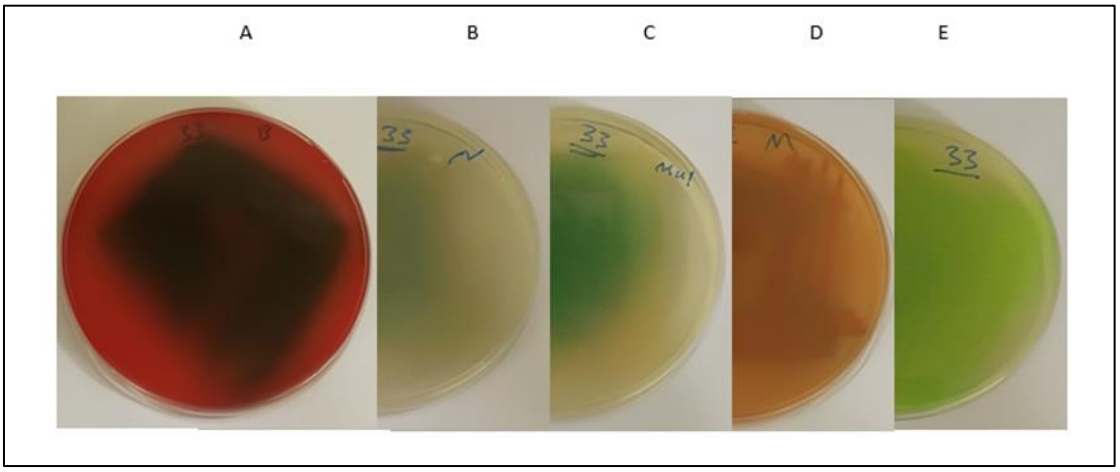

Figure 1 *P.aeruginosa* growth on different media A-Blood agar B- Nutrient agar C- Muller hinton agar D-MacConky agar E-King B agar

3.2. Biochemical Characterization

Following the schematic diagram proposed by [15], a series of biochemical tests were conducted to characterize *P. aeruginosa* from other Pseudomonas species. The results are shown in Table 1, which indicates that the isolates were positive for oxidase, and catalase, and for gram negative bacteria, growth at 4°C, urease, methyl red, triple sugar, MR-VP test, indol, hemolysis, pyocianin on cetrimide agar, motility, arginine dehydrolase and gelatin liquified.

Table 1 The biochemical tests of *P. aeruginosa* Isolates

Test	Result
Catalase test	+
Oxidase test	+
Gram-stain	-
Motility	+
Growth at 42°C	+
Growth at 4°C	-
Triple sugar test	K\k--
Hemolysis	-/+
Pyocianin on cetrimide agar	+
Gelatin liqufication	+
Indol test	-
Methyl red tast	-
MR-VP test	-
Arginine dehydrolase	+
Urease test	-
Citraite utilization	+

3.3. VITEK-2 System for Identification of *P. aeruginosa*

Pseudomonas aeruginosa ultimate identification was established using this approach. Using Identification Gram-Negative Bacteria (ID-GNB) cards, the system was able to identify bacteria more quickly, efficiently, and away from contaminants that might hinder pathogen identification. The results indicated that 20 isolates were *P. aeruginosa*. The manufacturer described the results as follows excellent identification: 96% to 100%, (very good identification); 93% to 95%, (good identification); 89% to 92%, and (acceptable identification); 5% to 88% represents [16].

3.4. Antibiotics Susceptibility Test

Susceptibility of *P. aeruginosa* isolates to 16 antibiotics from diverse class of antibiotics were obtained using disk diffusion method (Kirby-Bauer method). The results interpreted according to the recommendation of (CLSI, 2024), the results of the susceptibility of *P. aeruginosa* to antibiotics were shown in Table 2. The highest level resistance of antibiotic was against CPM, LEV and T 90%, on the other hands, the low level was against CIP 45%.

The sensitivity test findings demonstrated that *P. aeruginosa* isolates taken, a high level of resistance to the majority of the antibiotics utilized in the investigation. Table 2 shows the patterns of antimicrobial resistance in the isolates under study. *P. aeruginosa*, is becoming a common and significant opportunistic nosocomial infection. Antimicrobial managers are frequently categorized according on their primary mode of action. Mechanisms include interfering with synthesis of cell wall (e.g., glycopeptide agents and β-lactams), interfering with synthesis of nucleic acid (rifampin and fluoroquinolones), inhibition of a metabolic pathway (trimethoprim-sulfamethoxazole), disruption of protein synthesis (tetracyclines and macrolides), and disruption of bacterial membrane configuration (daptomycin and polymyxins) [17]. The modifications that affect efflux pump production, target site modifications, the development of enzymes, and membrane alteration, that block or alter antibiotics are some of these resistance mechanisms. Furthermore, the biofilm state reduces the effectiveness of antibiotics [18]. Genetically, it demonstrates a variety of antibiotic resistance pathways as well as *P. aeruginosa* capacity to acquire new resistance genes from other bacteria through conjugation, transformation, and transduction using mobile genetic elements (plasmids, transposons, and phages) [19]. Sura, (2015) reported., Various of the intrinsic factors, that impart resistance to antimicrobials in biofilms include: decreased oxygen and nutrient availability accompanied by altered metabolic activity, reduced diffusion of antibiotics through the biofilm matrix, increased production of oxidative stress, formation of per sisters, and additional specific molecules. These

mechanisms are activated during the development of biofilm and are essential components of biofilm structure and physiology. Although both induced, and innate mechanisms contribute to antibmicrobial resistance in biofilms, the mechanism of antibiotic resistance in biofilms has been linked to the altered microenvironment, the development of resistance phenotypes in biofilms, and failure to penetrate beyond the cell surface layer or slow penetration [20]. New methods for preventing and treating bacterial infections are essential due to the evolution, selection, and dissemination of bacterial resistance to a variation of antibiotics, and positive and negative gram bacterial including some eating-related pathogenic bacteria species be resistant to fungi in vitro, as well as yeasts and mycelial fungi, including dermatophytes and phytopathogens [21]. Numerous fungal species are a dependable source of natural antimicrobial chemicals because they have demonstrated efficacy against bacterial, viral, and fungal infections that are resistant to current treatment medications. Antimicrobial molecules that have been extracted from different stages of the fungal growth process can be identified using their antibacterial and antifungal activities [22].

Table 2 Antibiotics resistance percentage of *P. aeruginosa* isolates

Anti-microbial agents	**Resistance percentage**	**Intermediate Percentage**	**Sensitive percentage**
	R(%)	**I(%)**	**S(%)**
AK	12(60%)	5(25%)	3(15%)
AM	13(65%)	0(0%)	7(35%)
AZT	17(85%)	1(5%)	2(10%)
CZ	11(55%)	0(0%)	9(45%)
CPM	18(90%)	1(5%)	1(5%)
CTX	10(50%)	3(15%)	7(35%)
CIP	9(45%)	5(25%)	6(30%)
DXT	16(80%)	0(0%)	4(20%)
IMI	8(40%)	0(0%)	12(60%)
LEV	18(90%)	1(5%)	1(5%)
MEM	14(70%)	3(15%)	3(15%)
NIT	11(55%)	4(20%)	5(25%)
PTZ	17(85%)	0(0)	3(15%)
T	18(90%)	1 (5%)	1(5%)
TIM	13(65%)	3(15%)	4(20%)
TS	15(75%)	0(0%)	5(25%)

AK: Amikacin. AM: Ampicillin. AZT: Aztreonam. CZ: Cefazolin. CPM: Cefepime. CTX: Cefotaxime. CIP: Ciprofloxacin. DXT: Doxycycline. GM: Gentamicin. IMI: Imipenem. LEV: Levofloxacin. MEM: Meropenem. NIT: Nitrofurantoin PTZ: Piperacillin/ tazobactam. T: Tetracycline. TIM: Ticarcillin/clavulanate. TS: Trimethoprime/ sulphamethoxazole.

3.5. Antimicrobial of Bioactive Compound Extraction from Fungi

Soil is a significant source of bioactive substances that produce from microorganisms. Numerous of these fungal met demonstrated anti-disease efficacy. Secondary metabolites stimulate the host defenses through a variety of signal transduction mechanisms to produce. the bioactive compound appeared high level activity on *P. aeruginosa* the range of diameter was 0-34 mm with different four concentration as shown, figure 2 and Table 3.

Table 3 Determination of diameter zone of bioactive compound extract product of *P. aeruginosa* isolates

No.	C1	C2	C3	C4
1	18	15	8	0
2	24	21	17	11
3	20	16	8	0
4	31	24	17	0
5	32	25	0	0
6	33	18	14	11
7	21	15	0	0
8	0	0	0	0
9	33	23	17	11
10	28	21	18	0
11	18	13	8	0
12	32	28	17	6
13	17	13	0	0
14	22	17	0	0
15	34	26	17	7
16	22	12	0	0
17	33	21	17	13
18	23	16	8	0
19	26	17	8	0
20	0	0	0	0

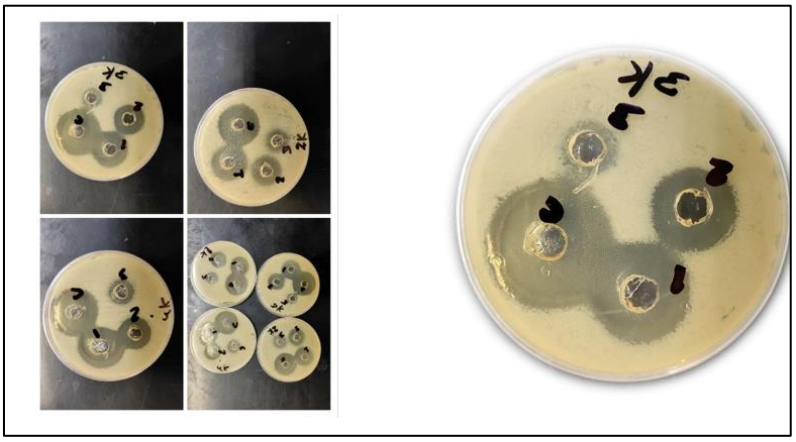

Figure 2 The results of bioactive extract product on *P. aeruginosa* isolates

According to previous study indicate that there has been a notable surge in the chemical analysis of soil-derived Aspergillus species fungi in latest years, because of the identification of novel molecular structures with a wide range of pharmacological characteristics and a useful source of antimicrobial agents [23]. In contrast, this study showed that the filamentous fungi have a massive amount for the production of a wide range of bioactive compounds, with application as among others antibiotic, antifungal and anticancer drugs [24]. A novel metabolite generated by the endophytic fungus

Aspergillus fumigatus CY018 is called asperfumin, and it has been reported in similar studies by other researchers to inhibit Candida albicans [25]. Aspergillus species are well-known for producing secondary metabolites, including as non-ribosomal peptides (like ferricrocin), polyketides (like aflatoxin), terpenes, indole terpenes, and which are crucial resources for the development of novel drugs [26]. Similar investigations by other researchers have revealed that four distinct fungal strains; Aspergillus fumigatus (NCIM No. 902), Penicillium marneffei, Aspergillus flavus (NCIM No. 524), and Trichophyton mentagrophytes, are resistant to the antifungal qualities of isochrontriazoles and thiadiazole. Derivatives of isochromen and dione that have been shown to have important biological properties [27]. This result is similar to reports observed that the isoquinoline derivatives from isochromen , dione found to exhibit interesting biological properties including narcotic, anti-fungal, anti-angiogenic, anti-inflammatory, antiallergic, and antimalarial, antibacterial, antivirus and anti cancer and this results in agreement with studies presented that the several metabolites of isocoumarins have several bioactivities: protease inhibitors, cytotoxic, acetylcholinesterase, antimicrobial, antimalarial, algicidal, immunostimulatory, allergic- and allergy-free, and plant growth regulators are only a few examples of the bioactivities of many isocoumarin metabolites [28]. Similar studies from other researchers imply that the dihydroisocoumarins, which are primarily natural, were extracted from a variety of natural sources, such as bacteria, fungi endophytic, marine fungi and soil [29].

4. Conclusion

One of the major sources of nosocomial infections in our hospitals is *P. aeruginosa*, which has the greatest isolation rate from burn infections and a greater prevalence in men than in women. *P. aeruginosa* isolates exhibited strong resistance to the majority of the antibiotics utilized in the study, according to the findings of the sensitivity test. Hemolysin, protease, and pyocyanin are among the phenotypic virulence factors that *P. aeruginosa* produces in varying patterns. The extract of the bioactive chemical exhibited substantial levels of activity against isolates of *P. aeruginosa* at varying concentrations.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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